The epidemiological data of a cohort of patients with early arthritis

Teodora SERBAN[1,2], Iulia SATULU[1], Oana VUTCANU[1], Mihaela MILICESCU[1,2], Carina MIHAI[1,2], Mihai BOJINCA[1,2], Victor STOICA[1,2]

[1]"Dr. I. Cantacuzino" Clinical Hospital, Bucharest
[2]"Carol Davila" University of Medicine and Pharmacy, Bucharest

Abstract

Objectives. *The aim of this study is to describe the epidemiologic characteristics of a cohort of patients with early arthritis and to identify the particularities that may help to identify the patients with early rheumatoid arthritis (ERA) from this cohort.*

Methods. *73 patients with ERA or early undifferentiated arthritis (EUA) were enrolled. Patients were recruited from those who presented in the "Early Arthritis Research Center" of "Dr. I. Cantacuzino" Hospital with inflammatory arthritis of one or more joints, lasting for at most 12 months.*

Results. *73 patients were included in this study, 44 females (60.3%) and 29 males (39.7%). 47 patients (64.3%) fulfilled the 2010 EULAR/ACR criteria for RA. The mean age of patients enrolled in the study was 49.81±15.93 years. The mean symptom duration was 3.39±3.42 months. The predominant form of presentation was polyarticular. While the values of acute phase reactants are comparable between groups and the differences are not significant ($p>0.05$ – Mann-Whitney test), in case of immunologic markers there is a difference represented by significantly higher values in the group with ERA ($p<0.001$). The NTJ and NSJ is significantly higher in patients with ERA ($p<0.001$). The values of VASd are significantly higher than that of VASp ($p<0.001$). CDAI and SDAI identified more patients with high disease activity than DAS28.*

Conclusion. *It was observed that there is a high degree of variation between results reported in different studies performed on cohorts of patients with early arthritis and we believe it is important to know the particularities of patients treated by one to improve clinical practice. The patients with ERA tended to have higher values of the parameters evaluated than the patients with EUA.*

Keywords: early arthritis, „window of opportunity"

BACKGROUND

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease with articular and extra-articular manifestations, with unknown etiology. By affecting articular bones and cartilage, it leads to important joint destruction associated with pain and, in time, it decreases quality of life and impairs self-assessment.

For a long period of time, RA was considered a chronic, debilitating disease, with no fatal outcome. Recent studies show that persons affected by RA present a higher morbidity and mortality compared to persons of the same sex and age and the life expectancy of this persons is decreased with about 7 years. (1,2)

Most rheumatologic diseases have a chronic evolution and the early stage of this disorders was considered a long period of time constituted by the first years of evolution. The early period of RA can be characterized by the presence of disease biomarkers in the absence of clinical

Corresponding author:

Teodora Serban, "Carol Davila" University of Medicine and Pharmacy, 37 Dionisie Lupu Street, Bucharest
E-mail: teodoramazdrag@yahoo.com

manifestations, this period being known as "preclinical RA". (3) Early RA (ERA) is considered to last a very short period of time, which is called "window of opportunity", and the prompt initiation of treatment during this period is significantly superior to the delay in starting specific therapy. (4)

It is supposed that ERA is characterized by different pathophysiological mechanisms than that seen in later stages and this theory is supported by the presence of a different population of cytokines in the early stages of disease. (5) Clinical remissions was more frequently obtained in patients with a disease duration no longer than 4 months. (6) Also, it was noted that by initiating as soon as possible the specific therapy a decline of radiographic progression can be obtained. (7)

Although at this point there is no consensus about the duration of the early period of RA, there is a consensus about the fact that initiation of specific therapy as soon as possible, no matter if structural damage is present or not, is necessary to prevent subsequent damage.

It is recommended that patients suspected of RA should be referred as soon as possible to specialized centers in diagnosis and treatment of ERA.

OBJECTIVES

The aim of this study is to describe the epidemiologic characteristics of a cohort of patients with early arthritis and to identify the particularities that may help to identify the patients with ERA from this cohort.

METHODS

For the present study, 73 patients with early arthritis were enrolled. Patients were recruited from those who presented in the "Early Arthritis Research Center" of "Dr. I. Cantacuzino" Hospital with inflammatory arthritis of one or more joints, lasting for at most 12 months. Patients who presented post-traumatic arthritis or who have fulfilled criteria for classification as other disease than RA at the end of the assessment were excluded from our study. In the study were evaluated only patients with ERA or early undifferentiated arthritis (EUA).

All the patients included in the present study underwent physical examination and medical history was obtained for all of them. Lab tests were performed for all the patients accordingly to local standard of care and included also the determination of rheumatoid factor (RF), anti CCP antibodies (ACPA) and any other immunological test considered suitable by the investigator. The clinical evaluation was done by means of number of tender joints (NTJ), number of swollen joints (NSJ), duration of morning stiffness, visual analogue scales (VAS) of patient (VASp) and doctor (VASd). The disease activity was evaluated by means of DAS28, CDAI and SDAI.

For the statistical analysis we used a version of SPSS and for graphic presentation we used a version of Microsoft Excel.

RESULTS

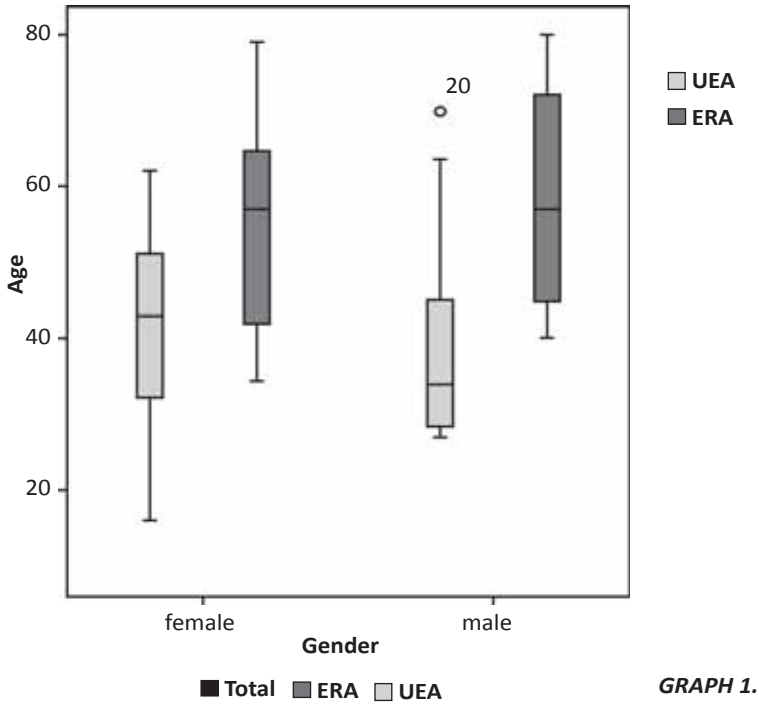
73 patients were included in this study, 44 females (60.3%) and 29 males (39.7%) (Graph 1). 47 patients (64.3%) fulfilled the 2010 EULAR/ACR criteria for RA. The mean age of patients enrolled in the study was 49.81±15.93 years, for patient with ERA was 55.17±14.62 years while UEA was 40.11±13.65 years. The values in terms of age are significantly higher in patients with ERA ($p<0.001$).

The mean duration of symptoms was 3.39±3.42 months and the difference between patient with ERA and those with UEA wasn't significant ($p>0.05$).

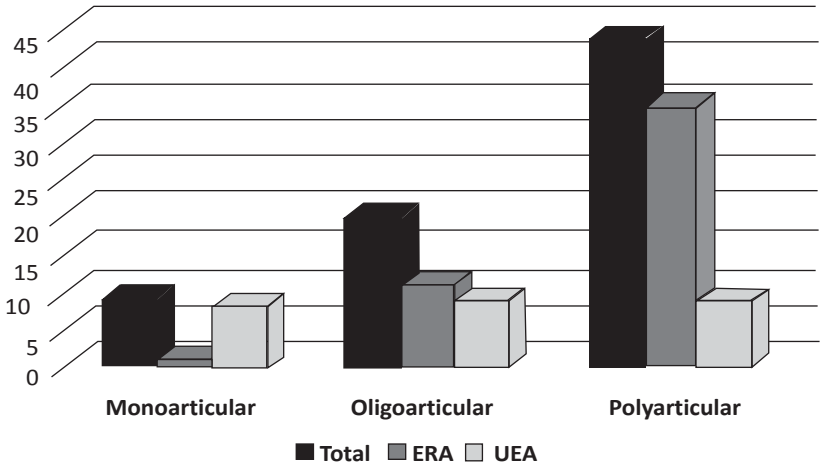
The initial presentation form was classified as monoarticular, oligoarticular or polyarticular. While the most frequent form of presentation for patients with ERA was polyarticular (74.5%) and only 1 patient (8.1%) presented with a monoarticular form, in case of patients with EUA the distribution was approximately equal between the three forms of presentation (Graph 2).

Smoking is the principal environmental factor involved in the pathogenesis of RA. 17 patients (36.2%) with ERA and 5 patients (19.2%) with EUA were smokers. We observe that the proportion of smokers in the group with ERA is almost double, but the difference is not significant ($p=0.156$ – Mann-Whitney test).

The median value and the interquartile range (IQR) for acute phase reactants (C reactive protein – CRP and erythrocyte sedimentation rate – ESR) and for immunologic markers (rheumatoid factor – RF and anti-citrullinated protein antibodies) are shown in Table 1.



GRAPH 1. *Distribution of patients by age and sex*



GRAPH 2. *Initial form of presentation*

It was observed that the values of acute phase reactants are comparable between groups and the differences are not significant (p>0.05 – Mann-Whitney test), in case of immunologic makers there is a difference represented by significantly higher values in the group with ERA (p<0.001).

The median value and IQR for clinical evaluation parameters are shown in Table 2.

The NTJ and NSJ is significantly higher in patients with ERA and this also applies to the duration of morning stiffness. The NTJ and NSJ correlated significantly with the level of ACPA (p<0.05 – Spearmen correlation) (Graph 3).

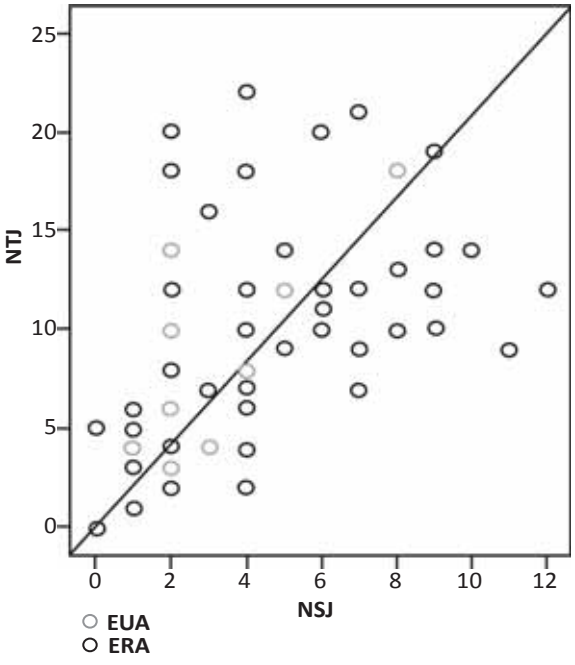
An important element is represented by the fact that, while the values of VASd are higher in patients with ERA and the difference is significant, the difference between groups is not sig-

TABLE 1. *Median and IQR range for acute phase reactants and immunologic markers*

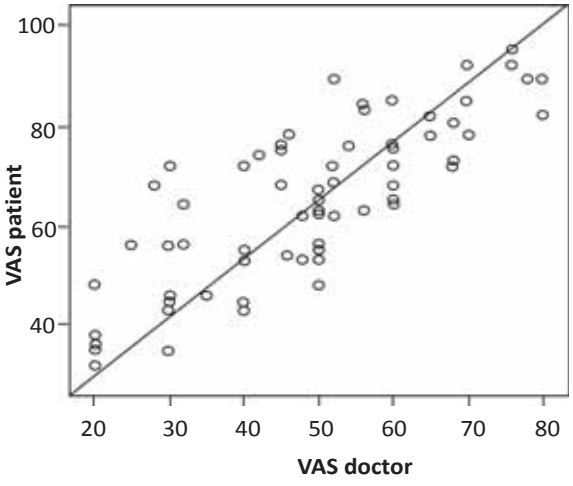
Parameter	Total Median (IQR)	ERA Median (IQR)	EUA Median (IQR)	p
CRP (g/dl)	8.63 (2.63-18.44)	9.23 (3.57-16.88)	7.65 (1.99-17.42)	0.710
ESR (mm/h)	27.00 (11.00-47.00)	27.00 (14.00-53.00)	27.50 (10.00-44.75)	0.067
RF (IU/ml)	34.00 (10.08-79.30)	68.02 (23.00-195.00)	9.47 (7.30-16.75)	**<0.001**
ACPA (IU/ml)	34.50 (5.00-134.77)	112.03 (42.15-211.30)	5.00 (0.50-5.00)	**<0.001**

TABLE 2. *Median value and IQR for clinical evaluation parameters*

Parameter	Total Median (IQR)	ERA Median (IQR)	EUA Median (IQR)	p
NTJ (28 joints)	7.00 (3.00-12.00)	9.00 (4.00-9.00)	4.00 (1.00-7.25)	**<0.001**
NSJ (28 joints)	3.00 (1.50-5.50)	4.00 (2.00-7.00)	2.00 (1.00-3.25)	**<0.001**
Morning stiffness (min)	60.00 (30.00-60.00)	60.00 (40.00-90.00)	45.00 (30.00-60.00)	**0.009**
VASp (mm)	64.00 (52.50-76.00)	65.00 (53.00-76.00)	64.00 (48.00-75.75)	0.484
VASd (mm)	50.00 (30.00-60.00)	50.00 (40.00-65.00)	41.00 (29.50-53.00)	**0.006**



GRAPH 3. *Distribution of NTJ and NSJ in patients with ERA and ERA*



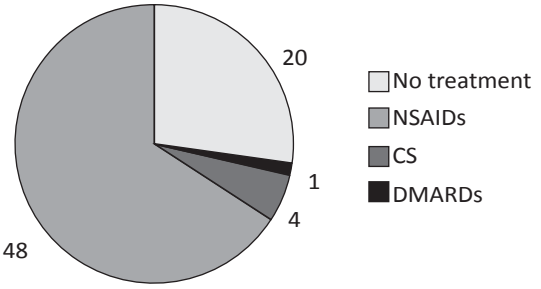
GRAPH 4. *Distribution of VASp and VASd*

nificant regarding the value of VASp. It was also observed that the values of VASp correlate with the values of VASd (p<0.001) but are significantly higher than those of VASd (p<0.001) (Graph 4).

Median values and IQR for DAS28, CDAI and SDAI are shown in Table 3.

The values of disease activity indices are significantly higher in patients with ERA. The disease activity indices correlated significantly with the level of RF and ACPA (p<0.05). CDAI and SDAI identified more patients with high disease activity than DAS28.

Regarding previous treatments followed before the first presentation, the majority of patients used NSAIDs (65.8% – 48 patients), while 20 patients didn't use any type of medication (27.3%). Only 4 patients used corticosteroids – CS (5.5%) and 1 patient used Methotrexate (1.4%) in absence of a rheumatologic diagnosis at the moment of the initiation of treatment. (Graph 5)



GRAPH 5. *Treatments administered before the first evaluation*

There was no significant difference regarding objective or subjective parameters between patients who received NSAIDs and those who didn't received any treatment (p>0.05). The number of patients who received CS is too small to analyze if there are significant differences between them and those who didn't received any treatment or those who received treatment with NSAIDs.

TABLE 3. *Median value and IQR for disease activity indices*

Parameter	Total Median (IQR)	ERA Median (IQR)	EUA Median (IQR)	p
DAS28	4.75 (3.63-5.35)	4.96 (4.27-5.60)	4.00 (3.26-4.98)	**<0.001**
CDAI	22.80 (14.70-29.55)	27.00 (17.10-33.20)	16.05 (10.52-22.82)	**<0.001**
SDAI	26.12 (14.94-32.13)	29.02 (18.90-34.78)	17.82 (11.98-26.03)	**<0.001**

DISCUSSION

In the cohort analyzed we observe a clear predominance of women, this being a feature of patients with RA that is highlighted in multiple studies performed on large cohorts of patients. (8,9). The mean age of patients with ERA (55.17±14.62 years) was higher than that of patients with EUA (40.11±13.65 years). Also, the mean age of patients with ERA is higher than that reported in studies performed on large cohorts of patients with ERA, for example the mean age reported for the ESPOIR cohort was 48.07±12.55 years. (8)

The mean duration of symptoms before the first evaluation was of about 3 months for both patients with ERA and patients with EUA. This duration of symptoms is higher than that reported for the ESPOIR cohort (74.89±76.59 days), but it still falls into what is understood by "window of opportunity". The predominant form of presentation was polyarticular.

Smoking is the principal environmental factor involved in the pathogenesis of RA. We observe that the number of smokers is higher in patients with ERA but the difference isn't significant. Also, the proportion of smokers is higher than that reported in other cohorts of patients with RA. (10)

Median value of ESR was higher than that reported in the ESPOIR cohort (24.0) but lower than that reported in the Leiden cohort (31.0). (141,146) The percent of patients with ERA who were positive for RF (87.2%) and ACPA (82.1%) are higher than that reported in the ESPOIR cohort (58.0% and 50.3%, respectively) and in the Leiden cohort (58.7% and 52.4%, respectively). (8,11)

The NTJ and NSJ is lower than that reported in other studies (11) and correlated with the level of ACPA. VASp had significantly higher values than VASd, and both had higher values in patients with ERA. The METEOR study showed that there is a large variation regarding the VAS reporting and that there are countries in which VASp is higher, while in other patients VASd is higher. (12)

The values of DAS28, CDAI and SDAI are higher in patients with ERA than in patients with EUA, but are lower than that reported in other studies. (11)

CONCLUSIONS

The patients with ERA tended to have higher values of the parameters evaluated than the patients with EUA. While the level of acute phase reactants didn't differ between groups, the level of immunologic markers was significantly higher in patients with ERA making them more suitable for differentiation of rheumatologic entities.

The better correlation of the level of ACPA than that of RF with different parameters makes this test a more suitable test for evaluating patients with RA.

The use of NSAIDs before the first evaluation didn't influence the clinical or laboratory parameters.

We observe that there is a high degree of variation between results reported in different studies performed on cohorts of patients with early arthritis and we believe it is important to know the particularities of patients treated by one to improve clinical practice.

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