Sleep quality and predictors of optimal sleep in patients with rheumatoid arthritis: data from a recent-onset cohort

G.A. Guaracha-Basáñez[1], I. Contreras-Yáñez[1], L.E. Bautista-Torres[2], A.B. Ortiz-Haro[1], V. Pascual-Ramos[1]

[1]Department of Immunology and Rheumatology, [2]Department of Internal Medicine, Instituto Nacional de Ciencias Médicas y Nutrición Salvador-Zubirán, Mexico City, Mexico.

Abstract

Objective

Sleep disorders are part of the symptomatology of rheumatoid arthritis (RA) patients and are related to disease characteristics and comorbidities. The study describes sleep quality among RA patients and identifies predictors of optimal sleep.

Methods

Patients whose data were analysed were identified from the recent-onset RA cohort initiated in 2004. In 2010, the Medical Outcome Study Sleep Scale (MOS-SS) was incorporated into the patients' assessments. Up to December 2019, the cohort comprised 187 patients with at least one MOS-SS application (in 78 patients at cohort entry) and six months of outcomes behaviour (cumulative) previous to the MOS-SS application: DAS28-ESR, pain-VAS, fatigue, HAQ-DI, SF-36, treatment (corticosteroids, DMARDs/patient and adherence), Charlson score, and major depressive episodes. A trained data abstractor retrospectively reviewed their charts. Multiple logistic regression analysis estimated odds ratios (95% confidence interval) to define baseline and cumulative variables predictive of optimal sleep (dichotomised variable derived from the quantity of sleep dimension of the MOS-SS).

Results

At the first MOS-SS application, patients were primarily middle-aged women with short disease duration and low disease activity. They scored higher on the "snoring" and "sleep non-adequacy" MOS-SS dimensions. There were 96 patients (51.3%) with optimal sleep. Lower baseline BMI, better baseline fatigue score, longer follow-up at the clinic, and better SF-36 physical summary score were predictors of optimal sleep (mental summary score also remained in the model when switched to the physical summary score).

Conclusion

Optimal sleep is achieved by half of the RA patients and predicted by BMI, patient-reported outcomes, and follow-up.

Key words

sleep quality, rheumatoid arthritis, Mexican patients

Guillermo A. Guaracha-Basáñez, MD, MSc
Irazú Contreras-Yáñez, MSc, PhD
Luis E. Bautista-Torres, MD
Ana B. Ortiz-Haro, MD, MSc
Virginia Pascual-Ramos, MD, PhD

Please address correspondence to:
Virginia Pascual-Ramos
Department of Immunology and Rheumatology, INCMyN-SZ,
Avenida Vasco de Quiroga 15,
Colonia Sección XVI,
Belisario Domínguez,
Tlalpan 14080,
Ciudad de México, México.
E-mail: virtichu@gmail.com
ORCID iD: 0000-0002-7368-498X

Received on January 7, 2023; accepted in revised form on April 26, 2023.

Competing interests: none declared.

Introduction

Rheumatoid arthritis (RA) is a worldwide chronic rheumatic disease characterised by pain, systemic inflammation, and extra-articular manifestations, which, if uncontrolled, might cause disability, reduced quality of life (QoL), and increased mortality (1).

Chronic medical illnesses can adversely affect sleep quality. Pain and inflammation can induce symptoms of excessive daytime sleepiness and fatigue, confirmed among patients with RA (2-5), who also have a high prevalence of sleep disturbances (4, 6). Zhang *et al*. (7) recently performed a systematic review and meta-analysis that included eight cross-sectional, case-control studies in RA patients and healthy controls (8-15); they showed that each domain of the Pittsburgh Sleep Quality Index (PSQI) was higher in RA patients than in healthy controls. Experimental observations have shown an alternative hypothesis where sleep disturbance activates clinical symptoms of pain, which then contributes to sleep loss and results in a vicious circle (16). Finally, in RA patients, sleep health has been associated with symptoms, disease activity/severity, functionality and QoL, mood disorders, disease-specific autoantibodies, perceived stress, and some treatments (3, 4, 10-13, 17-25).

Questionnaires are often the instrument of choice to assess sleep. Wells *et al*. (26) performed a systematic literature review and a patient perspective workshop on sleep to identify instruments assessing sleep quality that measure domains of sleep applicable to RA patients that were feasible and with appropriate psychometric properties. Four instruments were identified: the Athens Insomnia Scale, the Medical Outcome Study Sleep Measure/Scale (MOS-SS), the Pittsburgh Sleep Diary, and the Women's Health Insomnia Rating (26). A recent consensus report of a European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) combined committee examining outcome measures for assessing RA response to treatment recommends the study of sleep and disordered sleep (27). Meanwhile, longitudinal studies on sleep quality in RA patients are scarce, conducted in patients with substantial disease duration, or aimed to provide evidence for the therapeutic benefits of biologics (10, 16, 17, 18, 23, 24, 25). To complement the existing knowledge of the topic, the study aimed to describe sleep quality in patients with variable disease duration that belong to a recent-onset RA cohort (Objective 1), to identify predictors of optimal sleep (Objective 2), and to examine the relationship between sleep quality and patient-reported outcomes (PROs) behaviour at disease onset (Objective 3).

Materials and methods

Setting and study population: the recent-onset RA cohort

Patients whose data were analysed were identified from the early arthritis clinic of a national referral centre for rheumatic diseases located in Mexico City, the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMyN-SZ).

In 2004, we initiated a recent-onset dynamic RA cohort (28). Patients with symptoms of less than one year, at least one swollen joint, and non-specific rheumatic diagnosis at initial evaluation but with RA entered the cohort. From 2004 to 2010, ACR 1987 RA classification criteria were applied to all the patients, while ACR/EULAR 2010 RA classification criteria were incorporated from 2010 onwards (29).

At cohort inclusion, the primary rheumatologist recorded a complete medical history, demographic data, rheumatoid factor (RF), and anti-citrullinated protein antibodies (ACPA). At baseline and follow-ups, all the patients also had standardised rheumatic assessments, which included disease activity evaluation (66/68 swollen/tender joint counts, Disease Activity Score-28 joints evaluated by erythrocyte sedimentation rate (DAS28-ESR) (30), and Physician-overall disease evaluation), PROs, assessment of comorbidities (31) and major depressive episode (32), laboratory parameters and treatment evaluation. Laboratory parameters included, at minimum, blood biometry and chemistry, liver function tests, ESR, C-reactive protein, and urine analysis at every rou-

tine clinical assessment. Meanwhile, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, uric acid, and glycated haemoglobin were obtained every six months.

Since 2004, PROs have included disability as per the Health Assessment Questionnaire (HAQ-DI), QoL as per the Short-Form 36 (SF-36), pain (as per a pain-visual analogue scale [VAS], and overall disease status (overall-VAS) (33). Also, fatigue was assessed with the SF-36. In 2010, we incorporated the MOS-SS into PROs twice a year, and it has been applied once a year from 2019 onwards.

All the patients were assessed at baseline and then every two months during the first two years of follow-up. After that, visits were scheduled every two, four, or six months, depending on the patients and disease characteristics. Treatment was prescribed by the rheumatologist in charge of the clinic and was T2T oriented. Finally, hand and feet x-rays were scheduled at baseline and annually.

Study design and data collection

Up to December 2019, the cohort comprised 209 RA patients recruited from 2004 onwards. One hundred and ninety-four patients (92.8%) had at least one MOS-SS applied (at different follow-ups), and 187 patients had (at least) six months of outcomes behaviour previous a MOS-SS application; their data will be presented in the current study. Of them, ten (5.3%) patients were deceased, 41 (21.9%) were lost to follow-up, and 136 (72.7%) were currently active in the cohort (Fig. 1). We decided not to include patients' data corresponding to the 2020–2022 period, as early during 2020, the Mexican government declared our Institution a dedicated COVID-19 hospital, and visits to the outpatient clinic of the Department of Immunology and Rheumatology were interrupted and moved to phone medical consultations for at least six months.

Ending in 2019 and up to the last follow-up or death, all the charts were retrospectively reviewed by a trained data abstractor, who identified the first MOS-SS applied and corroborated the integrity of the data prospectively collected.

Sleep quality evaluation and definition of optimal sleep

The quality of sleep was assessed using the MOS-SS. It is a self-reported questionnaire integrated with 12 items regarding the patient's sleep over the last four weeks. MOS-SS scores six sleep dimensions as scales and two sleep problem indices (Table I). Dimensions were as follows: Sleep disturbance, daytime somnolence, snoring, awakening short of breath or with a headache, sleep adequacy, and quantity of sleep (which is the average number of hours spent asleep per night over the past four weeks). All items in the MOS-SS, except for the quantity of sleep, are given a numerical score, and the result is the sum of the individual scores, with the minimum value being 0 and the maximum 100. Higher scores indicate more of the named dimension, *i.e.* more sleep problems. The two indices – sleep problem indices I and II – are derived from several items, and as with dimensions, higher values indicate more sleep problems (4, 34).

Optimal sleep (dichotomised variable derived from the quantity of sleep) was defined when the reported duration of sleep/night was between 7 and 8 h (34).

Statistical analysis

Descriptive statistics were used with frequencies and percentages for dichotomous variables and mean ± standard deviation (SD) or median (interquartile range [IQR]) for continuous variables with normal and non-normal distribution, respectively.

The cumulative outcome behaviour (previous to the MOS-SS application) was restricted to six months. The following outcomes were considered: Disease activity (DAS28-ESR), pain (pain-VAS), fatigue (SF-36 corresponding component), disability (HAQ-DI), QoL (SF-36), treatment (corticosteroids use and the number of DMARDs/patient), persistence on therapy (29), comorbid conditions (Charlson score) and major depressive episodes (≥5 items from DSM-IV) (32). Cumulative outcomes behaviour (for continuous variables) was summarised as Area Under the Curve (AUC), calculated by the trapezoid method and presented standardised by the length of the study period evaluated (35). Dichotomous variables (prednisone use, persistence on therapy, and major depressive episodes) were summarised if present in the previous six months.

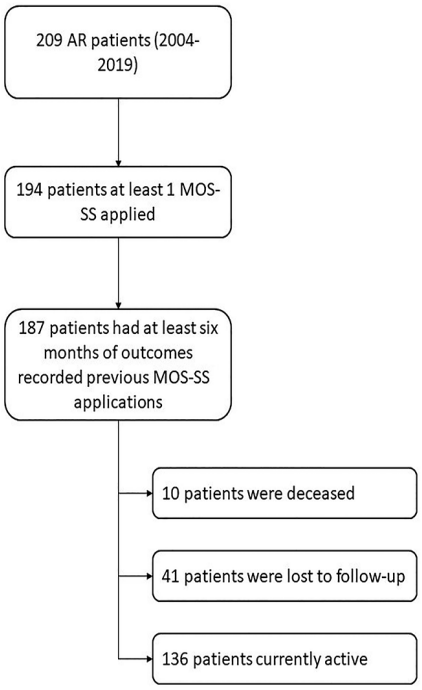

Fig. 1. Flowchart of patient cohort.

The patients' characteristics at cohort entry and cumulative previous MOS-SS application were compared among patients with and without optimal sleep using appropriate tests: The χ^2 test for the categorical variables and the Mann-Whitney U-test for continuous variables (non-normal distribution).

Multiple logistic regression analysis estimated odds ratios (ORs) (95% confidence interval [CI]) to define variables predictive of optimal sleep. We initially conceived a global model that considered variables at cohort entry (baseline) and cumulative variables (6 months of follow-up previous to MOS-SS application). Variables' inclusion was based on their statistical significance in the univariate analysis ($p \leq 0.05$) and clinical relevance. The variables finally included in the model were considered as simultaneous independent variables after collinearity was revised (variables were excluded if rho

Table I. Sleep quality description at first MOS-SS application.

Dimension scores (0-100, with higher scores indicating more of the named dimension)	n=187
Sleep disturbance (items 1, 3, 7, 8)	25 (10-42.5)
Daytime somnolence (items 6, 9, 11)	20 (13.3-33.3)
Snoring (item 10)	40 (0-60)
Awakening short of breath or with a headache (item 5)	0 (0-40)
Sleep (non)adequacy (items 4, 12)	40 (20-60)
Quantity of sleep, hours	7 (6-8)
Sleep problem indices I (items 4, 5, 7, 8, 9, 12)	26.7 (13.3-40)
Sleep problem indices II (items 1, 3, 4, 5, 7, 8, 9, 12)	26.7 (13.9-40)
Optimal sleep, number of patients (%)	96 (51.3)

Data presented as median (IQR) unless otherwise indicated.

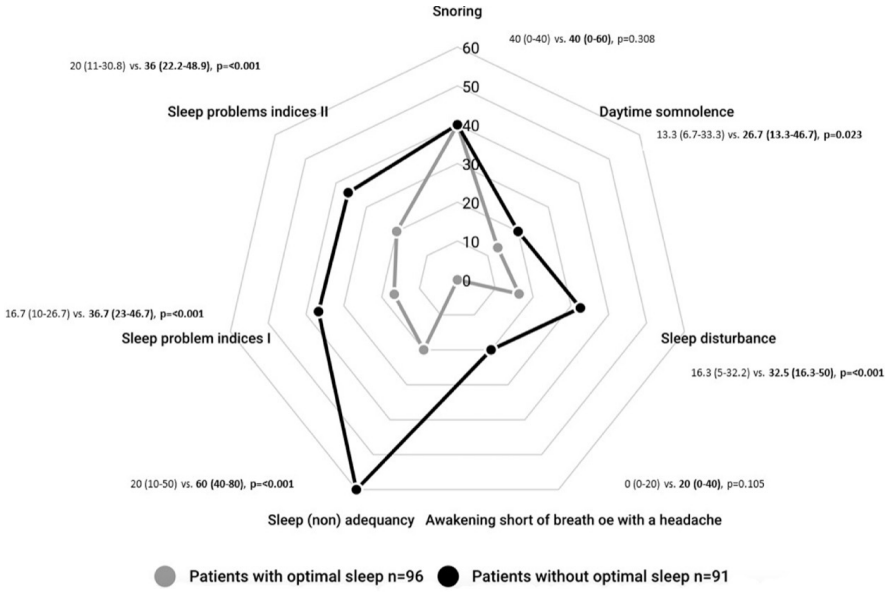

Fig. 2. Comparison of dimension and index scores between patients with optimal sleep and their counterparts.

>0.70). A test-based backward selection procedure defined the variables significantly associated with optimal sleep (dependent variable). The Nagelkerke R^2 test is reported as a measure of goodness of fit.

Finally, the Spearman correlation test was used to examine the relationship between sleep quality behaviour (MOS-SS dimension scores) and PROs behaviour in a subset of patients with five consecutive MOS-SS evaluations since RA diagnosis (up to two years of follow-up). Sleep quality dimensions and PROs behaviours were summarised as the mean of the respective consecutive scores.

Missing data were below 1.3%, and no imputation was performed.

All statistical tests were two-sided and evaluated at the 0.05 significance level. All analyses were performed using STATA (v. 16.0, Stata Corp LLC, College Station, TX) and SPSS (v. 21.0, IBM Corp., Armonk, NY, USA).

Ethics

The study was approved by the Institution's Internal Review Board "Comité de Ética del INCMyN-SZ" (IRE-274-10/11-1). Written informed consent was obtained from all patients.

Results

Characteristics of the study participants

In the study population (n=187), there were 78 patients (41.7%) in whom the first MOS-SS application coincided with clinical evaluation at cohort entry.

At first MOS-SS application, patients were primarily middle-aged (41 years of age [32–51.5]) females (n=164 [87.7%]) with short disease duration (1.01 years [0.19–2.34]) and overweight (Body Mass Index [BMI]: 26.71 kg/m^2 [23.9–29.9]). Few had erosive disease (n=42 [22.5%]), a coincident major depressive episode (3 [1.5%]), and additional comorbid conditions (Charlson score 1 [1–1]). Overall, patients had low disease activity (DAS28-ESR: 3 [2.2–4.9]), pain under control (pain-VAS: 7 [1–32]), and adequate function (HAQ-DI: 0.13 [0–1.13]), although fatigue was significant (62.5 [50–75]) and QoL was compromised (SF36 mental component score of 75 [55–90] and the physical component score of 70.5 [53–84.6]). Also, patients received corticosteroids (n=94 [48.5%]) and combined DMARDs (number of DMARDs/patients was 2 [1–2]), while persistence in therapy (the 83 patients with MOS-SS at baseline evaluation were excluded) was low n=62 [56.9%]).

At cohort inclusion (baseline evaluation), patients were middle-aged (38 years of age [28-49]), overweight (BMI: 26 [22.9–29]), married/living together (n=94 [45.8%]), had 12 years of formal education (9–15), and short symptom duration (5 months [3.2–6.8]). Menopause was present in 29 out of 171 females (17%). The majority had RF (n=161 [83.9%]) and ACPA (n=169 [87.6%]), while few had erosive disease (n=20 [10.7%]), a major depressive episode (n=29 [15.5%]), and additional comorbidities (Charlson score 1 [1–1]). Patients had high disease activity (DAS28-ESR: 5.7 [4.6–6.8]), which translated into pain (pain-VAS: 48 [28–72.5]), functional impairment (HAQ-DI score: 1.3 [0.75–2]), fatigue (50 [36–60]) and poor QoL (SF36 mental component score of 45 [30–60] and the physical component score of 40 [24–57]). Finally, 77 patients (41.2%) were already on corticosteroids and 112 (57.7%) on DMARDs; in these patients, the median DMARDs/patient was 1 (0–1).

Sleep quality description (Objective one)

Table I summarises the sleep quality results, with higher scores indicating more sleep problems. Overall, patients

scored higher on the "snoring" and "sleep non-adequacy" dimensions, followed by "sleep disturbance" and "Daytime somnolence" dimensions. In contrast, the "Awakening short of breath or with a headache" dimension received the lowest score. Overall, patients referred 7 hours (6–8) of sleep/night, and 96 patients (51.3%) were categorised with optimal sleep.

Figure 2 compares dimensions and indexes scores between patients with optimal sleep and their counterparts and highlights significantly lower scores among patients from the former group but for the snoring dimension score. Also, patients from the former group referred to 7 (7–8) sleep hours/ night, compared to 6 (5–6) hours/night in their counterparts.

Predictors of optimal sleep (Objective 2)

We first compared the patients' characteristics at cohort entry and cumulative previous MOS-SS data between patients with and without optimal sleep. The results are summarised in Table II. Briefly, at cohort inclusion, patients with optimal sleep (n=96) were younger, tested more frequently ACPA positive, had a lower BMI, and scored better on the fatigue dimension of the SF36 than their counterparts; in addition, female patients tended towards a lesser frequent menopause status. Regarding information at the MOS-SS application, patients with optimal sleep had longer follow-ups than their counterparts. Also, comparing cumulative outcomes behaviour between groups evidenced lower BMI and better scores on the DAS28, pain-VAS, HAQ-DI, SF-36 mental component summary, SF-36 physical component summary, and fatigue among patients with optimal sleep. Finally, these patients scored lesser frequently for a major depressive episode.

The global model considered baseline variables (age, ACPA status, BMI [highly correlated to cumulative BMI behaviour], and fatigue score [highly correlated to cumulative fatigue]), years of follow-up at MOS-SS application, and the following cumulative variables: major depressive episode, DAS28-ESR, pain-VAS (highly correlated to HAQ-DI-score) and SF-36 physical summary score (highly correlated to SF-36 mental summary score). This model considered data from 187 patients with (at least) six months of outcomes behaviour previous to a MOS-SS application, of whom 99 had an optimal sleep. Results are summarised in Table III. Lower baseline BMI, better baseline fatigue score, longer follow-up at the clinic, and better cumulative QoL (SF-36 physical summary score) were all predictors of optimal sleep (the SF-36 mental summary score remained in the model when switched to the SF-36 physical summary score). We repeated the global model and switched the BMI continuous variable to a variable that expressed a change in World Health Organisation (WHO) BMI-derived categories (healthy weight, overweight, and obesity [36]), and the results were similar. A change to a category with a higher BMI range (OR: 0.513, 95%CI:0.33–0.79, p=0.003), longer follow-up at the clinic (OR: 1.48, 95%CI:1.09–2.00, p=0.013) and better cumulative SF-36 physical summary score (OR: 1.02, 95%CI:1.01–1.04, p=0.013) were predictors of optimal sleep. At the same time, baseline fatigue showed a similar tendency (OR: 1.02, 95%CI:0.99–1.04, p=0.082).

Table II. Patients' characteristics at cohort inclusion and first MOS-SS between participants with/without optimal sleep.

	Patients with optimal sleep, n=96	Patients without optimal sleep, n=91	p-value
At cohort inclusion			
Years of age	35 (26-46.8)	40.4 (33-51)	0.010
Years of formal education	11 (9-13)	12 (9-16)	0.096
Female[1]	84 (87.5)	80 (88.4)	1
Patients married or living together[1]	47 (49)	42 (46.2)	0.770
Disease duration (months)	5.1 (3.2-7)	4.9 (3-6.9)	0.708
Patients with RF[1]	84 (87.5)	73 (81.1)	0.312
Patients with ACPA[1]	88 (92.6)	75 (82.4)	0.045
Patients with erosive disease[1]	11 (11.5)	9 (9.9)	0.815
Charlson score	1 (1-1)	1 (1-1)	0.661
Menopause status[1]	9 (10.7)	18 (22.5)	0.057
Patients with a major depressive episode[1]	12 (12.5)	17 (18.7)	0.313
Body Mass Index	24.8 (22-28)	27.3 (24-29.4)	0.003
DAS28-ESR	5.7 (4.5-6.8)	5.7 (4.5-6.8)	0.681
CRP, mg/dL	0.72 (0.29-2.38)	0.57 (0.18-2.45)	0.459
Pain-VAS (0-100)	48 (28.8-72.5)	48 (27-72.5)	0.975
HAQ-DI score (0-3)	1.25 (0.75-2)	1.38 (0.88-2.2)	0.648
SF-36 mental component summary (0-100)	48.5 (31.5-59)	43 (30-60)	0.292
SF-36 physical component summary (0-100)	40.5 (25.3-55)	40 (24-59)	0.670
Fatigue (0-100)	50 (40-63)	44 (35-60)	0.039
At MOS-SS application			
Years of age	42 (32.5-53)	40 (30.5-48.4)	0.251
Years of follow-up	1.69 (0.29-2.51)	0.28 (0.18-1.96)	0.003
Patients with erosive disease[1]	26 (27.1)	16 (17.6)	0.160
Charlson score[2]	1 (1-1)	1 (1-1)	0.752
Patients with a major depressive episode[1*]	13 (13.5)	24 (26.4)	0.042
Body Mass Index[2]	25.5 (22.6-29.1)	27.4 (24.7-30)	0.057
DAS28-ESR[2]	2.6 (2.1-3.3)	3 (2.1-4)	0.025
Pain-VAS[2]	5 (1-17.7)	12 (2-26.5)	0.016
HAQ-DI-score[2]	0 (0-0.6)	0.4 (0-7-0.8)	≤0.0001
SF-36 mental component summary[2]	83 (69.7-93.2)	71.7 (55.8-85.4)	≤0.0001
SF-36 physical component summary[2]	78.5 (68-5-87.4)	70.4 (53-79.7)	0.001
Fatigue[2]	70.7 (61.4-78.1)	62.5 (50-75)	0.002
Corticosteroids use[1*]	47 (49)	45 (49.5)	1
Number of DMARDs/patient[2]	2 (1-2)	2 (1-2)	0.085
Persistence on therapy[1*]	38 (39.5)	37 (40.7)	0.883

RF: rheumatoid factor; ACPA: anti-citrullinated protein antibodies; DAS: Disease Activity Score; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; VAS: visual analogue scale; HAQ: Health Assessment Questionnaire; SF: short form; DMARDs: disease-modifying anti-rheumatic drugs. Data presented as median (IQR) but [1]which represents the number (%) of patients. [2]AUC previous to MOS-SS application. *If ever present in the previous six months.

Table III. Multiple regression analysis to predict optimal sleep in the study population.

	OR	95% CI	*p*-value
Baseline BMI	0.897	(0.833-0.967)	0.005
Better baseline fatigue score	1.022	(1.002-1.042)	0.033
Longer follow-up at the clinic	1.575	(1.163-2.134)	0.003
Better cumulative SF-36 physical summary score	1.022	(1.003-1.041)	0.020

Nagelkerke R^2=0.210; OR: odds ratio; CI: confidence interval; BMI: Body Mass Index; SF: short form.

Table IV. Spearman correlations to examine the relationship between sleep quality and PROs behaviour.

	HAQ-DI score	Pain-VAS	Overall disease-VAS	Fatigue score	SF-36 score (EC)	SF-36 score (PC)
Sleep disturbance	0.125	0.206	0.285*	-0.473**	-0.357**	-0.338**
Daytime somnolence	0.193	0.244*	0.242*	-0.444**	-0.493**	-0.397**
Snoring	0.212	0.224	0.348**	-0.352**	-0.446**	-0.424**
Awakening short of breath or with a headache	0.190	0.252*	0.322**	-0.205	-0.287*	-0.260*
Sleep (non)adequacy	0.285*	0.143	0.159	-0.482**	-0.381**	-0.435**
Sleep problem indices I	0.240*	0.204	0.258*	-0.588**	-0.472**	-0.480**
Sleep problem indices II	0.270	0.213	0.278*	-0.574**	-0.455**	-0.455**

HAQ: Health Assessment Questionnaire; VAS: visual analogue scale; SF: short form; EC: emotional component; PC: physical component. *$p \leq 0.05$, **$p \leq 0.01$

Relationship between sleep quality and PROs (Objective 3)

Seventy-seven patients had five consecutive six-months-apart MOS-SS assessments and PROs behaviour since entry to the patient cohort (two years of follow-up). Table IV summarises the Spearman correlation between MOS-SS dimensions scores, MOS-SS indices scores, and PROs behaviour. Overall, sleep quality behaviour correlated with neither disability nor pain, while it showed a low correlation with patients' overall disease; meanwhile, moderate correlations were found with fatigue and the physical and emotional components of the SF-36.

Discussion

The current study involved patients from a well-characterised ongoing cohort of recent-onset RA. Patients received prospective evaluations of sleep health from 2010 onwards with a valid and reliable questionnaire to assess the construct in the target population. At the MOS-SS application, a significant proportion of the patients had achieved disease activity control after a T2T approach, translating into PROs characterised by pain control, absence of disability, and adequate QoL. This clinical context complements the current knowledge of the topic, mainly conceived from studies performed in patients with substantial disease duration and disease activity.

We observed that sleep quality was compromised, with the "snoring" and "sleep adequacy" dimensions scoring worse. Also, half of the patients (51.3%) were categorised with optimal sleep, which was predicted by lower patient baseline BMI, better baseline fatigue score, longer follow-up at the clinic, and better cumulative QoL. Finally, early during disease follow-up, sleep quality behaviour strongly correlated with fatigue and QoL.

Wolfe *et al*. (3) undertook a prospective study in 8676 RA patients, to whom the MOS-SS and a VAS-sleep scale were applied, to address sleep disturbances quantitatively. The study was performed on white USA patients not of Hispanic origin (92.7%), older than our patients, and with more pain, disability, and poorer QoL. Despite these differences, optimal sleep was found in 51.2%, with the average hours slept being 6.8/night (3). Similar to us, the MOS-SS dimensions scores were not uniform, with the "sleep adequacy" dimension scoring higher and the "awakening short of breath or with headache" dimension scoring lower. Grabovac *et al*. (20) detected optimal sleep in 43.2% of 95 RA patients from Vienna with a similar pattern in MOS-SS dimensions scoring. Our prevalence figure of optimal sleep follows studies and literature reviews that report sleep complaints and related symptoms in 52–81.5% of adult RA patients. In them, a wide range of sleep disturbances and alterations of sleep architecture are described (4-7, 10, 11, 18, 21), and the above studies have used additional (to the MOS-SS) tools to address sleep health.

The following variables were identified as predictors of optimal sleep: lower baseline BMI, better baseline fatigue score, longer follow-up, and better cumulative QoL.

Hamdi *et al*. (37) studied sleep characteristics in RA and knee osteoarthritis patients to determine the responsibility of disease activity in the occurrence of sleep disturbances, assessed with the MOS-SS. In RA patients, disease activity was a risk factor for sleep disturbances, while BMI significantly correlated with the MOS-SS snoring domain. Our finding might be particularly relevant considering that the prevalence of overweight and obesity has reached epidemic proportions. It is currently recognised that the growing rates of obesity have essential health consequences that extend to obesity-related respiratory disease (38, 39). Meanwhile, recent data suggest that short sleep duration and other dimensions of poor sleep are associated with obesity and appear to predict obesity risk and rate of weight gain longitudinally (38).

Previous publications had evidenced a (bidirectional) relationship between fatigue and sleep quality (6, 12, 16, 40-44). Following our results, Mahowald *et al*. (43) suggested that fatigue might manifest in sleep fragmentation in RA patients who had undergone polysomnography. Sariyildiz *et al*. (12) observed higher correlations between fatigue levels and sleep disturbance, evaluated with the PSQI. However, the logistic regression analyses indicated that depression and disease activity were the only predictors of poor sleep quality. Rodríguez-Muguruza *et al*. (45) described three stable fatigue trajectories (high, moderate, and low

fatigue) in 598 early RA patients who were followed for 120 months; they observed a linear relationship between fatigue level and sleep problems and increased risk of sleep problems among patients with high fatigue trajectories (*vs*. low fatigue trajectories patients). Interestingly, Katz *et al*. (46) recently identified the sources of fatigue in 158 RA patients with long-standing disease. In addition to disease activity, poor sleep, depression, and obesity were the primary predictors of fatigue and mediated the direct influence of inactivity on fatigue. These findings are inconsistent across studies (45), highlighting the complex interplay between sleep disturbances and RA characteristics, which might be sensitive to RA disease severity expression, disease duration, and comorbid conditions.

A longer follow-up has not been previously identified as a predictor of optimal sleep. We consider the result highly context-specific. In the recent-onset RA cohort, a longer follow-up summarises more visits and treatment adjustments according to a T2T approach. Consequently, (joint) inflammation is halted/reduced, which is more evident among patients persistent on therapy (28), and might result in less influence of some disease-related variables on sleep quality.

Previous studies have found pain/pain intensity (3, 5, 17, 18, 20), disease activity (3, 5, 10, 13, 18, 43, 47), flares (47), functional capacity (3, 7, 11, 17, 20), and mood disorders (3, 7, 10, 21, 48, 49) associated with sleep disturbances. We failed to demonstrate such associations, although our results might be due to our patient's characteristics at MOS-SS application with less disease activity and lower pain levels. Following our results, the association between health-related QoL and sleep disturbances has been previously reported. Guo *et al*. (10) used the PSQI in 131 RA patients and 104 controls and observed for the first time that sleep quality was independently and significantly associated with QoL, assessed with the SF-36.

Finally, we observed that early during disease follow-up, sleep quality behaviour showed the strongest correlation with fatigue (evaluated with SF-36) and QoL. There is a paucity of longitudinal studies on the relationship between PROs' behaviour and sleep quality behaviour (17, 18, 25). Drewes *et al*. (18) observed a relationship between pain and morning stiffness with sleep architecture. Nicassio *et al*. (17) confirmed that pain predicted subsequent adverse sleep outcomes. Threbarne *et al*. (25) found that self-reported frequency of sleep disruption related to perceived stress. Our results follow a recent literature review highlighting the relationship between poor sleep and poor health-related QoL (50). Also, QoL conceptualisation considers sleep and rest relevant facets.

Limitations of the study need to be addressed. First, the study was performed at a single academic centre and in a sample of patients with particular characteristics, limiting results generalisation. Second, sleep quality was assessed with a single instrument, while subjective and objective measures of sleep are important to fully understand sleep disturbances in adults with RA (6). Third, associated primary sleep disorders, including sleep apnea and periodic leg movement of sleep, were not investigated and are known to impair sleep health in RA patients (4). Fourth, we studied a limited number of variables associated with optimal sleep. Fifth, the MOS-SS refers to a time frame of the previous four weeks, and patients might be subject to information recall bias. Sixth, cohort studies have inherent biases, such as those related to losses to follow-up and the variability in assessment periodicity. Last, since cohort initiation in 2004, two different sets of RA classification criteria have been applied to patients, while the MOS-SS was incorporated into patients' assessments in 2011; however, we consider it might have little impact on our results as criteria for patients' cohort inclusion are not based on published RA classification criteria.

Considering the above, we may conclude that sleep deprivation and disturbances were frequent findings in Hispanic RA patients. A complex and dynamic interplay between the clinical aspects of RA and sleep quality has been described. In our study, optimal sleep was predicted by BMI, patient follow-up, fatigue, and QoL. Also, sleep impairment prevented optimal QoL early during disease follow-up. Rheumatologists' routine clinical assessments should incorporate sleep disturbances evaluation and tailor treatment strategies to reverse potential sleep pathology.

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