Age and Comorbidities Influence Initial Treatment of Patients with Early Rheumatoid Arthritis

To the Editor:

We are quite interested in the study recently published by Dr. Helga Radner, *et al*[1], in which they compared treatment profiles between multimorbid established rheumatoid arthritis (RA) patients and patients with RA only. They found a decrease in biologic disease-modifying antirheumatic drugs used for each additional chronic comorbidity[1]. We, too, have observed the influence of comorbidities on decision making in the initial treatment of patients with early RA. The aim of our study was to evaluate such influences. Our retrospective and observational study was done between March 2014 and March 2015. We included all medical records of patients with RA according to 2010 American College of Rheumatology/European League Against Rheumatism classification criteria[2]. Then we selected only the first-time medical evaluation. We made a descriptive analysis for clinical and demographic variables, initial treatments, and compared the comorbidities. We found 101 patients with RA; 91 (90.1%) were female, with a mean age of 53.2 years (SD 12.7). Patients had a median of 12 months [interquartile range (IQR) 42] from the onset of symptoms to diagnosis. Sixty-seven patients (66.3%) had a positive rheumatoid factor (RF) and 32 (31.7%) had anti-citrullinated peptide antibodies (anti-CCP). There were 77 patients (76.2%) with at least 1 comorbidity. The most common comorbidities observed were diabetes mellitus in 16 patients (15.8%), systemic hypertension in 26 (25.7%), and hypothyroidism in 13 (12.9%). The median 28-joint Disease Activity Score (DAS28) using erythrocyte sedimentation rate (ESR) was 2.37 (IQR 2.01).

Table 1 shows the different combinations of treatments used. No patient had triple therapy at baseline. In bivariate analysis, we did not find a significance in RF or anti-CCP levels, time from the onset of symptoms to diagnosis, or DAS28 ESR as predictors of the use of methotrexate (MTX) alone or in combination in the initial treatment. We observed a median age of 59.5 years (IQR 21) in the patients who used only MTX, versus 52 years (IQR 17) in patients with MTX in combination ($p = 0.028$). The presence of at least 1 comorbidity was associated with the use of MTX alone [35% vs 12.5%, $p = 0.027$, OR 3.78 (95% CI 1.03-13.8)]. We did not observe the influence of other variables studied in the treatment decision.

We observed that the patient's age and comorbidities influenced initial treatment of patients with early RA. The comorbidity in patients with RA affects morbidity-mortality, perhaps through the treatment choices. Previously, Dr. Radner, *et al* evaluated in a systematic review how gastrointestinal and liver comorbidities influence the choice of pain treatment in inflammatory arthritis, including in patients with RA[3]. Later, Listing, *et al* evaluated the increased risk of infections in patients with RA associated with the disease *per se*, the comorbidities, and its treatment[4]. Recently, Nakajima, *et al* found that comorbidity affects both treatment strategies and outcomes in disease activity, physical function, and quality of life in patients with RA[5]. It is noteworthy that all studies have been conducted in patients with established RA, unlike our observation. The window of opportunity that has been described not only helps us to initiate timely treatment to avoid complications or sequelae of the disease[6]. It also allows evaluation of the comorbidities in a systematic way, to reduce morbidity and mortality.

Table 1. Initial treatment of patients with early rheumatoid arthritis (RA).

Type of Treatment	n (%) of Patients
MTX alone or in combination	86 (85.1)
MTX alone	30 (29.7)
LFN	10 (9.9)
MTX + LFN	7 (6.9)
HCQ	20 (19.8)
CQ	31 (30.7)
MTX + HCQ/CQ	48 (47.5)
SSZ	25 (24.8)
MTX + SSZ	20 (19.8)
AZA	1 (1)
PDN	61 (60.4)
Biologic	3 (3)
MTX combination therapy	68 (67.3)

MTX: methotrexate; LFN: leflunomide; HCQ: hydroxychloroquine; CQ: chloroquine; SSZ: sulfasalazine; AZA: azathioprine; PDN: prednisone.

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