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Analysis of the association of fatigue with clinical and psychological variables in a series of 371 Brazilian patients with rheumatoid arthritis

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ABSTRACT

Objectives: Fatigue is a highly subjective and extremely common symptom in patients with rheumatoid arthritis although it is difficult to characterize and define. The aim of this study was to assess fatigue in a cohort of Brazilian patients, and to analyze the relationship between fatigue and disease-specific variables.

Methods: 371 Brazilian patients diagnosed with rheumatoid arthritis according to the 1987 American College of Rheumatology classification criteria were prospectively investigated. Demographic, clinical and laboratorial data were obtained from hospitals records. The number of painful joints, bone mass index, disease duration, quality of life, functional capacity, anxiety and depression were recorded. Fatigue was evaluated using the subscale of Fatigue Assessment of Chronic Illness Therapy (FACIT-FATIGUE scale).

Results: The median fatigue score was 42.0 (10.0), negatively correlated with functional capacity (-0.507; $P < 0.001$), anxiety and depression (-0.542 and -0.545; $P < 0.001$ respectively), and predominantly with physical domain of Short Form 36-item quality of life questionnaire (SF-36P: 0.584; $P < 0.001$). The scores were not associated with the erythrocyte sedimentation rate (-0.118; $P < 0.05$), C-reactive protein (-0.089; $P < 0.05$), disease activity (-0.250; $P < 0.001$) or the number of painful joints (-0.135; $P < 0.01$). Confidence interval of 95% was applied for all measures.

Conclusions: In this series of Brazilian patients with rheumatoid arthritis, we suggest a new significance for fatigue complains as an independent parameter not related with number of painful joints, disease or inflammatory activity scores. Psychological and functional im-

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pairments appear to be more related to fatigue. Additional studies and inclusion of standard measures for monitoring fatigue complaints are required.

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Análise da associação da fadiga com variáveis clínicas e psicológicas em uma série de 371 pacientes brasileiros com artrite reumatoide

R E S U M O

Palavras-chave:

Artrite reumatoide
Fadiga
Atividade da doença
Qualidade de vida
Dor

Objetivos: A fadiga é um sintoma altamente subjetivo e extremamente comum em pacientes com artrite reumatoide, embora seja difícil de caracterizar e definir. O objetivo desse estudo foi avaliar a fadiga em uma coorte de pacientes brasileiros e analisar a relação entre fadiga e variáveis específicas da doença.

Métodos: Foram prospectivamente investigados 371 pacientes brasileiros diagnosticados com artrite reumatoide, de acordo com os critérios de classificação do Colégio Americano de Reumatologia de 1987. Dados demográficos, clínicos e laboratoriais foram obtidos dos registros clínicos. Foram registrados o número de articulações dolorosas, índice de massa corporal, duração da doença, qualidade de vida, capacidade funcional, ansiedade e depressão. A fadiga foi avaliada com o uso da subescala específica da escala *Fatigue Assessment of Chronic Illness Therapy* (FACIT-FATIGUE).

Resultados: O escore mediano para fadiga foi 42 (10), negativamente correlacionado com a capacidade funcional (-0,507; $p < 0,001$), ansiedade e depressão (-0,542 e -0,545; $p < 0,001$, respectivamente) e predominantemente com o domínio físico do questionário Short Form-36 para qualidade de vida (SF-36P: 0,584; $p < 0,001$). Não houve correlação entre os escores e a velocidade de sedimentação das hemácias (-0,118; $p < 0,05$), proteína C reativa (-0,089; $p < 0,05$), atividade da doença (-0,250; $p < 0,001$) ou número de articulações dolorosas (-0,135; $p < 0,01$). Para todas as medidas foi aplicado um intervalo de confiança de 95%.

Conclusões: Nesta série de pacientes brasileiros com artrite reumatoide, sugerimos um novo significado para as queixas de fadiga como um parâmetro independente não relacionado com o número de articulações dolorosas ou escores de atividade inflamatória. Parece haver maior relação entre transtornos psicológicos e funcionais com a fadiga. Seriam importantes novos estudos e uso rotineiro de medidas padronizadas para a monitorização das queixas de fadiga.

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Introduction

Rheumatoid arthritis (RA) is a systemic inflammatory disease that can lead to significant morbidity, joint deformity and an impaired quality of life (QoL). This disease affects approximately 0.5%-1% of the general population, with considerable variations being observed among different populations.¹⁻³ Although the joints are the major loci of disease activity, fatigue is a notably common and disabling symptom experienced almost universally by patients with RA (88%-98%), who consider the effect and importance of fatigue similar to pain.⁴⁻⁹

There is no universally accepted definition of fatigue. It can be either defined as a progressive impairment of capacity to generate muscle or a lessened capacity to work, with reduced efficiency of accomplishment, that are usually accompanied by feelings of weariness, sleepiness or irritability.¹⁰ Belza *et al.* described fatigue as an "enduring the subjective sensation of generalized tiredness or exhaustion".¹¹

In the general population, 20% of men and 30% of women complain about frequent tiredness.¹²

Fatigue often accompanies various illnesses, and has been increasingly recognized and studied in a number of chronic diseases, such as liver disorders, infections and hematological diseases.¹²

Hewlett *et al.* observed that RA fatigue is a different phenomenon from normal tiredness because it is extreme, endless and unresolved described as an important and overwhelming complaint.⁴ Studies examining the predictive factors of fatigue in RA reported not only physical but also psychological and social aspects related to fatigue.^{4,13,14} Pain, physical disability, inactivity and poorer sleep quality and psychosocial factors, such as depressive symptoms, anxiety and social stress (as long-term symptoms or associated conditions) are predictive of fatigue in RA.^{13,14}

During the chronic course of RA, continuing inflammatory activity with periods of prolonged physical inactivity leads to muscle atrophy and instability of the periarticular structures with reduced strength and muscular endurance

that contribute to the onset of fatigue. Ekdahl *et al.* demonstrated that 80% of patients with RA exhibited changes in muscle strength and coordination of the lower extremities and decreased aerobic activity. These results were confirmed by Semble *et al.*^{15,16} In 1996, Rall *et al.* evaluated the effect of an exercise program to improve the muscle strength in patients with RA and observed a significant reduction in fatigue (38%).¹⁷

Due to fatigue's multifactorial and multidimensional nature, this condition is difficult to assess. Little is known concerning the correlations, adequate measurements or the clinical management and interventions for fatigue.^{4,18} Persistent fatigue is one of the most significant obstacles to optimizing function in these patients.¹⁹

The aim of this study was to analyze aspects of fatigue in 371 Brazilian RA patients, and the association of fatigue with disease-specific variables, such as inflammatory activity, pain, QoL, physical function, and psychological complaints, such as anxiety and depression.

Methods

A total of 371 patients with RA were recruited at the Department of Rheumatology of Hospital da Santa Casa da Misericórdia do Rio de Janeiro (HSCMRJ) and Hospital Universitário Pedro Ernesto (HUPE) into this cross-sectional prospective study from 2010-2011. Patients were between the ages of 18 and 65 years, diagnosed with RA according to the 1987 American College of Rheumatology (ACR) RA classification criteria.²⁰ For all of the patients invited and included in the study written informed consents were provided. The research was conducted with approval by and in accordance with the Ethics Committee of both hospitals.

The patients who were unable to understand and respond the questionnaires or who had any comorbidities that might interfere with the assessment of fatigue, such as anemia (hemoglobin > 9.0 mg/dl), endocrine diseases (diabetes type I and II, thyroid diseases), renal failure (creatinine < 2.0mg/dl), liver diseases including cirrhosis, pulmonary (Chronic Obstructive Pulmonary Disease) or cardiovascular disorders, were excluded.

Demographic and clinical data were collected including duration of disease, number of painful peripheral joints and body mass index (BMI). Disease activity was clinically measured, using the 28 joint count Disease Activity Score (DAS 28), and biologically, using the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels.

Physical function was assessed by the Health Assessment Questionnaire-Disability Index (HAQ DI), where scores range from 0 to 3, and higher scores indicate lower levels of physical functioning.^{21,22} The health-related quality of life (HRQoL) was assessed using physical and mental scores of the Short-Form 36-Items Health Survey (SF-36P and SF-36M) generic questionnaire.²³

The Hospital Anxiety and Depression Scale (HAD a/d) was used to evaluate the depression and anxiety symptoms. This questionnaire has 14 interlaced questions: one-half of the questions were related to anxiety, and one-half to depression. For each question, a value from 0 to 3 is added to each

domain separately, building the two sub-scales. Patients with results greater than 8 are considered at risk of anxiety and/or depression independently.¹² All questionnaires used were validated and culturally adapted to the Portuguese language.^{12,21-23}

Fatigue was evaluated using a subscale of the Functional Assessment of Chronic Illness Therapy (FACIT), which was initially validated to assess QoL in patients with cancer or other chronic illnesses. The scale was used for RA patients, who only scores the fatigue complains (FACIT-Fatigue). The total score ranges from 0 to 52, and higher scores represent less fatigue.²⁴ The FACIT-Fatigue was validated for Portuguese version through an authorization from the site <http://www.facit.org>.

Statistical analysis

Calculating the minimum patient number with precision measurements estimated under parameters of 90% with confidence interval of 0.20 and $\alpha = 0.05$, we got a minimum sample size of 258 patients.

Considering that both departments of Rheumatology treat approximately 800 patients with RA per year, 30%-40% of which fulfill the inclusion/exclusion criteria, the sample size could be about 240 to 320 patients.

Taking into account also that the fatigue complains could be present in 25% to 60% of RA patients,^{4,5,10,18,20,25,26,27} we found a sample size of 200 to 480 of those hospital's populations.

We decided to establish a final sample size between 320 to 480 patients. After two years of recruitment, 371 patients with useful data were finely included in this study.

All data were tested for normality by applying the Shapiro-Wilk Test. As all variables showed non-normal distribution, the variables were presented by median (interquartile range). Spearman's rank correlation coefficient (r_s) was calculated to determine correlations between fatigue and clinical or psychological measures. All tests were 2-sided, and P values ≤ 0.05 were considered statistically significant. Statistical analysis was performed using Statistica software, version 8.0 (Statsoft. Inc. Tulsa, USA).

Results

A total number of 371 patients were evaluated. The group studied included 335 women (90.3%) and 36 men (9.7%). The demographic and clinical data, which are summarized in Table 1, indicated the majority of our patients were white (66.8%), followed by mixed-race patients (20.5%), and black patients (12.7%). The median age was 51 (13) years and the BMI was 25.0 (3.6). The mean score of fatigue (FACIT-Fatigue) was 42.0 (10), and the mean number of painful joints was 6 (6). The median disease duration was 6 (6) years.

The median disease activity, as assessed by DAS 28, was 4.7 (2). The median ESR was 33 (27) mm, and the median of CRP level was 0.8 (1.7).

When the DAS 28 cut-off values for measuring inflammatory disease activity were applied, 7.0% of the patients were

Table 1 – Baseline characteristics of RA patients (n = 371)

Characteristics	Mean (sd) or n (%)	Median	Min	Max	- CI 95%	+ CI 95%
Women	335 (90.3)					
Ethnic group						
White	248 (66.8)					
Mixed-race	76 (20.5)					
Black	47 (1.7)					
Age	49.5 (10.2)	51.0	18.0	65.0	48.6	50.7
BMI	25.2 (3.9)	25.0	16.3	43.9	24.8	25.6
Disease duration (year)	7.8 (5.8)	6.0	1.0	43.0	7.2	8.4
Laboratory assessment of disease activity						
ESR	36.2 (22.7)	33.0	2.0	118.0	33.9	38.5
CRP	1.8 (3.2)	0.8	0.1	33.5	1.5	2.2
Clinical assessments						
DAS 28	4.6 (1.4)	4.7	0.0	8.1	4.4	4.7
HAQ DI	1.0 (0.7)	0.8	0.0	2.8	0.9	1.0
SF-36	86.9 (8.5)	87.5	51.0	99.6	86.0	87.7
Physical domain	39.1 (10.5)	39.5	12.1	68.3	38.1	40.2
Mental domain	47.6 (11.0)	50.1	12.4	96.1	46.5	48.8
HAD a	7.0 (3.4)	7.0	0.0	20.0	6.7	7.4
HAD d	5.4 (3.6)	5.0	0.0	20.0	5.0	5.7
FACIT-Fatigue	39.9 (8.6)	42.0	4.0	52.0	39.0	40.8
Number of Painfull joints	6.83(4.78)	6.0	0.0	28.0	6.4	7.3

BMI: Bone Mass Index, ESR: Erythrocyte Sedimentation Rate, CRP: C Reactive Protein, DAS 28: 28 Disease Activity Index, HAQ DI: Health Assessment Questionnaire Disability Index, SF-36: Short-Form 36-item, HAD a/d: Hospital Anxiety and Depression Scale, FACIT-Fatigue: Fatigue Assessment of Chronic Illness Therapy.

in remission (DAS 28 < 2.6), 7.8% had lower disease activity (DAS 28 ≥ 2.6 ≤ 3.2), 9.7% had moderate disease activity (DAS 28 ≥ 3.2 ≤ 5.1), and 75.5% of the sample had high disease activity (DAS 28 > 5.1).

The median score of the SF-36 was 87.5 (12.2). The means of the physical and mental subscales were 39.1 (10.5) and 47.6 (11.0), respectively. The mean of the HAQ DI was 1.0 (0.7). The anxiety and depression questionnaire (HAD a/d) showed means of 7.0 (3.4) for anxiety, and 5.4 (3.6) for depression, respectively.

The distribution of disease activity (DAS 28) and duration of illness (years) in this sample of RA patients are shown in Fig. 1.

The correlations between fatigue (FACIT-Fatigue), quality of life (SF-36), functional capacity (HAQ DI), painful joints, anxiety and depression (HAD a/d), DAS 28, ESR and CRP are shown in Table 2. The correlations of fatigue with QoL, anxiety and depression or functional capacity are shown in the graphs of Figs. 2 and 3.

Table 3 presents the correlations of fatigue with disease activity measured by ESR, CRP and DAS 28 and the QoL by the physical and mental domains of SF-36 (SF-36P and SF-36M), functional capacity by HAQ DI, the number of painful joints, and anxiety or depression as measured by HAD a/d in patients with moderate and high disease activity (DAS 28 ≥ 3.2).

Discussion

This study was the first in our country to analyze a sample of 371 Brazilian patients with RA, assessing fatigue by FACIT-Fatigue, a 13-items measure of fatigue that previously showed good internal consistency in patients with RA.

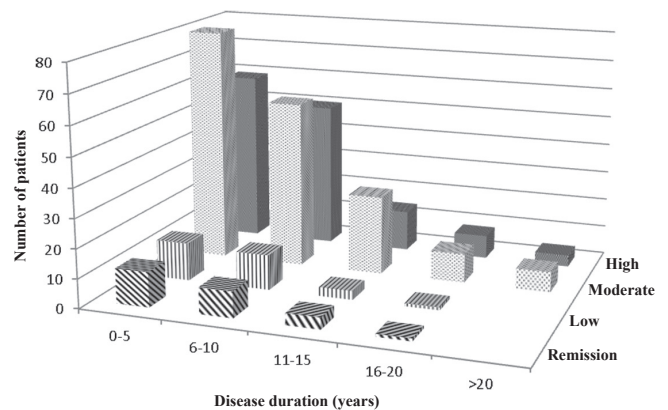


Fig. 1 – Distribution of disease duration with disease activity by DAS28 and number of patients.

In recent years, fatigue has emerged as an important outcome in RA,^{4,8,13,14} although the symptoms are largely ignored in terms of clinical care and educational and research endeavours. The multifactorial and multidimensional characteristics of fatigue demand a broad analysis that takes into consideration the clinical, cultural and social aspects of fatigue complaints and includes the patient's perspective. In Rio de Janeiro, a cosmopolitan coastal city, the mixed population and the tropical climate with a majority of sunny days could modify the perception of fatigue and its correlation to the indices of disease activity, QoL, functional capacity, pain, anxiety and depression.

Cella D *et al.* validated the FACIT-Fatigue, comparing it to other scales such as the Multidimensional Assessment of Fatigue (MAF) and the SF-36 in 636 patients with RA for 24 weeks in a double blind, randomized trial using anti-TNF

alpha monoclonal antibody and placebo, where the psychometric performance of the FACIT-Fatigue scale for assessment of fatigue was comparable to the other scales.²⁴

The demographic findings of gender and ethnicity are similar to previous reports, which indicate a female and white predominance, reflecting the typical incidence of RA

Table 2 – Analysis of Spearman’s correlations coefficient of all patients

	ESR	CRP	SF36-P	SF36-M	HAD-a	HAD-d	DAS28	HAQ-DI	Facit fatigue	Painful joints
ESR		0.467*	-0.203*	-0.161*	0.101	0.130*	0.472*	0.190*	-0.118*	0.220*
CRP	0.467*		-0.191*	-0.024	0.072	0.103*	0.356*	0.189*	-0.089	0.203*
SF-36P	-0.203*	-0.191*		0.121*	-0.328*	-0.406*	-0.439*	-0.672*	0.584*	-0.293*
SF-36M	-0.161*	-0.024	0.121*		-0.477*	-0.437*	-0.131*	-0.175*	0.405*	-0.019
HAD a	0.101	0.072	-0.328*	-0.477*		0.648*	0.169*	0.294*	-0.542*	0.060
HAD d	0.130*	0.103*	-0.406*	-0.437*	0.648*		0.244*	0.347*	-0.545*	0.101*
DAS 28	0.472*	0.356*	-0.439*	-0.131*	0.169*	0.244*		0.356*	-0.250*	0.725*
HAQ DI	0.190*	0.189*	-0.672*	-0.175*	0.294*	0.347*	0.356*		-0.507*	0.219*
Facit fatigue	-0.118*	-0.089	0.584*	0.405*	-0.542*	-0.545*	-0.250*	-0.507*		-0.135*
Painful joints	0.220*	0.203*	-0.293*	-0.019	0.060	0.101*	0.725*	0.219*	-0.135*	

ESR: Erythrocyte Sedimentation Rate, CRP: C-Reactive protein, SF-36: Short-Form 36-item, SF-36P: Short-Form 36-item Physical domain, SF-36M: Short-Form 36-item Mental domain, HAD a: Hospital Anxiety Scale, HAD d: Hospital Depression Scale, DAS28: Disease Activity Score, HAQ DI: Health Assessment Questionnaire – Disability Index, and FACIT fatigue: Fatigue Assessment of Chronic Illness Therapy. *Statistically significant (p < 0.05).

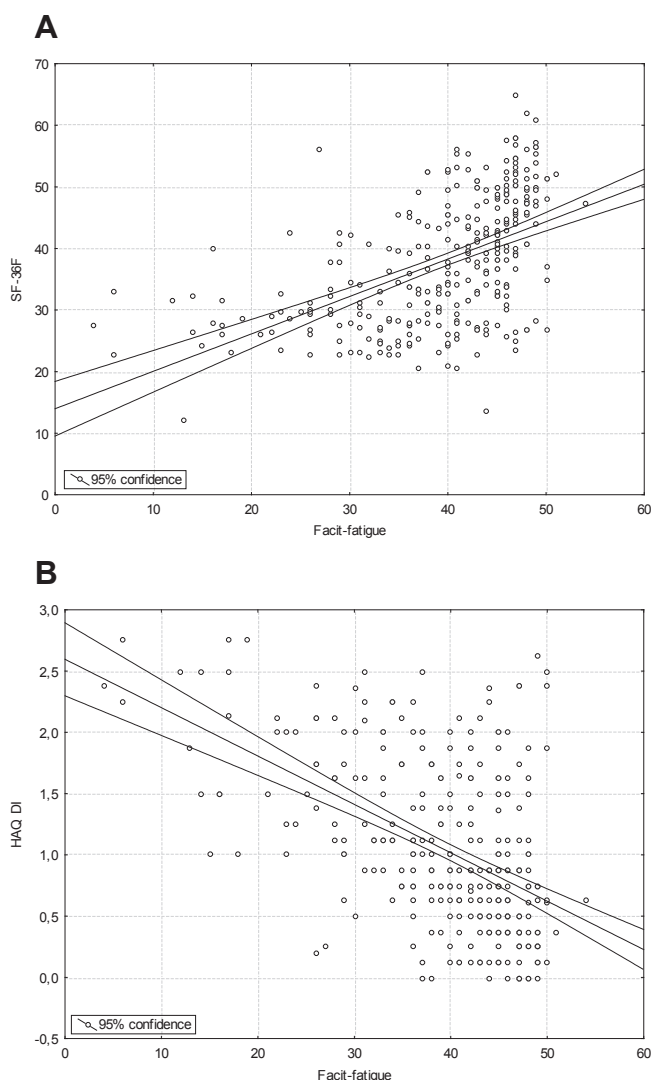


Fig. 2 – Spearman’s correlations coefficient between FACIT fatigue and SF-36 (A) and HAQ DI (B).

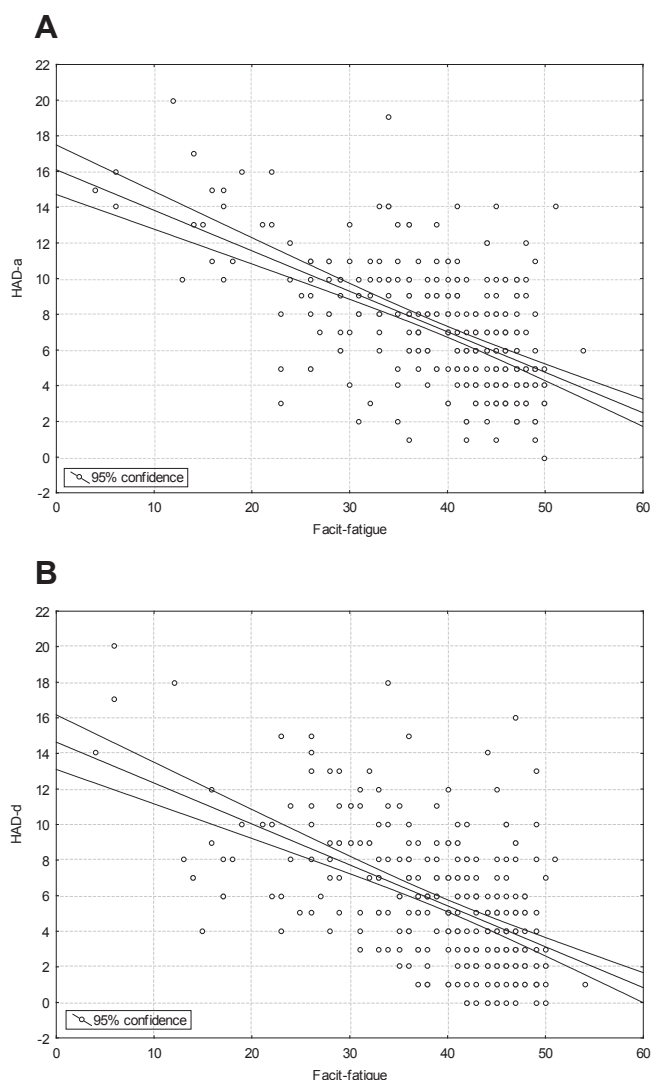


Fig. 3 – Spearman’s correlations coefficient between FACIT fatigue and HAD a (A) and HAD d (B).

Table 3 – Analysis of Spearman's correlations coefficient of patients with high and moderate disease activity (n = 316)

n = 316	ESR	CRP	SF-36P	SF36M	HAD a	HAD d	DAS 28	HAQ DI	Painful joints
Facit-fatigue	-0.108	-0.065	0.577*	0.456*	-0.539*	-0.528*	-0.218*	-0.489*	-0.080

ESR: Erythrocyte Sedimentation Rate, CRP: C Reactive Protein, SF36P: Short-Form 36-Item Physical domain, SF-36M: Short-Form 36-Item Mental domain, HAD a: Hospital Anxiety and Depression Scale-anxiety domain, HAD d: Hospital Anxiety and Depression Scale-depression domain, DAS 28: Disease Activity Score, HAQ DI: Health Assessment Questionnaire Disability Index, and FACIT fatigue: Fatigue Assessment of Chronic Illness Therapy. *Statistically significant (p < 0.001).

patients. These results differ in ethnic characteristics of Brazilian population, in which 47.7% are white according to data from the Brazilian Institute of Geography and Statistics (IBGE).²⁸

The disease duration was under 10 years, and for the largest number of patients there had been less than 5 years since symptoms onset and diagnosis confirmation. The mean disease activity quantified by DAS 28 score of 4.6, shown in Table 1, confirms that most of our cohort exhibit moderate or high disease activity.

Based on our findings, fatigue did not correlate with disease activity. As shown in Table 2, the FACIT-Fatigue has not demonstrated correlation with CRP, ESR and DAS 28, which are routinely evaluated as inflammatory disease activity indexes. The FACIT- Fatigue demonstrated a moderate correlation with functional capacity (HAQ DI), as shown in Fig. 2B, Table 2; anxiety and depression (HAD a/d), shown in Fig. 3, and predominantly with the physical domain of quality of life (SF-36P), shown in Fig. 2A.

A similar analysis with moderate and high disease activity (DAS 28 > 3.2) subgroups of this sample confirmed the absence of a correlation between fatigue and disease activity, shown in Table 3. This finding is in accordance with Huyser *et al.*, who suggested that fatigue in RA is not related to disease activity and showed that many of the variables that were significantly correlated with fatigue had a psychosocial basis.²⁵ Such factors, as anxiety and higher depressive symptoms, were significantly associated with increased fatigue, as was seen in this study (Fig. 3). The best predictors of fatigue were higher levels of pain, more depressive symptoms and female gender, which were independent of disease activity.²⁵ Our study showed that the number of painful joints, measured by the first item of DAS 28, did not correlate with fatigue independently of the level of pain or the patient global assessment.

Bergman *et al.* showed that fatigue is not an inflammatory variable and has virtually no correlation with the number of swollen or tender joints. These researchers showed a moderate association of fatigue with DAS 28, and 79% of the complaints could be explained by the patient global assessment.²⁹

Yacoub *et al.* assessed fatigue in 248 patients with RA, finding a prevalence of fatigue in approximately 90% and, in contrast to our results, a significant association with disease activity.³⁰ Thyberg *et al.* suggested that disease activity is among the factors closely related to fatigue.³¹

This study, using the HAD a/d scale, determined a correlation between fatigue and emotional aspects, such as depression and anxiety, shown in Fig. 3 and Table 2, which was reported by Huyser *et al.* Depression is a frequent complaint

associated with fatigue in RA patients with a prevalence of 13%-20%, which is 2 to 3 times higher than observed in healthy people.^{25,32,33} The presence of pain, joint swelling and deformities, as well as functional disabilities and work or leisure restrictions in RA patients, could explain the higher number of depression cases. Functional disabilities result in reduction of self-confidence and QoL, leading to a depressive mood. Several authors attempted to correlate depression, anxiety and fatigue.^{25,34-36} Tack *et al.* found that in the RA population, higher fatigue was strongly associated with depressive symptoms, pain, and poorer overall mood.³⁶ A recent study by Munsterman *et al.* confirms earlier results that depressive symptoms are associated with fatigue.²⁷

We observed a moderate correlation of fatigue with QoL (SF-36) and functional capacity (HAQ DI), as presented in Fig. 2. Yacoub *et al.* report that fatigue was significantly associated with functional disability.³⁰ Pollard *et al.* found similar results with a significant relationship between fatigue and functional disability, suggesting that severe fatigue had a negative impact on patients QoL.³⁷ Thyberg *et al.* suggest that fatigue is related to physical aspects of disability such as pain, activity limitation and mental aspects, which may be a psychological reaction to physical disability.³¹ Each of these studies measures fatigue by different questionnaires, scales and methods, achieving results that are not directly comparable.

Regarding the application of FACIT-Fatigue as a specific instrument of fatigue evaluation in RA patients, these data showed consistency and significant correlation with other protocols (SF-36, HAD a/d, HAQ DI) demonstrated in Figs. 2 and 3, with significant values being observed in Table 2. These findings indicate that patient's complaint of fatigue is an independent data in the analysis of disease evolution.

We suggest a new significance for fatigue complaints in RA patients, which is an independent parameter that is not related to inflammatory activity. Fatigue appears to be related to the physical capacity and emotional symptoms associated with the negative effect of disability on the quality of life of some patients. Reports in the literature are conflicting, most likely because of the multifactorial etiology of fatigue and its correlation with physiological, psychological, social, personal and individual disease aspects, as well as the non-existence of a standardized evaluation method. These results emphasize the need for a better understanding of fatigue in RA patients with additional studies and an inclusion of standard measures for monitoring the symptoms and clinical management of fatigue. As recently recommended by OMERACT, psychological and psychosocial interventions, taking into account considerations that the

patient's perspective should be considered in studies and clinical practice to improve the results of treatment of fatigue.³⁸

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

- Alamanos Y, Voulgari PV, Drosos AA. Incidence and prevalence of rheumatoid arthritis, based on the 1987 American College of Rheumatology criteria: a systematic review. *Semin Arthritis Rheum.* 2006;36:182-8.
- Lee DM, Michael L. Weinblatt rheumatoid arthritis. *The Lancet.* 2001;358:903-9.
- Symmons DP, Barrett EM, Bankhead CR, Scott DG, Silman AJ. The incidence of rheumatoid arthritis in the United Kingdom: results of the Norfolk Arthritis Register. *Br J Rheumatol.* 1994;33:735-9.
- Hewlett S, Cockshott Z, Byron M, Kitchen K, Tipler S, Pope D et al. Patient's perception of fatigue in rheumatoid arthritis: overwhelming, uncontrollable, ignored. *Arthritis Rheum.* 2005;53:697-702.
- Wolfe F, Hawley DJ, Wilson K. The prevalence and meaning of fatigue in rheumatic disease. *Journal of Rheumatology.* 1996;23:1407-17.
- Carr A, Hewlett S, Hughes R et al. Rheumatology outcomes: the patient's perspective. *J Rheumatol.* 2003;30:880-3.
- Katz PP. The stresses of rheumatoid arthritis: appraisals of perceived impact and coping efficacy. *Arthritis Care Res.* 1998;11:9-22.
- Hewlett S, Carr M, Ryan S, Kirwan J, Richards P, Carr A. et al. Outcomes generated by patients with rheumatoid arthritis: how important are they? *Musculoskeletal Care.* 2005;3:131-42.
- Belza BL, Henke CJ, Yenli EH, Epstein WV, Gilliss CL. Correlates of fatigue in older adults with rheumatoid arthritis. *Nurs Res.* 1993;42:93-9.
- Golgenberg DL. Fatigue in rheumatoid diseases. *Bull Rheum Dis.* 1995;44:4-8.
- Belza BL. The impact of fatigue on exercise performance. *Arthritis Care Res.* 1994;7:176-80.
- Zigmund AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr.* 1983;67:361-70.
- Nikolaus S, Bode C, Taal E, van de Laar MA. Four different patterns of fatigue in rheumatoid arthritis patients: results of a Q-sort study. *Rheumatology.* 2010;49:2191-9.
- Nierengarten MB. ACR/ARHP Annual Meeting 2012: Fatigue for people with rheumatoid arthritis rooted in physiological and psychological factors. *The Rheumatologist.* march 2013.
- Ekdahl C, Andersson SI, Moritz V, Suensson B. Dynamic versus static training in patients with rheumatoid arthritis. *Scand J Rheumatol.* 1990;19:17-26.
- Semle EL, Loeser RF, Wise CM. Therapeutic exercise for rheumatoid arthritis and osteoarthritis. *Semin Arthritis Rheum.* 1990;20:32-40.
- Rall LC, Kehayinas JJ, Dawson-Hughes B, Roubenoff R. The effect of progressive resistance training in rheumatoid arthritis. Increased strength without changes in energy balance or body composition. *Arthritis Rheum.* 1996;39:415-426.
- Belza B. Comparison in self-reported fatigue in rheumatoid arthritis and controls. *J Rheumatol.* 1995;22:639-43.
- Davis MC, Okun MA, Kruszewski D, Zautra AJ, Tennen H. Sex differences in the relations of positive and negative daily events and fatigue in adults with rheumatoid arthritis. *J Pain.* 2010;11:1338-47.
- Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum.* 1988;31:315-24.
- Bruce B, Fries JF. The Stanford health assessment questionnaire: dimensions and practical applications. *Health Qual Life Outcomes.* 2003;1:20.
- Ferraz MB. Tradução para o português e validação do questionário para avaliar a capacidade funcional "Stanford health assessment questionnaire" [tese]. São Paulo: Universidade Federal de São Paulo, 1990.
- Ciconelli RM, Ferraz MB, Santos WS, Meinão I, Quaresma MR. Tradução para a língua portuguesa e validação do questionário genérico de qualidade de vida SF-36 (Brasil SF-36). *Rev Bras Reumatol.* 1999;39:143-50.
- Cella D, Yount S, Sorensen M, Chartash E, Sengupta N, Grober J. Validation of the functional assessment of chronic illness therapy fatigue scale relative to other instrumentation in patients with rheumatoid arthritis. *J Rheumatol.* 2005;32:811-9.
- Huysen BA, Parker JC, Thoreson R, Smarr KL, Johnson JC, Hoffman R. Predictors of subjective fatigue among individuals with rheumatoid arthritis. *Arthritis Rheum.* 1998;41:2230-7.
- Katz PP, Yelin EH. Prevalence and correlates of depressive symptoms among persons with rheumatoid arthritis. *J Rheumatol.* 1993;20:790-6.
- Munsterman T, Takken T, Wittink H. Low aerobic capacity and physical activity not associated with fatigue in patients with rheumatoid arthritis: a cross-sectional study. *J Rheumatol Med.* 2013;45:164-9.
- Instituto Brasileiro de Geografia e Estatística. Censo Demográfico 2010. Disponível em: www.ibge.gov.br/home/estatistica/populacao/censo2010/. Acesso em: 8 de abril de 2014.
- Bergman MJ, Shahouri SS, Shaver TS, Anderson JD, Weidensaul DN, Busch RE, et al. Is fatigue an inflammatory variable in rheumatoid arthritis? Analyses of fatigue in rheumatoid arthritis, osteoarthritis, and fibromyalgia. *J Rheumatol.* 2009;36:2788-94.
- Yacoub YI, Amine B, Laataris A, Wafki F, Znat F, Hajjaj-Hassouni N. Fatigue and severity of rheumatoid arthritis in Moroccan patients. *Rheumatol Int.* 2012;32:1901-7.
- Thyberg I, Dahlström Ö, Thyberg M. Factors related to fatigue in women and men with early rheumatoid arthritis: the Swedish TIRA study. *J Rehabil Med.* 2009;4:905-12.
- Dickens C, McGowan L, Clark-Carter D, Creed F. Depression in rheumatoid arthritis: a systematic review of the literature with meta-analysis. *Psychosom Med.* 2002;64:52-60.
- Dickens C, Creed F. The burden of depression in patients with rheumatoid arthritis. *Rheumatology.* 2001;40:1327-30.
- Zautra AJ, Yocum DC, Villaneuva I, Smith B, Davis MC, Attrep J, Irwin M. Immune activation and depression in women with rheumatoid arthritis. *J Rheumatol.* 2004;31:457-63.
- Repping-Wust H, van Riel P, van Achterberg T. Rheumatologist's knowledge, attitude and current management of fatigue in patients with rheumatoid arthritis (RA). *Clin Rheumatol.* 2008;27:1549-55.
- Tack BB. Self-reported fatigue in rheumatoid arthritis: a pilot study. *Arthritis Care Res.* 1990;3:154-7.

-
37. Pollard LC, Choy EH, Gonzalez J, Khoshaba B, Scott DL. Fatigue in rheumatoid arthritis reflects pain, not disease activity. *Rheumatology*. 2006;45:885-9.
38. Kirwan JR, Hewlett SE, Heiberg T, Hughes RA, Carr M, Hehir M et al. Incorporating the patient perspective into outcome assessment in rheumatoid arthritis-progress at OMERACT 7. *J Rheumatol*. 2005;32:2250-6.