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## Original article

# Rheumatoid arthritis seems to have DMARD treatment decision influenced by fibromyalgia

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### ABSTRACT

**Objective:** To compare DMARD use in patients with and without FM over time, including overtreatment and undertreatment rates in both groups.

**Methods:** A prospective cohort study with patients attending an RA outpatient clinic was conducted. Participants were consecutively recruited between March 2006 and June 2007 and were followed through December 2013. Data on DMARD use (prevalences, doses and escalation rates), DAS28, HAQ and radiographic progression were compared among RA patients with FM and without FM. Mistreatment clinical scenarios were allegedly identified and compared between groups.

**Results:** 256 RA patients (32 with FM) were followed for  $6.2 \pm 2.0$  (mean  $\pm$  SD) years comprising 2986 visits. At baseline, RA duration was  $11.1 \pm 7.4$  years. DAS28 and HAQ were greater in RA with FM group, and were closer to RA without FM group towards the end. RA patients with FM used higher doses of tricyclic antidepressants, leflunomide and prednisone, and lower doses of methotrexate. When compared to RA patients without FM, participants with RA and FM used more often tricyclic antidepressants, leflunomide, prednisone, continuous analgesics and less often methotrexate. Groups presented similar 7-year biologic-free survival, and radiographic progression-free survival in Cox regression. RA patients with FM had greater proportions of visits in mistreatment scenarios when compared to RA patients without FM (28.4 vs. 19.8%,  $p < 0.001$ ).

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E-mail: [rafaelchakr@gmail.com](mailto:rafaelchakr@gmail.com) (R.M. Chakr).<http://dx.doi.org/10.1016/j.rbre.2017.01.004>2255-5021/© 2017 Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Conclusions:** RA patients with FM used more leflunomide and prednisone, and RA mistreatment was more frequent in FM patients. Certainly, RA patients with FM will benefit from a personalized T2T strategy, including ultrasound (when suitable) and proper FM treatment.

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## As decisões de tratamento com DMARD na artrite reumatoide parecem ser influenciadas pela fibromialgia

### RESUMO

#### Palavras-chave:

Fibromialgia

Artrite reumatoide

Tratamento farmacológico

**Objetivo:** Comparar o uso de fármacos antirreumáticos modificadores da doença (DMARD) em pacientes com e sem fibromialgia (FM) ao longo do tempo, incluindo as taxas de tratamento excessivo e subtratamento em ambos os grupos.

**Métodos:** Estudo de coorte prospectiva com pacientes atendidos em um ambulatório de artrite reumatoide (AR). Os participantes foram recrutados consecutivamente entre março de 2006 e junho de 2007 e foram seguidos até dezembro de 2013. Compararam-se os dados de uso de DMARD (prevalências, doses e taxas de escalonamento), 28-Joint Disease Activity Score (DAS28), Health Assessment Questionnaire (HAQ) e progressão radiográfica entre pacientes com e sem FM. Os cenários clínicos de tratamento supostamente incorreto foram identificados e comparados entre os grupos.

**Resultados:** Seguiram-se 256 pacientes com AR (32 com FM) por  $6,2 \pm 2,0$  (média ± DP) anos, período que abrangeu 2.986 consultas. No início do estudo, a duração da AR era de  $11,1 \pm 7,4$  anos. O DAS28 e o HAQ foram maiores no grupo AR com FM e estavam mais próximos do grupo AR sem FM no fim do estudo. Os pacientes com AR com FM usaram doses mais altas de antidepressivos tricíclicos, leflunomida e prednisona e doses mais baixas de metotrexato. Quando comparados com os pacientes com AR sem FM, os participantes com AR e FM usaram mais frequentemente antidepressivos tricíclicos, leflunomida, prednisona e analgésicos contínuos e menos frequentemente metotrexato. Os grupos apresentaram sobrevida em sete anos sem agentes biológicos e livres de progressão radiográfica semelhantes na regressão Cox. Os pacientes com AR com FM apresentaram uma maior proporção de consultas em cenários de tratamento supostamente incorreto quando comparados com os pacientes com AR sem FM (28,4 vs. 19,8%,  $p < 0,001$ ).

**Conclusões:** Os pacientes com AR e FM usaram mais leflunomida e prednisona e o tratamento supostamente incorreto na AR foi mais frequente em pacientes com FM. Os pacientes com AR com FM certamente se beneficiarão de uma estratégia personalizada de tratamento por metas (T2T), incluindo ultrassonografia (quando apropriado) e controle da FM.

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## Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic destructive polyarthritis that may cause severe functional impairment and death.<sup>1</sup> To stop joint destruction and prevent worse outcomes clinicians should use disease-modifying antirheumatic drugs (DMARD) in a treat-to-target (T2T) strategy, where lower disease activity is pursued.<sup>1-3</sup> Disease activity level can be clinically estimated by 28-joint disease activity score (DAS28), a score that includes objective (number of swollen joints and erythrocyte sedimentation rate) and subjective parameters (number of tender joints and patient's global health evaluation using a visual analogue scale).<sup>4,5</sup>

Fibromyalgia (FM) is a chronic painful condition affecting up to 20% of RA patients. FM may falsely increase RA activity by augmenting the subjective components of DAS28

and, therefore, bias treatment decision. Both overtreatment (DMARD escalation when a higher DAS28 is due to FM) and undertreatment (no DMARD escalation when a higher DAS28 is due to RA) are possible.<sup>6-10</sup>

The primary goal of this study is to compare DMARD use in patients with and without FM over time. Also, we intend to compare overtreatment and undertreatment rates in both groups.

## Patients and methods

A prospective cohort study was conducted with patients attending the RA outpatient clinic at Hospital de Clínicas de Porto Alegre since biologic DMARD became available in the institution. Participants were consecutively recruited between March 2006 and June 2007 and they were followed through December 2013. To be included patients had to fulfil 1987

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