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Brief communication

# Rheumatoid arthritis in elderly and young patients

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*Ariane Carla Horiuchi, Luiz Henrique Cardoso Pereira, Bárbara Stadler Kahlow, Marilia Barreto Silva, Thelma L. Skare**

*Hospital Universitário Evangélico de Curitiba, Serviço de Reumatologia, Curitiba, PR, Brazil*

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## Introduction

There is a wide variability in the forms of presentation of rheumatoid arthritis (RA). The age of onset of this disease seems to be a critical factor in its clinical spectrum.[1] It is considered that a patient suffers elderly onset rheumatoid arthritis (EORA) when the disease began at the age of ≥60 years.[1,2] This form of RA contributes with 10–33% of cases of disease.[3]

The prevalence of RA increases with age and is estimated to occur in up to 2.2% of the population >55 years.[4] The genetic influence, especially of HLA class 2 genes,[5,6] acts not only in the incidence rate, according to the age of onset,[4,7,8] but also in promoting the appearance of clinical peculiarities in each age group.[9] Individuals with disease onset at a younger age have a higher prevalence of HLA DRB1*04; in those with a late onset, HLA DRB1*01 prevails.[8] On the other hand, elderly patients with the seronegative, polymyalgia-like form show increasing prevalence of HLA DRB1*13/*14.[10]

In contrast to the disease beginning in young individuals (young onset rheumatoid arthritis, or YORA), EORA seem to follow a more acute course, in association with systemic phenomena such as fever, fatigue and weight loss, as well as with the involvement of larger joints and higher prevalence of atypical forms of onset as RS3PE (remitting seronegative symmetrical synovitis with pitting edema) and polymyalgia rheumatica-like forms.[1] However, the statement that, with increasing age, the prognosis becomes more severe or even that there are differences in the course of the disease for young and elderly people, as some authors claim,[1,4,5,11] is a controversial matter, since the literature is not unanimous on this point.[5,8,11] A Brazilian study could not detect differences in prognosis for both groups.[6]

The treatment of EORA patients pursuits the same goals as those of YORA patients, *i.e.* to control the clinical manifestations, prevent structural damage, preserve function and autonomy of the individual, and also prevent excess mortality caused by the disease.[1] But some authors have observed that the treatment of elderly patients is carried out differently, with less aggressiveness opposed to that for YORA patients.[2,4] This finding is justified for the fear of prescribing modifying-disease drugs in more vulnerable people, with greater possibility of drug interaction due to multiple co-morbidities to which the elderly individual is usually subject.[2,3]

* *Corresponding author.*
E-mail: tskare@onda.com.br (T.L. Skare).
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**Table 1 – Comparison of demographic, clinical and serological data between patients with elderly onset rheumatoid arthritis (EORA) and young onset rheumatoid arthritis (YORA).**

| | EORA $n = 62$ | YORA $n = 111$ | $p$ |
|---|---|---|---|
| Gender (male/female) | 14/48 | 11/100 | 0.02 |
| Tobacco exposure (current smokers and former smokers) | 34/60 (56.5%) | 52/110 (47.2%) | 0.24 |
| Race[a] (African descent/Caucasian) | 14/62 | 32/100 | 0.19 |
| Rheumatoid nodules | 3/54 (5.5%) | 5/106 (4.7%) | 1.00 |
| Interstitial pneumonitis[b] | 7/51 (13.7%) | 4/91 (4.3%) | 0.056 |
| DAS-28 | 1–6.7<br>Mean = 3.45 ± 1.49 | 1–7.2<br>Mean = 3.69 ± 1.56 | 0.39 |
| Health Assessment Questionnaire (HAQ) | 0–3<br>Median = 1<br>IQR = 0.12–1.62 | 0–2.75<br>Median = 1.43<br>IQR = 0.62–2.00 | 0.04 |
| Presence of rheumatoid factor (RF) | 49/62 (79.0%) | 61/104 (58.6%) | 0.007 |
| Presence of antinuclear antibodies (ANA) | 16/58 (27.5%) | 41/104 (39.0%) | 0.13 |
| Association with hypothyroidism | 7/56 (12.5%) | 22/106 (20.7%) | 0.19 |

[a] According to the patient's self-declaration.
[b] Found by high-resolution CT of the chest.

With increasing longevity and growth of the population over 60 years, it is important to recognize the characteristics of the local population with EORA to improve the quality of health care offered to these patients. In this study, we sought to evaluate the demographic, clinical, serological and treatment profiles of the local population with EORA compared to patients with YORA.

## Patients and methods

This is a study approved by the Research Ethics Committee. RA patients who met at least four of the classification criteria of the American College of Rheumatology (1987) for RA[12] and being diagnosed with EORA[1] who attended to a single rheumatology outpatient clinic of a tertiary care center during the period of one year (August 2012 to August 2013) were studied. This is an observational, analytical, cross-sectional study of a convenience sample where patients with EORA ($n = 62$) and with YORA ($n = 111$) properly matched for disease duration were compared. Data about demographics, presence of nodules, extra-articular manifestations of RA, the presence of autoantibodies as rheumatoid factor (RF) and antinuclear antibody (ANA), and use of medications were obtained retrospectively through a review of their medical records. Inflammatory activity indexes such as DAS (Disease Activity Score) 28[13] and of functional capacity measured by HAQ (Health Assessment Questionnaire)[14] were obtained during the study period.

Data were gathered in frequency and contingency tables; Chi-squared and Fischer tests were used for comparison of nominal data; and Mann–Whitney and non-paired $t$ tests were applied to numerical data. The sample distribution was studied by D'Agostino and Person test. Measures of central tendency were expressed as mean and standard deviation for Gaussian variables; and as median and interquartile range (IQR) for non-Gaussian variables. Results with $p \leq 0.05$ were considered statistically significant. The calculations were made with the aid of the Graph Pad Prism (version 5.0) software.

## Results

At disease onset, YORA patients ($n = 111$) were aged 32–58 (median = 45, IQR = 39.0–51.0) years; and EORA patients ($n = 62$) were aged 60–83 (median = 63.0, IQR = 60.7–70.0) years. In EORA group, the disease duration time was 1–16 (median = 3.0; IQR = 1.0–6.5) years; and in YORA group, the disease duration time was 1–13 (median = 5.0; IQR = 2.0–8.0) years ($p = 0.21$). In Table 1, one can observe the comparison between these two groups regarding demographic, serological and clinical characteristics; it is worth noting the difference found for gender, HAQ and RF between the groups. In EORA group there were 41.6% patients with low activity or remission by DAS 28 (<3.2) as opposed to 38.7% in YORA group ($p = 0.85$). As regards the use of medications, no difference was found between groups, as can be seen in Table 2.

## Discussion

The results of this study demonstrate that EORA in Brazil is more common in male individuals, and that patients with this form of RA have better HAQ that of patients with YORA with the same disease duration. The finding that males are more affected in older age groups is a fact already widely recognized in the literature.[1,15] The Norfolk Arthritis Register,[11] *i.e.* the English arthritis registry, shows that the incidence of RA in men gradually increases with age, while in women it increases from 45 years, reaching a plateau at 75 years, from which the incidence starts to decline. Bajocchi et al.[16] described a gender distribution ratio of 1.5–2 women to 1 man in the elderly *versus* 4–4.5 women for 1 man in younger people.

It was also observed in the present study that the functional state measured by HAQ had lower values in elderly individuals. This fact is interesting and is opposed to the idea that older people, despite whether or not suffering from a rheumatic disease, may show functional impairment related to the weakness inherent to older people. This can be explained, if a higher disease severity is ascribed to YORA. Pease et al.[17] reported

**Table 2 – Comparison of treatments used in patients with elderly onset rheumatoid arthritis (EORA) *versus* young onset rheumatoid arthritis (YORA).**

| | EORA $n = 62$ | YORA $n = 111$ | $p$ |
|---|---|---|---|
| Corticosteroid use (number of patients) | 48/62 (77.4%) | 85/103 (82.5%) | |
| Dose of corticosteroid mg/day (prednisone or equivalent) | 2.5 and 20.0<br>Median = 10.0<br>IQR = 5.0–10.0 | 2.50–20.00<br>Median = 5.0<br>IQR = 5.0–10.0 | 0.17 |
| Methotrexate | 49/62 (79.0%) | 82/105 (78.0%) | 0.88 |
| Antimalarials | 32/62 (51.6%) | 44/105 (41.0%) | 0.22 |
| Leflunomide | 15/62 (16.1%) | 28/105 (26.2%) | 0.72 |
| Anti-TNFα | 4/62 (6.4%) | 6/104 (5.7%) | 1.00 |

that patients with EORA had a better prognosis and achieved easier and faster remission. On the other hand, a Spanish study[18] shows that patients with elderly onset rheumatoid arthritis have worse functional and anatomical indexes *versus* corresponding younger subjects. Data from this study favor the concept that RA in the elderly is not a more serious condition than in young subjects. However, Naz et al.[19] showed that older age at the time of diagnosis is associated with increased cardiovascular mortality, suggesting the need for an aggressive treatment to avoid premature death.

Tutuncu et al.[7] investigating prescribing habits of 192 rheumatologists, describe that patients with EORA receive less treatment than those with YORA, despite an identical duration of disease and comparable activity and severity. As already mentioned, older people have more co-morbidities, are at higher risk of polypharmacy and are subject to a higher prevalence of side effects by changes in drug pharmacodynamics and pharmacokinetics.[1,2] The recognition that RA is a disease with a poor prognosis and that the control of the inflammatory process impacts decisively on functional capacity and survival of the patient, may have been responsible for a change of attitude toward this age group in recent years. In this study, we could not detect differences in the use of drugs in the two disease onset ranges, showing that currently the aggressiveness in treatment does not vary according to the age of onset, and a similar control of inflammation, measured by DAS 28, was obtained in both populations.

This study has some limitations. Due to the retrospective nature of the study, it was not possible to access certain information such as, for instance, the prevalence of secondary Sjögren syndrome in both groups. Interestingly, we observed a lower tendency for investigation of such kind of symptoms in the older age group. It may be that such fact occurred by attributing the sicca symptoms to their own age, or to the concomitant use of other drugs, such as diuretics and antidepressants, common in older people. Another limitation is the fact that only individuals who already have completed four ACR (1987) classification criteria for RA were included. This choice was made because this is a retrospective study; thus, the quality of information is dependent on the correct completion of medical records. It is therefore important to stress that the above findings are only valid for this type of patients. Subjects with atypical forms of RA, such as those with preferential involvement of large joints, polymyalgia rheumatica-like forms and RS3PE have not been studied. On the other hand, this same selective process allowed the inclusion of individuals with a more accurate diagnosis, with the exclusion of other diseases that, in the elderly, may simulate RA, such as microcrystalline diseases. The strategy used for our inclusion criterion of patients may also have been responsible for the higher prevalence of positive RF in EORA found in this study, since most authors have described this variable as being lower than that found in young subjects.[1,11] Although the literature mentions that healthy elderly are likely to have a higher prevalence of RF, a fact attributed solely to age, it is interesting to note that this finding could not be proven in a study of 336 healthy patients in our region.[20] Therefore, the higher prevalence of this autoantibody found in this study cannot be justified by immune system changes associated with the aging process. Furthermore, it is worth noting that the cutoff point used for defining EORA in this study was 60 years,[1] which makes this population somewhat younger and less subject to immunosenescence than that from other studies, where the cutoff point of 65 years was adopted.[8]

Moreover, in this study a comparison group matched for disease duration was included, which allowed a more realistic analysis of the effects of the disease on the functional capacity of the different groups.

An interesting observation was the finding of a trend toward the appearance of interstitial pneumonitis in EORA individuals. Although this extra-articular manifestation was not associated with age at disease onset, it has been found more frequently in male individuals[21] who, in turn, are more common in EORA groups. One should take into account that this finding may be influenced by the fact that this study was performed in a tertiary center, with a heavier referral of patients with more severe disease.

In conclusion, it can be said that, in our region, patients with EORA have higher prevalence of male individuals and that, despite equal treatment and control of inflammatory activity in both groups, patients with YORA have a worse functional performance.

## Conflicts of interest

The authors declare no conflicts of interest.

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