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# Late onset rheumatoid arthritis: Clinical and laboratory comparisons with younger onset patients

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**Abstract**

We aimed to compare the clinical and laboratory profiles of the patients presenting late onset rheumatoid arthritis (LORA) with younger onset rheumatoid arthritis (YORA) patients. During the period between January 1995 and December 2004, 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 $71.7 \pm 5.9$ years, and $52.1 \pm 11.5$ years, respectively. The gender ratio (female/male) was 1.48 in LORA and 2.85 in YORA ($p = 0.012$). The average ages of the disease onset were $42.2 \pm 10.4$ years in YORA and $68.4 \pm 4.6$ years in LORA. The duration of the diagnosis was longer in LORA than in YORA ($20.7 \pm 14.3$ months versus $10.3 \pm 6.2$ months, $p < 0.001$). Rheumatoid arthritis (RA) duration was shorter in LORA than in YORA ($43.5 \pm 64.4$ months versus $126.3 \pm 101.0$ months, $p < 0.001$). Although LORA patients had more significant frequent shoulder joint involvements ($p < 0.001$), proximal interphalangeal (PIP), metacarpophalangeal (MCP), elbow, metatarsophalangeal (MTP) and ankle involvements were common in YORA. Wrist, knee and hip involvements were not different in the groups. Classical rheumatoid hand deformities, interstitial lung disease and Sjögren's syndrome (SS) were significantly lower in LORA than in YORA. LORA patients had more common weight loss, myalgia, lympha-

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denopathy, polymyalgia rheumatica (PMR)-like syndrome and neuropathy. The frequencies of RF, ANA, anti-SSA/Ro and anti-SSB/La positivities were lower in LORA than in YORA, whereas elevated erythrocyte sedimentation rates (ESR), C-reactive protein (CRP) and anemia associated with chronic disease were higher in LORA. Patients with LORA, according to the accepted international criteria, present with different clinical and laboratory profiles when compared with younger patients. These results suggest that age may influence the presentation of RA at onset.


*Keywords:* Late onset rheumatoid arthritis; Early onset rheumatoid arthritis; Polymyalgia rheumatica

## 1. Introduction

Rheumatoid arthritis (RA) is a chronic and destructive inflammatory disease characterized especially in the involvement of small joints. RA usually develops in middle aged adults; however, it may occur at childhood or old age, too (Goronzy and Weyand, 2001). RA is the second most common rheumatic disease after osteoarthritis but it is the most destructive for synovial joints. The disease beginning over 60 or 65 years is described as a late onset rheumatoid arthritis (LORA) and the one at middle age is defined as a younger onset rheumatoid arthritis (YORA) (Healey, 1986). These two presentations of RA may differ significantly with respect to the mode of onset, the prevalence of associated systemic symptoms, the diagnostic criteria, the progression of diseases and the functional outcomes. The onset may be acute and severe or slow and insidious, making the diagnosis difficult and often delayed (Erlich et al., 1970; Healey, 1986; Yazici and Paget, 2000). Polymyalgia rheumatica (PMR) is diagnosed in elderly patients presenting with pain and stiffness of at least a four-week duration in the muscles of the neck, shoulder and pelvic girdles. Moreover, peripheral synovitis may be present in up to 25% of the patients with PMR. Since both PMR and LORA patients have similar clinical presentations, the differential diagnosis of these disorders may be difficult and LORA may overlap PMR, or LORA patients may have PMR-like symptoms, too (Salvarani et al., 2004). In the literature, there are papers emphasizing that LORA and YORA have similar clinical presentations; besides, there are some papers emphasizing that they have different clinical entities (Yazici and Paget, 2000; Papadopoulos et al., 2003).

The aim of the study was to compare the clinical and laboratory presentations of LORA with that of YORA in this retrospective analysis.

## 2. Patients and methods

During the period between January 1995 and December 2004, we identified retrospectively 124 LORA patients and 150 YORA patients in whom a diagnosis of RA was made at the age of 18–64 years in outpatient or inpatient clinics of the Rheumatology and Geriatric Medicine Departments of Ankara University. LORA was defined as the patients developing RA after the age of 65 years. The hospital records of the patients were reviewed to assess the age at onset, disease duration, gender, characteristics of the joint involvements, duration of morning stiffness, systemic symptoms such as weight

loss, fever and fatigue, extra-articular features such as PMR symptoms, lymphadenopathy, hepatosplenomegali, neuropathy, rheumatoid nodules, pulmonary involvement, Sjögren's syndrome (SS), malignancy, and laboratory findings such as complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), anti-nuclear antibodies (ANA), anti-neutrophile cytoplasmic antigen (ANCA), anti-SSA/Ro and anti-SSB/La. The duration from the beginning of RA symptoms to the time of diagnosis was accepted as the duration of the diagnosis. The diagnoses of RA and SS were based on the criteria for the classification of RA and SS (Arnett et al., 1988; Vitali et al., 2002). Radiological evaluation was not done because the data from hand radiographs were not available. All the patients fulfilled American College of Rheumatology criteria for the classification of RA though their radiological criteria were unknown.

### 2.1. Statistical analysis

The differences between YORA and LORA, with regard to the clinical and laboratory parameters, were calculated by either chi-square test or Fisher's exact test for the categorical data and the *t*-test for the quantitative data. All the statistical tests were two-sided and the statistical significance was assigned to $p$ values less than 0.05.

## 3. Results

Table 1 shows the pattern of the joint involvements in YORA and LORA patients. Mean ages of the patients with LORA and YORA were $71.6 \pm 5.9$ years (range 66–88), and $52.1 \pm 11.5$ years (range 20–66), respectively. The gender ratio (female/male) was 1.48 (74/50) in LORA and 2.85 (111/39) in YORA ($p = 0.012$). The average ages of the disease onset were $42.2 \pm 10.4$ years in YORA and $68.4 \pm 4.6$ years in LORA. The duration of the diagnosis was longer in LORA than in YORA ($20.7 \pm 14.3$ months versus $10.3 \pm 6.2$

Table 1
The features of joint involvements in patients with LORA and YORA

| | LORA ($n = 124$) | YORA ($n = 150$) | $p$ |
|---|---|---|---|
| Age (mean ± S.D.) (years) | 71.7 ± 5.9 | 52.1 ± 11.5 | <0.001 |
| Female/male | 1.48 (74/50) | 2.85 (111/39) | 0.012 |
| Diagnose duration (mean ± S.D.) (months) | 20.7 ± 14.3 | 10.3 ± 6.2 | <0.001 |
| RA duration (mean ± S.D.) (months) | 43.5 ± 6.4 | 126.3 ± 101.0 | <0.001 |
| PIP | 58 (46.8) | 117 (78.0) | <0.001 |
| MCP | 74 (59.7) | 129 (86.0) | <0.001 |
| Wrist | 81 (65.3) | 112 (74.7) | NS |
| Elbow | 31 (25.0) | 61 (40.7) | 0.007 |
| Shoulder | 29 (23.4) | 8 (5.3) | <0.001 |
| MTP | 8 (6.5) | 23 (15.3) | 0.022 |
| Ankle | 33 (26.6) | 76 (50.7) | <0.001 |
| Knee | 87 (70.2) | 100 (66.7) | NS |
| Hip | 5 (4.0) | 3 (2.0) | NS |

NS: not significant.

Table 2
Extra-articular features of LORA and YORA

| | LORA ($n = 124$) (%) | YORA ($n = 150$) (%) | $p$ |
|---|---|---|---|
| Fever | 24 (19.4) | 21 (14.0) | NS |
| Loss of weight | 47 (37.9) | 33 (22.0) | 0.005 |
| Myalgia | 11 (8.9) | 4 (2.7) | 0.032 |
| Fatigue | 105 (84.7) | 124 (84.4) | NS |
| Lymphadenopathy | 18 (14.5) | 9 (6.0) | 0.024 |
| Hepatomegaly | 10 (8.1) | 5 (3.3) | NS |
| Splenomegaly | 5 (4.2) | 6 (4.0) | NS |
| Neuropathy | 26 (21.0) | 7 (4.7) | <0.001 |
| SS | 4 (3.23) | 12 (8.0) | <0.05 |
| Interstitial lung disease | 28 (18.7) | 39 (31.5) | 0.017 |
| Rheumatoid nodules | 11 (8.9) | 19 (12.7) | NS |
| PMR-like syndrome | 8 (6.5) | 0 | 0.002 |
| Malignancy | 6 (4.8) | 3 (2.0) | NS |
| Swan-neck | 20 (16.13) | 65 (43.33) | <0.001 |
| Boutonniere | 18 (14.52) | 76 (50.67) | <0.001 |
| Ulnar deviation | 68 (54.84) | 136 (90.67) | <0.001 |

months, $p < 0.001$). RA duration was shorter in LORA than in YORA ($43.5 \pm 64.4$ months versus $126.2 \pm 101.0$ months, $p < 0.001$). Morning stiffness was not different in both groups (132 min versus 142 min). Although the patients with LORA had more significant frequent shoulder joint involvements ($p < 0.001$), proximal interphalangeal (PIP), metacarpophalangeal (MCP), elbow, metatarsophalangeal (MTP) and ankle joint involvements were common in YORA. Wrist, knee and hip joint involvements were not different in both groups.

Extra-articular manifestations and associated diseases in LORA and YORA are shown in Table 2. The patients with LORA had more significant common weight loss, myalgia, lymphadenopathy, PMR-like symptoms and neuropathy ($p < 0.05$). However, the frequencies of rheumatoid nodules, fever, fatigue, hepatomegaly, splenomegaly, and malignancy were not different in the groups ($p > 0.05$). The patients with YORA had more frequent interstitial lung disease and SS than LORA patients did ($p < 0.05$). Classical rheumatoid hand deformities including ulnar deviation, swan neck and boutonniere were significantly lower in LORA patients than in YORA patients ($p < 0.05$).

The laboratory parameters including elevated ESR, CRP and anemia associated with chronic diseases were higher in LORA than in YORA, but RF, ANA, anti-SSA/Ro, and anti-SSB/La positivities had a lower incidence in LORA than in YORA ($p < 0.05$) (Table 3).

Table 3
The laboratory features of YORA and LORA

| | LORA | YORA | $p$ |
|---|---|---|---|
| ESR (mean ± S.D.) (mm/h) | $74.31 \pm 26.41$ | $48.13 \pm 16.23$ | <0.001 |
| CRP | $36.41 \pm 24.35$ | $24.37 \pm 12.41$ | <0.001 |
| RF | 36 (29.03) | 98 (65.33) | <0.001 |
| ANA | 4 (3.23) | 20 (13.33) | <0.001 |
| SSA/Ro | 5 (4.03) | 18 (12.0) | <0.05 |
| SSB/La | 3 (2.42) | 12 (8.0) | <0.05 |

## 4. Discussion

RA is the most prevalent inflammatory synovitis affecting 2–2.3% of the geriatric population (Rasch et al., 2003). Differential diagnostic possibilities for LORA including PMR, pseudogut, reflex sympathetic dystrophy and osteoarthritis must be excluded (Kerr, 2004). Since LORA is difficult to diagnose exactly, its diagnosis takes a long time. Meanwhile, we found that the duration of the diagnosis was longer in LORA than in YORA ($20.7 \pm 4.3$ months versus $10.3 \pm 6.2$ months, $p < 0.001$).

A striking female preponderance characterizes many autoimmune diseases and estrogens activate humoral immunity. Sex steroids contribute to the expression of autoimmune diseases (Masi and Crofford, 2001). It is well-known that women are affected approximately three times as common as men, but gender differences have been diminishing in the studies of the older age group (Yazici and Paget, 2000; Goronzy and Weyand, 2001). In our study, the gender ratio in LORA was similar to that in literature (male:female 1.48) and it is the predominance of postmenopausal females with respective hormonal changes.

With regard to morning stiffness, Deal et al. (1985) emphasized that there were no differences between LORA and YORA. However, Pease et al. (1999) found that LORA patients had longer morning stiffness than that in YORA patients, but we found no differences in both groups.

A substantial proportion of LORA patients had features similar to those found in PMR-like syndrome. The occurrence of peripheral arthritis particularly in both hands may lead to some difficulties in the differential diagnosis between PMR and LORA. It was noted that patients developed episodes of PMR and LORA at different times during the follow up. They had a different clinical condition from classical RA, closely similar to PMR. A diagnosis of PMR or RA could therefore be made in the same patient at a different time depending on the clinical expression of the disease (Healey and Sheets, 1988; Healey, 1992). Moreover, in other studies (Salvarani and Hunder, 1999; Salvarani et al., 2004), the patients were considered to have PMR, manifesting the broader clinical spectrum of this disease at the end of the period of observation. In our study, PMR-like symptoms were found to be 6.5% in LORA patients and it is similar to other studies (Healey, 1992; Salvarani et al., 2004; Gonzalez-Gay et al., 2001).

That large joint involvements especially of the shoulders are common in LORA patients is commonly held. It is reported that older patients had an acute onset, in both small and large joint involvements and PMR-like symptoms more frequently (Van der Heijde et al., 1991). In some papers, shoulder involvements in LORA are reported in 48–64%; however, it was found in 29% in our study, which was statistically higher than that in YORA. More significant frequent shoulder joint involvements in the LORA group may testify to the degenerative-destructive changes of non-rheumatoid nature and other joints are involved in the YORA group frequently. Although PIP, MCP, elbow, MTP and ankle joints were more commonly involved in YORA than in LORA, we found that wrist, knee and hip involvements were not different in both. Classical rheumatoid hand deformities, interstitial lung disease and SS were significantly lower in LORA patients than in YORA patients, whereas LORA patients had more common constitutional features such as weight loss and myalgia, lymphadenopathy, rheumatoid nodules and neuropathy.

There are controversial results about RF seropositivity in LORA. It was found higher in LORA than in YORA (89% versus 78%) by Van der Heijde et al. (1991), but we found RF seropositivities higher in YORA than in LORA, similar to that reported by other investigators (Erlich et al., 1970; Ferraccioli et al., 1984; Inoue et al., 1987). In our study, the frequencies of RF, ANA, anti-SSA/Ro and anti-SSB/La seropositivities were lower in LORA than in YORA, but anemia-associated chronic diseases, elevated ESR and CRP were more common in LORA patients and these results are similar to those literatures (Erlich et al., 1970; Pease et al., 1999; Tishler et al., 2001).

In conclusion, we found some differences between LORA and YORA in clinical and laboratory patterns and these differences were shown via this study once more, which suggests that age may influence the disease expressions of RA. Taking the age at onset into consideration, these differences must be kept in mind while making RA diagnosis.

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