ORIGINAL PAPER

# Comparison between Young and Elderly Onset of Rheumatoid Arthritis in a Romanian Cohort

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## Abstract

Rheumatoid arthritis (RA) is a chronic inflammatory disease that predominantly affects middle-aged adults in the third to fifth decades of life, but can also occur at any age. Significant differences were observed between patients with the diagnose of the disease under the age of 65 years – young- onset of RA (YORA) and those with the onset over the age of 65 years -elderly-onset of RA (EORA). The literature has shown that patients in the EORA group, in comparison to the young, have more severe onset, shorter duration of morning stiffness, lower frequency of sero-positivity and a more important biological inflammatory syndrome.

**Objective:** Describe and compare the clinical characteristics, laboratory features, functional status, therapeutic approach and disease progression in elderly-onset and young-onset rheumatoid arthritis (RA) patients.

**Materials and methods:** This retrospective, transversal study included 102 patients diagnosed with rheumatoid arthritis according to the ACR / EULAR criteria and who had at least 3 visits to our clinic, the last one during 2019-2020. Depending on the age at disease onset, we divided them into 2 groups- EORA and YORA and analyzed them comparing the clinical, laboratory and treatment data obtained at diagnosis. Subsequently we studied the evolution of the disease activity and the therapy efficiency at 6 months of follow-up and at the last hospitalization for each group.

**Results:** The percentage of women is similar and predominant in both groups, YORA and EORA (68.3% and 71.8%). YORA was associated with a longer disease length and a prolonged symptom duration prior to the diagnosis in comparison to EORA (p<0.001 and P=0.002). Extra-articular manifestations were more frequent in elderly-onset RA patients at diagnosis, especially the presence of rheumatoid nodules (46.2% vs 22.2%. p=0.011) and weight loss (82.1% vs 34.9%, p<0.001). Anemia was statistically associated with the EORA group (p=0.037). Analyzing the radiological findings, there was a greater number of patients who showed erosions (48.7%) and geodes (28.2%) in EORA, than in YORA group (33.3% and 19.0%). The prevalence of specific auto-antibodies positivity as anti-CCP was higher in YORA (76.2% vs 53.8%, p=0.019), as well as the positivity of Rheumatoid factor (RF) (84.1% vs 61.5%, p=0.010). The majority of patients began treatment with synthetic DMARD monotherapy, 54.0% of YORA and 64.1% of EORA. Methotrexate was the main drug administrated in both groups (61.5% in EORA and 54.0% in YORA, p-value= 0.602). Other medications, such as Sulfasalazine and Leflunomide, were less preferred in the two groups. Biologic therapy was preferred in younger patients than in those with RA at 65 years of age or over (69.8% vs 35.9%, p=0.001). Disease activity measured with DAS28(CRP) score was similar between the two groups at baseline, but significantly lower for YORA patients measured at the last hospitalization (p=0.020), treat to target (low disease activity and remission) being achieved in 53% of cases in the YORA group versus 23% of EORA patients (p=0.002).

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**Conclusions:** The definite diagnosis of RA was delayed in YORA patients in comparison to EORA patients and the extra-articular manifestations of the disease were more frequently found in the EORA group. Seropositivity was statistically significantly associated with the YORA group. Anemia was predominant in patients with disease onset over 65 years old. Both groups underwent DMARDs therapy in the early stages of the disease, but biologic therapy was more often administered in younger patients. Disease activity at diagnosis was similar in both groups, but in dynamic, the treat to target endpoint was achieved more frequent in YORA population.

**Keywords:** rheumatoid arthritis, study, cohort, young patients, elderly persons.

## Rezumat

Poliartrita reumatoidă (PR) este o boală inflamatorie cronică care afectează predominant adulții de vârstă mijlocie, începând cu decada a treia și până la a cincea de viață, dar poate apărea la orice vârstă. S-au observat diferențe semnificative între pacienții cu diagnosticul de boală sub vârsta de 65 de ani – PR cu debut precoce (YORA- young- onset of RA) și cei cu debut peste 65 de ani – PR cu debut tardiv (EORA- elderly-onset of RA). Literatura de specialitate a arătat că pacienții din grupul EORA, în comparație cu tinerii, au debut mai sever, rigiditate matinală cu durată mai scurtă, frecvență mai mică a sero-pozitivității și un sindrom inflamator biologic mai important.

Obiectiv: Descrierea și compararea caracteristicile clinice, caracteristicile de laborator, starea funcțională, abordarea terapeutică și progresia bolii la pacienții cu poliartrită reumatoidă (PR) cu debut precoce si respectiv tardiv.

Materiale și metode: Acest studiu retrospectiv, transversal, a inclus 102 pacienți diagnosticați cu poliartrită reumatoidă, conform criteriilor ACR/EULAR și care au avut cel puțin 3 vizite în clinica noastră, ultima în perioada 2019-2020. În funcție de vârsta la debutul bolii, pacienții au fost împărțiți în 2 grupe - EORA și YORA și au fost comparate datele clinice, de laborator și strategia terapeutică, la prima vizită. Ulterior au fost analizate evoluția activității bolii și eficiența tratamentului la 6 luni de urmărire și la ultima spitalizare pentru fiecare grup.

Rezultate: Procentul de femei este similar și predominant în ambele grupuri, YORA și EORA (68,3% și 71,8%). YORA a fost asociată cu o durată mai lungă a bolii și o durată prelungită a simptomelor înainte de diagnostic, în comparație cu EORA (p<0,001 și p=0,002). Manifestările extra-articulare, la diagnostic au fost mai frecvente la pacienții cu PR cu debut tardiv, în special prezența nodulilor reumatoizi (46,2% vs 22,2% p=0,011) și pierderea în greutate (82,1% vs 34,9%, p<0,001). Anemia a fost asociată statistic cu grupul EORA (p=0,037). Analizând constatările radiologice, a existat un număr mai mare de pacienți care au prezentat eroziuni (48,7%) și geode (28,2%) în EORA, decât în grupul YORA (33,3% și 19,0%). Prevalența sero-pozitivității din punct de vedere a auto-anticorpilor specifici ca anti-CCP a fost mai mare în YORA (76,2% vs 53,8%, p=0,019), precum și sero-pozitivitatea factorului reumatoid (RF) (84,1% vs 61,5%, p=0,010). Majoritatea pacienților au început tratamentul cu DMARD sintetic în monoterapie, 54,0% din YORA și 64,1% din EORA. Metotrexatul a fost principalul medicament administrat în ambele grupuri (61,5% în EORA și 54,0% în YORA, valoarea p= 0,602). Alte medicamente, cum ar fi sulfasalazina și leflunomida, au fost mai puțin preferate în cele două grupuri. Terapia biologică a fost o opțiune pentru pacienții mai tineri decât la cei cu PR cu debut peste 65 de ani (69,8% vs 35,9%, p=0,001). Activitatea bolii măsurată cu scorul DAS28(CRP) a fost similară între cele două grupuri la momentul inițial, dar semnificativ mai scăzută pentru pacienții din YORA măsurați la ultima spitalizare (p=0,020), treat-to-target (activitate scăzută a bolii și remisiune) fiind atins în 53% de cazuri din grupul YORA, față de 23% dintre pacienții cu EORA (p=0,002).

Concluzii: Diagnosticul de certitudine de RA a fost întârziat la pacienții din grupul YORA în comparație cu pacienții EORA și manifestările extra-articulare ale bolii au fost mai frecvent întâlnite în grupul EORA. Sero-pozitivitatea a fost asociată semnificativ statistic cu grupul YORA. Anemia a fost predominantă la pacienții cu debut de boală peste 65 de ani. Ambele grupuri au fost supuse terapiei cu DMARD în stadiile incipiente ale bolii, dar terapia biologică a fost mai des administrată la pacienții mai tineri. Activitatea bolii la diagnostic a fost similară în ambele grupuri, dar în dinamică, obiectivul treat-to-target a fost atins mai frecvent în populația YORA.

Cuvinte-cheie: poliartrita reumatoidă, studiu, cohortă, pacienți tineri, vârstnici.

## INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, immune-mediated inflammatory disease that damages the synovial joints, especially the small ones, having a destructive pattern. RA mainly develops in middle-aged adults, in the third to fifth decades of life and the prevalence of this pathology in people over 60 years is 2% [1,2]. Starting from the principle that the manifestations and prognosis is influenced by the onset age of RA, appeared the definitions of elderly-onset rheumatoid arthritis (EORA)- age at diagnose over 65 years and younger onset RA (YORA), the onset age in this group being between 16 and 60 years [3].

Some studies have illustrated a more abrupt onset in EORA patients, with severe symptoms including weight loss, fatigue, fever, lymphadenopathy, myalgia and involvement of large joints, especially the shoulder girdle. Also, there was a significant number of patients suffering from polymyalgia rheumatic-like symptoms [2, 4]. Other observed features were the associations between the YORA group and interstitial lung disease, Sjogren's syndrome or joint deformities[11]124 patients with LORA were identified from a retrospective chart review of inpatients and outpatients. They were compared with 150 YORA patients examined during the same period including their clinical and laboratory findings. The mean ages of the patients with LORA and YORA were 71.7 ± 5.9 years, and 52.1 ± 11.5 years, respectively. The gender ratio (female/male. As in the clinical characteristics, there is an important difference in laboratory findings regarding the two subsets of patients, especially regarding the frequency of rheumatoid factor (RF) and inflammatory biological syndrome (erythrocyte sedimentation rates (ESR) and C-reactive protein (CRP)). In the EORA group the serum test results shown a lower frequency of positive rheumatoid factor [4,5].

The purpose of this study is to describe and compare the demographic characteristics, clinical features, laboratory findings and prognosis between YORA and EORA.

## MATERIALS AND METHODS

In this study, we included 102 patients diagnosed with Rheumatoid Arthritis according to the ACR/EULAR 2010 criteria and evaluated in the Department of Rheumatology and Internal Medicine of „Dr. Ion Cantacuzino" Clinical Hospital, Bucharest who had at least three visits to our clinic, the last one during 2019-2020. Depending on the age at disease onset, we divided them into 2 groups- EORA and YORA and analyzed them comparing the clinical, laboratory and treatment data obtained at diagnosis. Subsequently we studied the evolution of the disease activity and the therapy efficiency at 6 months of follow-up and at the last hospitalization for each group.

The patient's data remained confidential according to the Helsinki Declaration.

Data features were collected from the patient's chart not only during the initial presentation (at diagnose), but also from another two routine visits, at 6 months post-diagnosis and respectively at the last hospitalization. Demographic variables analyzed were current age, gender, age at diagnosis, the type of onset, the smoking status of the patients and the duration of the disease. Clinical findings were also recorded and included the duration of symptoms prior to diagnosis, duration of morning stiffness (>30 minutes), presence of fatigue and weight loss, as well as the presence of subcutaneous nodules. The involvement of the small or large joints was also registered. The presence of geodes and the joint erosions were the main radiological manifestations described.

Regarding the laboratory tests, the following data was collected: complete blood (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, hemoglobin concentration and presence of RF and ACPA.

The disease activity was measured using DAS28(CRP) score at every visit.

The therapeutic approach included data about the initial medication: monotherapy or combined synthetic therapy (DMARDs), the dosage of Methotrexate and the frequency of glucocorticoid usage.

The treat to target strategy was followed according to the EULAR recommendations. This status was separately aimed, which included Remission or Low disease activity according to DAS28(CRP) at the 6 months follow-up and the last evaluation in our clinic. The efficacy of the therapy was analyzed in dynamics, examining the duration between diagnosis and the introduction of biological treatment and

the timelenght from diagnosis to treat to target achievement, respectively.

**Statistical analysis**

The differences regarding the clinical and laboratory parameters between YORA and EORA were calculated using IBM SPSS Statistics (Statistical Package for the Social Sciences) version 20.0. Values of continuous variables were presented as mean and standard deviation (SD) and categorical variables were presented as numbers and percentages. The variables were analyzed and compared using Student t-test, Mann-Whitney U test and Pearson Chi-square test. For all tests, a significant statistical result was considered at P-value < 0.05.

## RESULTS

This study included 102 patients with Rheumatoid Arthritis divided in two groups based on the age at disease onset, 63 patients with YORA (61.8%) and 39 patients with EORA (38.2%). In the YORA group, 43 patients (68.3%) were female with a mean age at onset of 42.11±12.72 years, while in the EORA group, 28 patients were female (71.8%), with a mean age at onset 68.54±4.73 years.

The duration of the disease and the duration of symptoms were longer in the YORA group compared to the EORA group (p <0.001, p = 0.02). Morning stiffness measured in minutes was significantly increased in YORA (p=0.004). Regarding the other clinical features, weight loss and the presence of rheumatoid nodules were statistically more important in elderly patients (p<0.001, p=0.011).

**Table 1.** Clinical characteristics of YORA and EORA at diagnosis

| | YORA n=63, %=61.8 | EORA n=39, %=38.2 | P-value |
|---|---|---|---|
| Age (year) at disease onset, mean ± SD | 42.11±12.72 | 68.54±4.73 | <0.001 |
| Actual age ( year), mean ± SD | 57.43±10.364 | 75.54±4.599 | <0.001 |
| Female n, (%) | 43, 68.3% | 28, 71.8% | 0.702 |
| Disease duration (year), mean ± SD | 14.97±11.49 | 6.90±3.70 | <0.001 |
| Symptoms duration (month), mean ± SD | 9.06±4.60 | 6.64±4.02 | 0.002 |
| Smoking (%) | 15, 23.8% | 6, 15.4% | 0.306 |
| Abrupt onset (%) | 27, (42.9%) | 20, (51.3%) | 0.407 |
| Morning stiffness (minute), mean ± SD | 68.41±62.481 | 50.90±31.931 | 0.004 |
| Presence of rheumatoid nodules (%) | 14, 22.2% | 18, 46.2% | 0.011 |
| Fatigue at disease onset (%) | 43, 68.3% | 30, 76.9% | 0.346 |
| Weight loss at disease onset (%) | 22, 34.9% | 32, 82.1% | <0.001 |

**Table 2.** Joint involvement and radiographic damage in YORA and EORA at diagnosis

| | | YORA n=63, %=61.8 | EORA n=39, %=38.2 | P-value |
|---|---|---|---|---|
| Joint involvement | Wrist | 40, 63.5% | 25, 64.1% | 0.950 |
| | MCP | 42, 66.7% | 21, 53.8% | 0.195 |
| | Elbow (%) | 16, 25.4% | 10, 25.6% | 0.978 |
| | Shoulder (%) | 19, 30.2% | 17, 43.6% | 0.103 |
| | Ankle (%) | 13, 20.6% | 11, 28.2% | 0.381 |
| | Knee (%) | 20, 31.7% | 20, 51.3% | 0.049 |
| Rx findings | Geodes + Erosions | 33, 52.3% | 30, 76.9% | 0.006 |

Small joints of the hand (wrist and metacarpophalangeal) were commonly affected in both groups, but involvement of large joints, such as the knee and the shoulder were particularly more present in EORA group, 43.6% patients having shoulder damages and 51.3% of patients having knee involvement (p> 0.005).

Analyzing the radiological findings, there was a greater number of patients who showed erosions (48.7%) and geodes (28.2%) in EORA, than in YORA (33.3% and 19.0%). The elderly had significantly more radiographic joint damage than the young patients (p= 0.006).

**Table 3.** Laboratory features in YORA and EORA at diagnosis

| | YORA n=63, %=61.8 | EORA n=39, %=38.2 | P-value |
|---|---|---|---|
| Anti-CCP positivity n, % | 48, 76.2% | 21, 53.8% | 0.019 |
| RF positivity n, % | 53, 84.1% | 24, 61.5% | 0.010 |
| CRP (mg/dl) | 19.79±30.98 | 23.44±28.09 | 0.193 |
| ESR (mm/ h) | 37.32±25.68 | 43.33±25.04 | 0.206 |
| Hemoglobin level g/L | 12.87±1.69 | 12.25±1.26 | 0.037 |
| Thrombocyte level | 295.86±116.83 | 298.31±100.34 | 0.498 |
| Leucocyte level | 7.89±2.77 | 8.36±3.38 | 0.300 |

Inflammatory markers such as ESR and CRP level were higher in both groups, with a higher mean value in EORA than in YORA group. The number of seropositive patients (RF and ACPA positive) was significantly higher in YORA compared to the EORA group (p=0.010 for RF positivity, p=0.019 for ACPA positivity). Considering the thrombocyte and leucocyte levels there were no differences between the two groups.

Regarding the disease activity at diagnosis, 36.5% patients of the YORA group had high disease activity (HDA), while 48.7% of the EORA patients had moderate disease activity (MDA) at disease onset.

With reference to the therapy strategy between YORA and EORA subjects, the majority of patients began treatment with synthetic DMARD monotherapy, 54.0% of YORA and 64.1% of EORA. Methotrexate was the main drug administrated in both groups, with some, but not consistent differences between YORA and EORA (61.5% in EORA and 54.0% in YORA, p-value= 0.602). Other medications, such as Sulfasalazine and Leflunomide, were less preferred in the two groups. Glucocorticoids were used more often in EORA group (66.7% versus 57.1% in YORA, p= 0.235).

Subsequently we studied the evolution of the disease activity and the therapy efficiency at 6 months of follow-up and at the last hospitalization for each group.

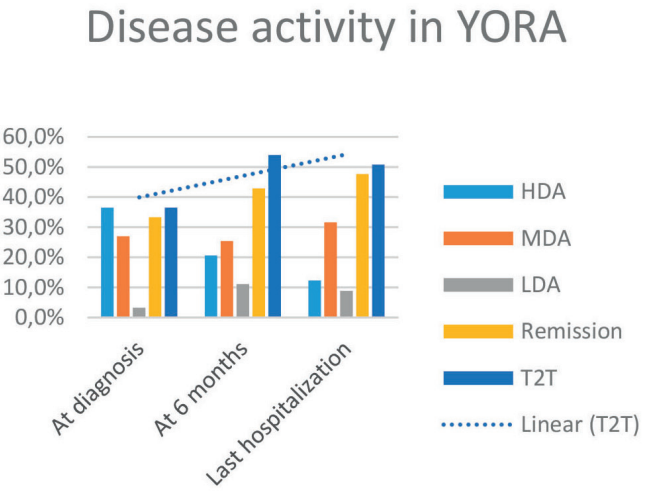


**Figure 1.** Evolution of disease activity in YORA according to DAS28-CRP score

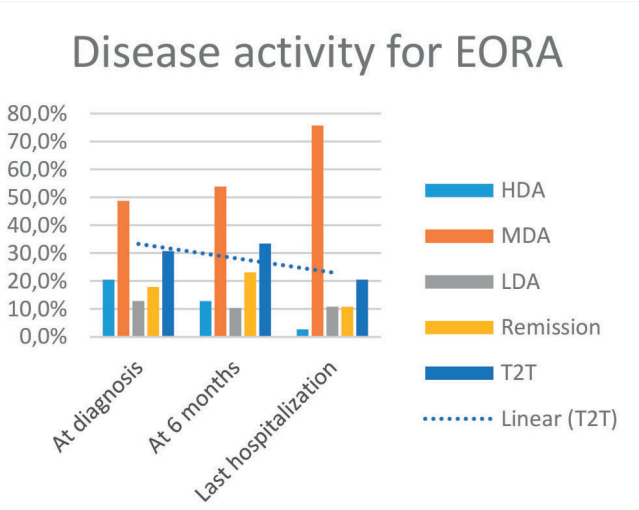


**Figure 2.** Evolution of disease activity in EORA according to DAS28-CRP score

Regarding the disease activity in the YORA group, 36.5% had high disease activity (HDA) at baseline while the majority (42.9%) achieved remission at 6 months of follow up. The percentage of patients in remission increased to 47.4% at the last check-up. In comparison, 48.7% of the EORA patients had moderate disease activity (MDA) at diagnosis. Similar results were obtained after 6 months, 53.8% being in remission while the percentage increased to 75.7% at the last evaluation.

**Table 4.** Biologic therapy in YORA and EORA

| | YORA n=63, %=61.8 | EORA n=39, %=38.2 | P-value |
|---|---|---|---|
| Biologic therapy | 44, 69.8% | 14, 35.9% | 0.001 |
| Months from diagnosis to first biologic mean ±SD | 7.07±5.04 | 3.36±1.74 | 0.008 |

Biologic therapy was more frequently used in YORA group (p=0.001), while the period between the diagnosis and the initiation of this treatment was shorter in the EORA group (p=0.008). Treat to target status was achieved earlier for the EORA subset of patients as opposed to YORA, 5.36±2.33 months versus 6.33±2.91 months, with a significant statistical difference, where p-value= 0.035.

Treat to target goal refers to patients who are in remission or have low disease activity. In our study, this target was achieved more often in the YORA group, regardless of whether we refer to 6 months after the diagnosis (p = 0.042) or to the last hospitalization (p = 0.002).

## DISCUSSION

The purpose of this study is to identify the significant differences in clinical, laboratory, radiological and therapeutic approaches between patients diagnosed with Rheumatoid Arthritis prior to 65 years old, and those diagnosed after the age of 65. In this study, 102 patients were included, divided in 2 groups, 63 subjects belonging to the YORA group and 39 to the EORA group. The proportion of female was higher in both groups, with a slightly difference in favor of EORA, which is in accordance with other studies that evaluated similar populations from Egypt or the USA[6,7]. In YORA population it is important to take in account the fertility of these patients, as well as for male and females groups, for this entity exists data even from Romania[8,9].

This study concluded that the EORA patients had symptoms for a shorter period than YORA before a certain diagnosis was made, making these findings comparable to those found by Murata and colleagues [10]. Nevertheless, we demonstrated that the duration of the disease was longer in the YORA group than in the EORA group. These findings are different than the ones found in other publications where EORA patients had a longer disease duration[4,11].

Regarding morning stiffness. Deal, as well as Turkcapar, in theirs extended populations showed that there are no differences between the two groups [4, 11], but in our cohort, the results emphasized that morning stiffness measured in minutes was significantly increased in YORA in comparison to the elderly patients. Meanwhile, Abdou S. El-Labban and his colleagues found that elderly onset RA patients had increased morning stiffness[6].

About one half of the patients from both groups had an abrupt onset (42.9% in YORA and 51.3% in EORA), the data from literature define an abrupt onset more specific for elderly RA patients[4,12].

Similar to others studies, the results had shown that seropositivity (the presence of ACPA and/ or FR) was more frequently associated with the YORA group[10, 11,13,14]. Although there is no significant difference between the two groups regarding CRP and ESR mean value, the elderly onset RA patients tend to have higher levels of these inflammatory markers, especially regarding ESR, and they also associate lower hemoglobin levels.

Completely compatible with the data obtained by the Egyptian group, in YORA population arthritis affects predominantly the small joints (MCP), while in the EORA group the knee is the main joint involved (p=0.049)[6]. Wrist, elbow, shoulder and ankle joint involvements were similar in both groups.

The extra-articular manifestations were substantially more common in EORA in comparison to YORA, with a significant difference for the presence of rheumatoid nodules (p=0.011) and weight loss (p<0.001) at disease onset, which is consistent with the results obtained by Deal, Turkcapar and theirs colleagues[4,11].

Radiographic progression at diagnosis (geodes and joint erosions) was more important in the EORA patients (p=0.006), even though an elderly onset RA was not associated with a higher disease activity DAS28(CRP) score calculated at diagnosis. The results obtained by Lance and colleagues attest that in the EORA group there is a destructive pattern with important erosive changes[15].

The treatment for RA improved dramatically in recent years with the development of new therapies while early administration of disease-modifying anti-rheumatic drugs (DMARDs) and treat-to-target strategies have been able to stop the destructive outcome and reduce morbidity and mortality. The main goal of the RA treatment is to control the disease so there should not be major differences between YORA and EORA. In this study, most patients diagnosed with RA began treatment with monotherapy, the preferred drug among both YORA and EORA being methotrexate (58.7% in YORA vs 53.8% in EORA), with a mean dosage slightly higher in EORA. The literature evidence regarding the use of DMARDs in RA patients diagnosed at 65 years or over is limited and in the same time contradictory, but there is a general accordance that these patients are receiving less aggressive treatment, due to drug pharmacodynamics and side-effects[10]. This study demonstrated that YORA patients were more likely treated with biologic therapy (69.8%) versus EORA, due to the presence of multiple comorbidities and drugs interaction[16]. Regarding the antirheumatic drugs adverse events in EORA group, we have to take in account the haematological manifestations, especially now in pandemic times, there is a publication regarding severe thrombocytopenia induced by SARS-COV2 infection in a EORA patient[17].

Furthermore, there was an important difference analyzing the period from disease diagnosis to first biologic drug administration. EORA patients needed much earlier this therapy (p=0.008). In agreement with our findings, there is some evidence that physicians prefer the use more corticosteroids and less DMARDs and biologic treatment when dealing with rheumatoid arthritis in elderly patients[12,18]. During follow-up treat to target was achieved more often in the YORA group, regardless of whether we refer to 6 months after the diagnosis (p = 0.042) or to the last hospitalization (p = 0.002).

## CONCLUSIONS

Both entities, YORA and EORA, show different patterns regarding the onset, the clinical involvement, extra-articular manifestations, the autoimmune status and radiographic progression. Nevertheless, the YORA group received more frequently biological therapy, the treat to target strategy was achieved and maintained more often for the younger patients. A more decisive result regarding the impact of the treatment by comparing the two populations would be demonstrable in an extended cohort.

**Compliance with ethics requirements:** The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

## References


1. Rasch, E. K., Hirsch, R., Paulose-Ram, R. & Hochberg, M. C. Prevalence of rheumatoid arthritis in persons 60 years of age and older in the United States: Effect of different methods of case classification. Arthritis Rheum. 48, 917–926 (2003).
2. Negoescu A & Ostör, A. J. K. Early recognition improves prognosis in elderly onset RA | Request PDF. Practitioner Jan 258, 11–4 (2014).
3. Quintana, G. et al. Comparative study of elderly-onset rheumatoid arthritis and young-onset rheumatoid arthritis in a Colombian population : clinical , laboratory and HLA-DRB1 findings. 40–46.
4. Deal, C. L. et al. The clinical features of elderly-onset rheumatoid arthritis. A comparison with younger-onset disease of similar duration. Arthritis Rheum. 28, 987–994 (1985).
5. Schaardenburg, V. & Breedveld, F. C. Elderly-Onset By. 23, 367–378 (1994).
6. El-Labban, A. S., Abo Omar, H. A. S., El-Shereif, R. R., Ali, F. & El-Mansoury, T. M. Pattern of young and old onset rheumatoid arthritis (YORA and EORA) among a group of Egyptian patients with rheumatoid arthritis. Clin. Med. Insights Arthritis Musculoskelet. Disord. 3, 25–31 (2010).
7. Richter, M. D., Matteson, E. L., Davis, J. M., Achenbach, S. J. & Crowson, C. S. Comparison of Biologic Discontinuation in Patients With Elderly-Onset Versus Younger-Onset Rheumatoid Arthritis. ACR Open Rheumatol. 1, 627–631 (2019).
8. Micu MC, Ostensen M, Bojincă V, Șerban O, Mihai M, Suta C, Ramazan A, Enache L, Bobircă A, Pătcaș SF, Micu R, Ionescu R. Pregnancy Outcomes in Couples with Males Exposed to Longterm Anti-tumor Necrosis Factor-α Inhibitor Therapies: A Prospective Study. J Rheumatol. 2019 Sep;46(9):1084-1088. doi: 10.3899/jrheum.180588. Epub 2019 Mar 1. PMID: 30824658.
9. Bobirca A, Bobirca F, Ancuta I, et al Pregnancy in rheumatoid arthritis – a romanian cohort Annals of the Rheumatic Diseases 2017;76:1151-1152
10. Murata, K. et al. Elderly onset of early rheumatoid arthritis is a risk factor for bone erosions, refractory to treatment: KURAMA cohort. Int. J. Rheum. Dis. 22, 1084–1093 (2019).
11. Turkcapar, N. et al. Late onset rheumatoid arthritis: Clinical and laboratory comparisons with younger onset patients. Arch. Gerontol. Geriatr. 42, 225–231 (2006).
12. Kobak S, Bes C. An autumn tale: geriatric rheumatoid arthritis. Ther Adv Musculoskelet Dis. 2018 Jan;10(1):3-11. doi: 10.1177/1759720X17740075. Epub 2017 Nov 7. PMID: 29290762; PMCID: PMC5724645.
13. Ranganath, V. K. & Furst, D. E. Disease-modifying antirheumatic drug use in the elderly rheumatoid arthritis patient. Clin. Geriatr. Med. 21, 649–669 (2005).
14. Mueller, R. B. et al. Is radiographic progression of late-onset rheumatoid arthritis different from young-onset rheumatoid arthritis? Results from the swiss prospective observational cohort. Rheumatol. (United Kingdom) 53, 671–677 (2014).
15. Lance, N. J. & Curran, J. J. Late-onset, seropositive, erosive rheumatoid arthritis. Semin. Arthritis Rheum. 23, 177–182 (1993).
16. Innala, L. et al. Age at onset determines severity and choice of treatment in early rheumatoid arthritis : a prospective study. (2014).
17. Bobircă A, Bobircă F, Ancuța I, Florescu A, Bojincă M, Muscă A, Florescu DN, Florescu LM, Sima RM, Florescu A, Mușetescu AE. COVID-19-A Trigger Factor for Severe Immune-Mediated Thrombocytopenia in Active Rheumatoid Arthritis. Life (Basel). 2022 Jan 6;12(1):77. doi: 10.3390/life12010077. PMID: 35054471.
18. Mueller, R. B. et al. Does addition of glucocorticoids to the initial therapy influence the later course of the disease in patients with early RA? Results from the Swiss prospective observational registry (SCQM). Clin. Rheumatol. 36, 59–66 (2017).