European Review for Medical and Pharmacological Sciences 2022; 26: 3212-3229

The impact of sleep disorders on the daily activity and quality of life in rheumatoid arthritis patients – a systematic review and meta-analysis

W. TAŃSKI[1], N. ŚWIĄTONIOWSKA-LONC[2], A. TOMASIEWICZ[3], K. DUDEK[4], B. JANKOWSKA-POLAŃSKA[2]

[1]Department of Internal Medicine, [2]Clinical Research Support Center, 4th Military Teaching Hospital, Wrocław, Poland
[3]Student Research Club of Surgical Specialties, Faculty of Medicine, Wrocław Medical University, Poland
[4]Wrocław University of Science Technology, Wrocław, Poland

Abstract. – OBJECTIVE: We aimed at determining the relationship between sleep disorders and daily activity and quality of life (QoL) of patients with rheumatoid arthritis (RA).

MATERIALS AND METHODS: A systematic search of databases was carried out. We used the Cochrane guidelines to perform the meta-analysis following the PRISMA statement. Fifteen full-text papers were ultimately included in the subsequent statistical analyses. The study was registered in the PROSPERO database (No. CRD42021245664).

RESULTS: In group 1, the mean sleep quality score measured with the Pittsburgh Sleep Quality Index (PSQI) was 6.93. The mean QoL score for the physical domain and the mental domain of the Short Form (36) Health Survey (SF-36) was 38.15 and 41.83, respectively. In group 2, the mean PSQI score was 7.21. The mean daily activity score measured with the Health Assessment Questionnaire (HAQ) was 0.80. A strong negative correlation was observed between the PSQI scores, and the SF-36 total score each unit increase in the SF-36 total score was associated with an average decrease of 0.35 points in the PSQI score. A one-point increase in the PSQI score was associated with an average decrease of 2.4 points in the QoL score measured with SF-36.

CONCLUSIONS: RA patients have a low quality of sleep. Sleep disorders correlate negatively with the QoL scores in the physical and mental domains.

Key Words:
Rheumatoid arthritis, Sleep disorders, Quality of life.

Abbreviations

AIS: the Athens Insomnia Scale; BDI: Beck Depression Inventory; CES-D: the Center for Epidemiologic Studies Depression Scale; CG: Control Group; CRP: C-Reactive Protein; DAS28: 28-joint Disease Activity Score; DMARD: Disease-Modifying Anti-Rheumatic Drugs; EBBS: Exercise Benefits and Barriers Scale; ESS: the Epworth Sleepiness Scale; HAQ: Health Assessment Questionnaire; HAQ-DI: Health Assessment Questionnaire-Disability Index; IG: Intervention Group; MFI: the Multidimensional Fatigue Inventory; mHAQ: Multidimensional Health Assessment Questionnaire; NSAIDs: Nonsteroidal Anti-Inflammatory Drugs; OA: Osteoarthritis; OSA: Obstructive Sleep Apnea; PHQ: Patient Health Questionnaire; PSQI: Pittsburgh Sleep Quality Index; QoL: Quality of Life; RA: Rheumatoid arthritis; RADAI: the Rheumatoid Arthritis Disease Activity Index; RADAR: the Rapid Assessment of Disease Activity in Rheumatology; RAQoL: the Rheumatoid Arthritis Quality of Life questionnaire; RDI: the Rheumatology Distress Index; RLS: Restless Legs Syndrome; SF-36 MCS: the Short Form (36) Health Survey mental component summary; SF-36 PCS: the Short Form (36) Health Survey physical component summary; VAS: Visual Analogue Scale; YDS: Yesavage Depression Scale.

Introduction

Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune, connective tissue disease. It causes functional limitations, disability and even a loss of full independence. RA affects 0.8% of the adult population in Europe[1]. The

Corresponding Author: Beata Jankowska-Polańska, MD; e-mail: bpolanska@4wsk.pl

prevalence of RA increased by 7.4% and its incidence increased by 8.2% globally between the 1990s and 2017[2]. Even at an early stage of the disease, typical muscular and joint symptoms can start to be accompanied by systemic symptoms. The latter, apart from the dominating joint and bone pain, also include sleep disorders[3]. RA patients have a significantly lower quality of sleep compared with healthy individuals[4]. Over 80% of RA patients experience sleep disturbances. These include increased sleep latency, multiple awakenings during the night and early morning awakening, which leads to excessive sleepiness during the day as well as fatigue[5,6]. Little is known about the pathogenesis of sleep disturbances. They may be primarily related to the underlying disease, or they may be caused by the treatment used. Various primary sleep disorders have been reported in patients with RA. The highly prevalent ones are obstructive sleep apnea (OSA), restless legs syndrome (RLS) and insomnia[7-9]. Some studies have reported a link between sleep and the immune system. Sleep disturbances and sleep deprivation result in increased plasma levels of pro-inflammatory cytokines, which increases inflammation and aggravates RA[7]. Sleep disturbances may contribute to increased plasma levels of C-reactive protein (CRP), interleukin 6 and TNF-α[8]. Increased inflammation levels have been reported in both short-term and chronic sleep deprivation. Therefore, it is vital that sleep disorders associated with RA are diagnosed and treated early. This will allow for better control of the disease and thus reduce the frequency and severity of RA flares. The muscle and joint pain associated with RA may increase sleep latency or prevent deep sleep, which most often results in fatigue after waking up in the morning and excessive sleepiness during the day[9]. RA patients describe the fatigue associated with their condition as overwhelming and distinct from normal fatigue. Fatigue results in increased pain intensity, has an impact on sleep and mood disorders, and leads to disability[10]. In studies using polysomnographic assessment, disease activity is associated with a decrease in sleep efficiency and in the amount of slow-wave sleep. It is also related to sleep fragmentation and an increase in the number of awakenings[10].

In many conditions, including RA, a vicious circle develops: pain makes sleeping difficult and sleep deprivation worsens or aggravates pain. Difficulty falling asleep and fatigue after sleeping are linked to a reduced pain threshold, increased pain intensity, depression and inflammation in RA patients[11].

It has been found that there is a relationship between low sleep quality and the stage of disease, pain and depression[4,5,7]. Furthermore, it is believed that sleep disorders, daily activity limitations and the symptoms associated with the underlying condition have a significant impact on quality of life and cognitive dysfunction. They are also thought to be linked to a higher risk of mortality in RA patients[12]. Moreover, RA patients report that they consider sleep problems to be of high personal importance.

In conclusion, sleep disorders are an important clinical problem in RA patients. However, the precise mechanisms underlying disease activity and sleep problems have not been identified. Similarly, there are few reports regarding the relationship between sleep disturbances and quality of life. It is vital that sleep disorders are properly diagnosed and treated, as they may aggravate the underlying condition. The aspect of treating sleep disorders should not be overlooked. The main role of pharmacological treatment of insomnia is to support non-pharmacological therapy, which is based on behavioral methods (sleep-restriction, stimulus-control). In addition to habit formation, non-pharmacological therapy usually emphasizes the importance of physical activity, which can be difficult to achieve in patients with RA[10].

The purpose of the study was to determine the prevalence of sleep disturbances and relationship between sleep disorders and physical daily activity (HAQ) and quality of life in RA patients.

Materials and Methods

Search Strategies

A systematic search of the PubMed, Scopus, MEDLINE, Academic Search Ultimate, CINAHL Complete and Health Source: Nursing/Academic Edition databases was carried out. The Cochrane guidelines were used to perform the meta-analysis following the PRISMA (Preferred Reporting Items for Systematic review and Meta-Analysis) statement[13].

During the search, we identified all published articles that investigated the issue of QoL in RA patients and used the term (rheumatoid arthritis [Title/Abstract] OR rheumatoid-arthritis [Title/Abstract] OR RA [Title/Abstract]) AND (sleep disorders [Title/Abstract] OR sleep distur-

bance [Title/Abstract] OR sleep disorder [Title/Abstract] OR sleep problem [Title/Abstract] OR insomnia [Title/Abstract]) AND (quality of life [Title/Abstract] OR wellbeing [Title/Abstract] OR well-being [Title/Abstract] OR health-related quality of life [Title/Abstract]) (665). The following search limits were used: "English" (language), "1 January 2010" and "31 December 2021" (date of publication) as well as "full text" (276) (Figure 1).

The following exclusion criteria were applied: review articles, case studies, meta-analyses, study protocols, no numerical data, studies on children, and duplicates. Relevant studies were then selected by 3 reviewers (WT, NŚL, BJP) for inclusion based on an examination of the remaining titles, abstracts and full papers (n = 15). The analysis took into account publication bias, duplication of publications and selective reporting as part of research. In order to ascertain the validity of eligible randomized trials, the reviewers worked independently. They determined the adequacy of randomization and concealment of allocation, as well as blinding of patients, data collectors and outcome assessors with adequate reliability. Any disagreements were resolved by consensus, which was reached through discussion. The meta-analyses were conducted by computing relative risks (RRs) using the random-effects model. Quantitative analyses were carried out on an intention-to-treat basis and were limited to data derived from the follow-up period. RRs and 95% confidence intervals were calculated for each type of intervention.

The first stage involved the identification of all records from searches of electronic databases. In the next stage, the titles and abstracts were screened independently by 3 researchers (WT, NŚL, BJP) in order to identify potentially eligible studies and to remove duplicates. In the third stage, potentially eligible studies were selected for full-text review. Any disagreements were resolved through discussion in order to reach consensus. Fifteen full-text papers were ultimately included in the subsequent statistical analyses (Figure 1, Table I). The authors made every effort to ensure that all basic studies that met the adopted criteria were included in the review. The quality of basic research was evaluated. It was assessed how many studies met the reliability criteria and to what extent. The selection and evaluation process of the basic research was repeated.

The study was registered in the PROSPERO database (No. CRD42021245664).

Data Extraction

Once an initial database was developed, it was pilot-tested and refined in order to ensure consistency with the outcomes reported in the literature. Data were extracted from eligible articles

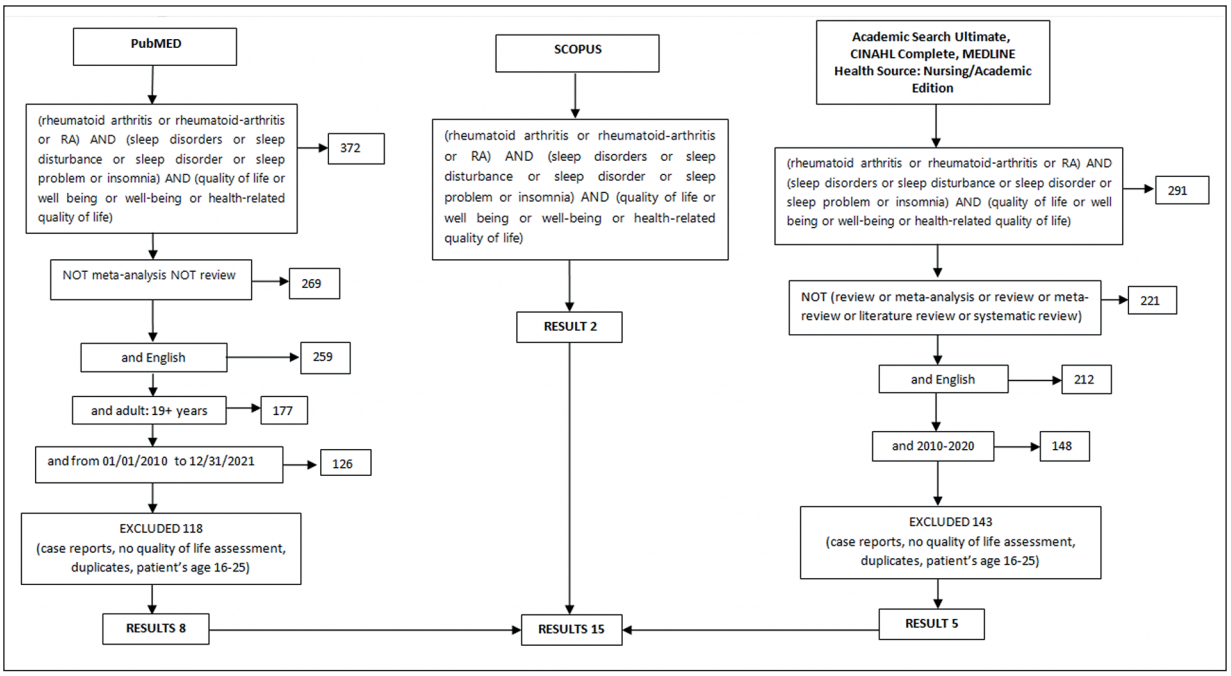

Figure 1. Study flow diagram.

Table I. Summary of studies on QoL and daily activity in RA patients with sleep disturbances.

No.	Author and year	Study group	Study design	Questionnaire used to assess 1) QoL 2) sleep disturbances 3) daily activity	Main results	Intervention	Factors decreasing QoL	Factors increasing QoL
1.	Nicassio et al[14]	106 RA patients (83% females), mean age 56.09 ± 12.45 years, illness duration 11.23 years	An observational, cross-sectional study	1) SF-36 2) PSQI	A correlation analysis showed the following: RADAR total joint (-0.381), RADAR disease (-0.411), CES-D total (-0.357), perceived stress scale Total (0.318), PSQI Sleep efficiency (-0.212), PSQI daily disturbances (-0.544)	No	Low disease activity, depression, perceived stress, sleep disturbances	– -
2.	Taylor-Gjevre et al[15]	270 patients (145 RA and 78 OA), the mean age of RA patients was 54.21 ± 15.72, 88% female	A self-administered questionnaire study	1) SF-36 2) ESS 3) mHAQ, VAS	RADAI 3.7 ± 2.25 RLS 0.27 Berlin high risk OSA 0.39 VAS 4.39 ± 2.71 Fatigue 4.77 ± 3.0 Global function 6.65 ± 2.58 Stress 6.41 mHAQ 12.65 ± 4.36 SF-36 PCS 35.7 ± 10.77 SF-36 MCS 50.18 ± 11.04 CES-D 14.06 ± 10.69 ESS 7.09 ± 4.59	No	Sleep disturbances	-

Continued

Table I ***(Continued).*** Summary of studies on QoL and daily activity in RA patients with sleep disturbances.

No.	Author and year	Study group	Study design	Questionnaire used to assess 1) QoL 2) sleep disturbances 3) daily activity	Main results	Intervention	Factors decreasing QoL	Factors increasing QoL
3.	Gjevre et al[16]	25 RA patients (including 7 men), divided into two groups: • I - ESS > 10 (n = 10 mean age 58.2 ± 7.63 years); • II - ESS ≤ 10 (n = 15; mean age 61.8 ± 11.07 years)	a case-control study	1) SF-36 2) PSQI 3) mHAQ	I. VAS 5.16 ± 2.88 atigue 6.25 ± 3.79 fglobal function 7.19 ± 2.72 RADAI 5.18 ± 2.19 mHAQ 14.70 ± 3.89 SF-36 PCS 33.62 ± 7.52 SF-36 MCS 49.72 ± 9.74 high risk of OSA 80% PSQI 9.30 ± 4.24 CES-D 15.80 ± 8.35 stress 6.70 ± 2.31 II. VAS 3.73 ± 2.39 fatigue 3.64 ± 2.71 global function 7.72 ± 1.59 RADAI 3.41 ± 2.06 mHAQ 9.87 ± 2.64 SF-36 PCS 39.32 ± 10.07 SF-36 MCS 55.98 ± 6.81 high risk of OSA 7% PSQI 7.33 ± 3.68 CES-D 6.93 ± 5.65 stress 5.13 ± 2.23	No	Poor sleep quality	-

Continued

Table I *(Continued)*. Summary of studies on QoL and daily activity in RA patients with sleep disturbances.

No.	Author and year	Study group	Study design	Questionnaire used to assess 1) QoL 2) sleep disturbances 3) daily activity	Main results	Intervention	Factors decreasing QoL	Factors increasing QoL
4.	Taylor-Gjevre et al[17]	423 patients (26% male) aged 52.07 ± 16.31, including 145 RA patients, 93 patients with seronegative arthritis, 78 with OA and crystalline 61 with connective tissue diseases and 46 with soft tissue musculoskeletal disorders. The patients were divided into two groups depending on the ESS score: • I: ESS ≥ 11 (n = 106, 30% male, aged 51.08 ± 14.09) • II: ESS ≤ 10 (n = 306, 25% male, aged 52.32 ± 16.92)	A comparative study	1) SF-36 2) PSQI, ESS 3) mHAQ	I. PSQI 10.33 ± 3.55 mHAQ 13.47 ± 3.98 SF-36 PCS 33.25 ± 10.39 SF-36 MCS 45.80 ± 12.65 pain 45.48 ± 2.7 fatigue 6.91 ± 2.44 CES-D 19.16 ± 10.62 II. PSQI 7.33 ± 4.13 mHAQ 10.91 ± 3.52 SF-36 PCS 39.29 ± 10.94 SF-36 MCS 51.50 ± 10.20 pain 3.87 ± 2.93 fatigue 4.25 ± 3.09 CES-D 12.42 ± 9.61	No	Poor sleep quality	-

Continued

Table I ***(Continued).*** Summary of studies on QoL and daily activity in RA patients with sleep disturbances.

No.	Author and year	Study group	Study design	Questionnaire used to assess 1) QoL 2) sleep disturbances 3) daily activity	Main results	Intervention	Factors decreasing QoL	Factors increasing QoL
5.	Albayrak Gezer et al[18]	136 patients with RA were divided into 2 groups depending on age: • I: ≥ 65 (n = 52), mean age 67.69 ± 4.33, 14.5% male, median disease duration - 120 months, 94.2% treated with DMARDs, 5.8% treated with TNF-alpha blockers • II: < 65 (n=84), mean age 45.71 ± 10.46, 21.4% male, median disease duration - 72 months, 88.1% treated with DMARDs, 11.9% treated with TNF-alpha blockers	A cross-sectional study	1) SF-36 2) PSQI	I. PSQI 7.07 ± 4.21 VAS 4.42 ± 2.23 BDI 16.44 ± 9.39 II. PSQI 5.01 ± 2.89 VAS 3.32 ± 1.92 BDI 12.17 ± 7.24	No	Poor sleep quality	-
6.	Løppenthin et al[19]	443 patients with RA, 20% male, mean age 60 years, disease duration (median) 11 years, divided into 2 groups depending on physical activity: • I. regular (n = 96) • II. low (n = 342)	A cross-sectional study	1) - 2) PSQI 3) HAQ	I. MFI general 12.0 [8.7-15.0] PSQI 6.0 [4.0-10.0] DAS28 2.25 [1.8-2.9] patient global assessment 29 [7.5-4.7] VAS 1.7 [5.0-3.95] HAQ 0.37 [0-0.8] II. MFI general 15.0 [12.0 -18.0] PSQI 7.0 [4.0-10.0] DAS28 2.25 [2.0-3.7] patient global assessment 39.5 [16-68] VAS 3.1 [14.0-61.0] HAQ 0.87 [0.4-1.4]	No	Pain, sleep disturbances, depression, higher RDI	-

Continued

Table I *(Continued)*. Summary of studies on QoL and daily activity in RA patients with sleep disturbances.

No.	Author and year	Study group	Study design	Questionnaire used to assess 1) QoL 2) sleep disturbances 3) daily activity	Main results	Intervention	Factors decreasing QoL	Factors increasing QoL
7.	Katz et al[20]	158 RA patients, mean age 59.2 ± 11.3, 15.2% male, RA duration 21.1 ± 12.5 years, treatment: glucocorticoid use 72%, biologic agent use 50.6%	A cross-sectional study	1) - 2) PSQI 3) HAQ	HAQ 0.90 ± 0.72 PSQI 8.4 ± 3.8 PHQ 4.7 ± 4.8	No	High CRP levels, prednisolone use, fitness (resting heart rate), low sleep quality, depressive symptoms, obesity, physical inactivity	Muscle weakness, lean to fat mass ratio
8.	Fragiadaki et al[21]	15 RA patients (2 men), mean age 48.0 ± 6.54 years, disease duration 8.4 ± 6.54 years	A clinical trial	1) - 2) PSQI, ESS 3) HAQ	The following was observed: statistically significant improvement in PSQI score from baseline to 6 months (from 7.5 ± 2.3 to 6.8 ± 2.5, $p = 0.005$), significant decrease in daytime sleepiness (ESS score decreased from 6.9 ± 4.8 to 5.5 ± 4.5 in 1 month, $p = 0.01$) decrease in HAQ-DIscore from baseline (1.5 ± 0.8) to 6 months (0.7±0.6) as well as a decrease in DAS28 from baseline (5.77 ± 1.2) to 2.5 ± 0.9 after 6 months	6 monthly infusions of tocilizumab 8 mg/kg		Treatment with tocilizumabat a dose of 8 mg/kg
9.	Westhovens et al[22]	305 RA patients, mean age 57.0 ± 12.38, disease duration 11.77 ± 9.94 years, treatment: 56.4% conventional DMARDs only, 43.6% biologic DMARDs, 45.8% lucocorticoids	An observational cross-sectional multicenter study	1) SF-36 2) PSQI, ESS 3) HAQ	VAS 39.04 ± 26.21 VAS fatigue 45.22 ± 26.29 DAS28-CRP 3.54 ± 1.5 PSQI 7.8 ± 4.3 ESS 39.04 ± 26.21 HAQ-DI 1.08 ± 0.75 SF-36 general health 14.75 ± 3.89	No	Insomnia	-

Continued

Table I ***(Continued).*** Summary of studies on QoL and daily activity in RA patients with sleep disturbances.

No.	Author and year	Study group	Study design	Questionnaire used to assess 1) QoL 2) sleep disturbances 3) daily activity	Main results	Intervention	Factors decreasing QoL	Factors increasing QoL
10.	Løppenthin et al[23]	384 RA patients, 20% male, 48% were < 60 years old	A cross-sectional study	1)- 2) PSQI 3) HAQ	VAS 2.8 [1.1-5.5] DAS-28 2.6 [1.9-3.5] HAQ 0.75 [0.25-1.25] general fatigue 13.67 ± 4.62 PSQI 7.54 ± 4.17	No	Sleep disturbances	-
11.	Guo et al[24]	IG: 131 RA patients (19 male), mean age 54.5 ± 11.5 years, RA duration 8.7 ± 9.1 years, DMARD use 98.5% CG: 104 persons (15.4% male), mean age 54.77 ± 11.2 years	A cross-sectional study	1) SF-36 2) PSQI	PSQI 7.93 ± 3.98 the group was divided into 2 sub-groups depending on the PSQI score: I. PSQI < 5 (n = 28); SF-36 PCS 49.30 ± 20.27, SF-36 MCS 66.33 ± 22.72 II. PSQI ≥ 5 (n = 103); SF-36 PCS 38.68 ± 19.95, SF-36 MCS 49.30 ± 20.27 PSQI 3.88 ± 1.89	No	Poor sleep quality	-
12.	Kim et al[25]	IG: 123 RA patients, aged 56 [47-61] years, RA duration 113 [68-199] months. Medication used: 52% NSAIDs, 27.6% biologics	A case-control study	1) SF-36 2) PSQI	IG: DAS28-ESR 2.69 [2.2-3.11] PSQI 5 [3-6.75] SF-36 PCS 44.61 [37.52-50.43] SF-36 MCS 49.14 [41.96-54.8] PSQI 7 [5-11] SF-36 PCS 50.54 [45.11-54.16] SF-36 MCS 53.23 [44.69-57.29]	No	Low quality of sleep, cognitive dysfunction, high disease activity	-
		CG: 76 persons aged 54 [45-61]						

Continued

Table I *(Continued)*. Summary of studies on QoL and daily activity in RA patients with sleep disturbances.

No.	Author and year	Study group	Study design	Questionnaire used to assess 1) QoL 2) sleep disturbances 3) daily activity	Main results	Intervention	Factors decreasing QoL	Factors increasing QoL
13.	Durcan et al[26]	IG: 40 RA patients (25% male), mean age 61 ± 8, disease duration 11 ± 11.2 years CG: 38 RA patients (47.4% male) aged 59 ± 12 years, disease duration 16 ± 10.9 years	A randomized controlled study	1) - 2) PSQI 3) HAQ	IG: HAQ 0.8 ± 0.4 VAS 29 ± 21.5 PSQI 7.2 ± 4.4 EBBS 125.8 ± 5.5 CG: HAQ 0.9 ± 0.4 VAS 41.4 ± 25.5 PSQI 5.6 ± 5.2 EBBS 126 ± 3.0 After 12 weeks, a significant improvement in quality of life, pain intensity, joint stiffness, fatigue levels and sleep quality was observed both in the intervention group and in the control group.	12-week home exercise program (resistance exercise 3 times per week)	-	Regular physical activity
14.	Elazeem and Salem[27]	IG: 100 RA patients (16 males), mean age 48.1 ± 12.4 years, disease duration of 6.9 ± 5.9 years CG: 40 persons (6 males) aged 42.4 ± 12.4 years	A cross-sectional study	1) SF-36 2) PSQI, ESS, AIS 3) HAQ	IG: PSQI 6.98 ± 2.8 AIS 9.6 ± 4.4 ESS 7.4 ± 2.6 CG: PSQI 2.6 ± 1.9 ESS 3.3 ± 2.03	No	High ESS, AIS and PSQI scores	-
15.	Pehlivan et al[28]	182 RA patients, divided into 2 groups: • adult (n=99, 19 male patients; 22.9% male) diagnosed with RA. • elderly (n =83), 15 15 male Drug groups used: • adult: DMARDs 30.3%; anti-TNF 69.7%; steroid 77.8% • elderly: DMARDs 44.6%; anti-TNF 55.4%; steroid 75.9%	A cross-sectional and observational study	1) - 2) PSQI 3) HAQ	Adult: VAS 52.2 ± 24.1 HAQ 0.7 ± 0.5 PSQI 5.9 ± 3.4 elderly: VAS 60.6 ± 23.7 HAQ 1.1 ± 0.8 PSQI 7.2 ± 4.0	No	Poor sleep quality	-

independently by two reviewers. Discrepancies between the reviewers regarding data extraction were resolved by consensus.

The following information was extracted from each included trial: (1) characteristics of trial participants (including age, gender as well as the stage and severity of disease), the trial's inclusion and exclusion criteria; (2) type of intervention; (3) type of outcome measure, improvement in quality of life score (using a validated scale), factors affecting quality of life, length of follow-up. The risk of bias was determined using the Newcastle-Ottawa scale.

Definitions and Outcomes

The main outcomes of interest for the review were: (1) the prevalence of sleep disturbances and sleep quality; (2) influence of sleep disturbances on QoL and physical daily activity.

Questionnaires Used to Assess QoL, Health, and Sleep Quality

The Short Form (36) Health Survey (SF-36) is a 36-item questionnaire designed to assess patient health. The original version of the questionnaire was developed in the Medical Outcome Study (MOS). The SF-36 consists of eight domains: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning and mental health. Responses for each domain are converted into scores on a 0-100 scale. All items are assigned the same weight. The higher the score, the better a patient's quality of life[14].

The Pittsburgh Sleep Quality Index (PSQI) is used to measure sleep quality over the past month. It consists of 19 items across 7 components, which produce a global score. The PSQI measures several different aspects of sleep: subjective sleep quality, sleep latency, duration of sleep, habitual sleep efficiency (i.e., the percentage of time in bed that one is asleep), sleep disturbances, use of sleeping medication, and daytime dysfunction. Each item is weighted on a 0-3 interval scale. A global PSQI score is then derived by adding up the seven component scores. This yields an overall score ranging from 0 to 21, where lower scores denote a better quality of sleep[15].

The Health Assessment Questionnaire (HAQ) is used to evaluate the long-term effects of a chronic illness on a patient's life. The HAQ was developed to enable a comparison of the degree of improvement at particular treatment stages in patients with rheumatic conditions. The HAQ is a tool which evaluates the impact of disease symptoms on the life and functioning of a patient in five main dimensions: death, disability, drug side effects, discomfort and economic costs. The questionnaire consists of 20 questions divided into 8 sections. The patient is asked to rate, on a 4-point scale, their difficulty in performing the activities described. The scores for the 8 sections are then summed and divided by 8. The final score ranges between 0 (no functional impairment) and 3[16].

Statistical Analysis

Correlations between quality of life (SF-36) and sleep disorders (PSQI) were analyzed using Spearman's rank correlation coefficients (*rho*) and significance levels (*p*-value). A meta-analysis was used to synthesize the available research results on the relationship between sleep disorders and quality of life. Since the studies present the data as correlations, the same correlation coefficient was used as effect values. The correlation was transformed using the Fisher's *z* transformation and the analysis was performed using this index. Then the totals were converted back to a correlation for presentation. Calculations were performed using STATISTICA v.13.3 (TIBCO Software Inc.).

Considering the questionnaire used, patients were divided into 2 groups for statistical analysis: group 1 included patients examined with the SF-36 questionnaire (n = 1177), while group 2 included patients examined with the HAQ questionnaire (n = 975).

Results

The meta-analysis focused on quality of life in the 2507 RA patients with sleep disturbances studied (Table I)[17-32]. Male patients comprised 26.1% of the groups analyzed.

Description of the Studies

The 15 studies included in our meta-analysis were conducted in 10 countries on 3 continents. The meta-analysis included research papers in English published between 2010 and 2021 in one of the databases listed above. Another in-

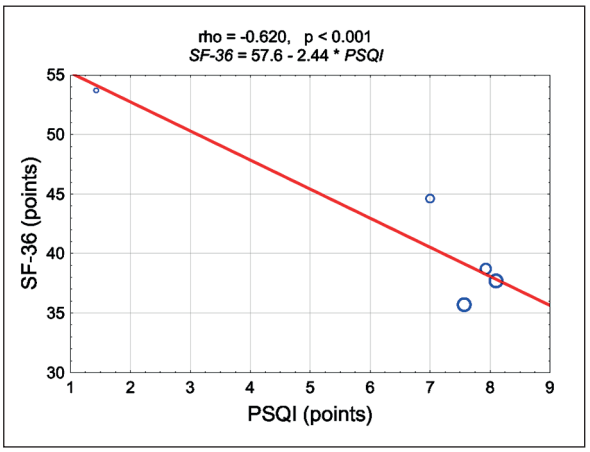

Figure 2. Correlation diagram between sleep disturbances (PSQI) and quality of life (SF-36 total scores) in a group. SF-36: Short Form Health Survey; PSQI: Pittsburgh Sleep Quality Index.

clusion criterion was the use of one of the following questionnaires designed to evaluate QoL and functional status: the Short Form (36) Health Survey (SF-36) and the Health Assessment Questionnaire (HAQ). Studies on children, review articles, other meta-analyses, duplicates, and study protocols as well as studies with incomplete data were excluded from the meta-analysis.

Sleep Quality According to PSQI (Prevalence of Sleep Disturbances)

Sleep quality in the study group was assessed using the PSQI in 9 articles. The lowest PSQI scores, i.e., the most severe sleep disturbances, were found in patients in the study by Nicassio et al[32], whereas the best quality of sleep was observed in patients in the study by Gjevre et al[19] (1.43 *vs.* 9.30).

Analysis of the Correlation between Sleep Disturbances and QoL

A strong negative correlation was observed between the PSQI scores and the SF-36 total scores (Figure 2). The correlation works in both directions. Each unit increase in the SF-36 total score is associated with an average decrease of 0.35 points in the PSQI score: PSQI = 21.0 - 0.35 * SF-36. A one-point increase in the PSQI score is associated with an average decrease of 2.4 points in the SF-36 total score.

Correlation Between Quality of Life, Daily Activity and Sleep Quality – Meta-Analysis

An analysis of 9 articles containing information on sleep quality (as assessed using the PSQI) and quality of life in the physical (SF-36 PCS) and mental (SF-36 MCS) domains was carried out (Table II). The studies related to 1177 RA patients (group 1). In this group, the mean sleep quality score on the PSQI was 6.93, whereas the mean quality of life score for the physical domain and the mental domain was 38.15 and 41.83, respectively.

The linear correlation coefficients between the PSQI scores and the SF-36 PCS scores related to

Table II. Results of a correlation analysis for quality of life (SF-36), daily activity (HAQ) and sleep quality (PSQI).

Study	N	PSQI	SF-36 PCS	SF-36 MCS	rPSQI *vs.* PCS	rPSQI *vs.* MCS	HAQ	rPSQI *vs.* HAQ
Nicassio et al[14]	106	2.43	53.73	-	-0.544	-	-	-
Taylor-Gjevre et al[15]	145	7.57	35.70	50.18	-0.174	-0.302	-	-
Albayrak Gezer et al[18]	52	7.07	44.56	46.81	-0.431	-0.206	-	-
Albayrak Gezer et al[18]	84	5.01	46.74	49.33	-0.477	-0.022	-	-
Westhovens et al[22]	305	7.80	21.90	17.45	-	-	-	-
Guo et al[24]	131	7.93	38.68	49.30	-0.204	-0.158	-	-
Guo et al[24]	131	7.93	56.63	66.33	-0.204	-0.158	-	-
Kim et al[25]	123	7.00	44.61	49.14	-0.211	-0.341	-	-
AbdElazeem and Salem[27]	100	6.98	31.40	44.30	-0.740	-0.300	-	-
Løppenthin et al[19]	100	7.00	-	-	-	-	0.87	-
Løppenthin et al[19]	96	6.00	-	-	-	-	0.37	-
Katz et al[29]	158	8.40	-	-	-	-	0.90	0.549
Fragiadaki et al[21]	15	7.50	-	-	-	-	1.50	0.600
Løppenthin et al[23]	384	7.54	-	-	-	-	0.75	-
Durcan et al[26]	40	7.20	-	-	-	-	0.80	-
Pehlivan et al[28]	99	5.90	-	-	-	-	0.70	0.426
Pehlivan et al[28]	83	7.20	-	-	-	-	1.10	0.403

only 872 patients, whereas the linear correlation coefficients between the PSQI scores and the SF-36 MCS scores related to only 766 patients (Figure 3).

Correlation Between Physical Daily Activity and Sleep Quality PSQI v HAQ – Meta-Analysis

An analysis of 8 articles containing information on sleep quality (as assessed using the PSQI) and physical daily activity (as assessed using the HAQ) was carried out (Table III). The studies related to 975 patients (group 2). In this group, the mean sleep quality score on the PSQI was 7.21, whereas the physical daily activity score on the HAQ was 0.80. The linear correlation coefficients between the PSQI scores and the HAQ scores related to only 355 patients (Figure 4).

Discussion

Our analysis confirmed the main outcomes of interest for the review. Firstly, as researchers report, sleep disorders are very common in RA patients. Secondly, sleep disorders have a significant impact on the quality of life and experience in this group of patients. Our meta-analyses demonstrated a relationship between sleep disorders and daily activity and quality of life (QoL) inpatients with RA. The literature indicates that chronic insomnia increases the risk of mortality, morbidity and healthcare use. Pharmacological interventions aimed at improving sleep quality have been found to have short-term efficacy. However, their long-term usefulness is limited by increased mortality, dependency, and rapid development of tolerance[33].

Additionally, our meta-analysis showed that there is a strong relationship between sleep disturbances, physical disease activity and quality of life[14,17-23,25-28,31,33]. The tools included in our study were reproducible and standardized questionnaires for the assessment of sleep disorders and quality of life. In the studies included in the meta-analysis, sleep disorders were most frequently assessed using the PSQI, whereas QoL was most frequently assessed using the SF-36. SF-36 is considered a reliable and valid tool for measuring health-related quality of life. It allows for a comparison of patient HRQoL to that of the healthy population[28].

The few available studies on the subject indicate a relationship between sleep disorders and QoL[28,34], as well as a link between underlying daily activity and QoL. Kim et al[28] found that sleep disorders have a strong significant impact on the physical component (PCS) of HRQoL, especially as regards the role physical, bodily pain and general health dimensions. Naturally, in this case, the authors also stress that sleep quality is closely associated with bodily pain and daily functioning[28]. It should be emphasized that the

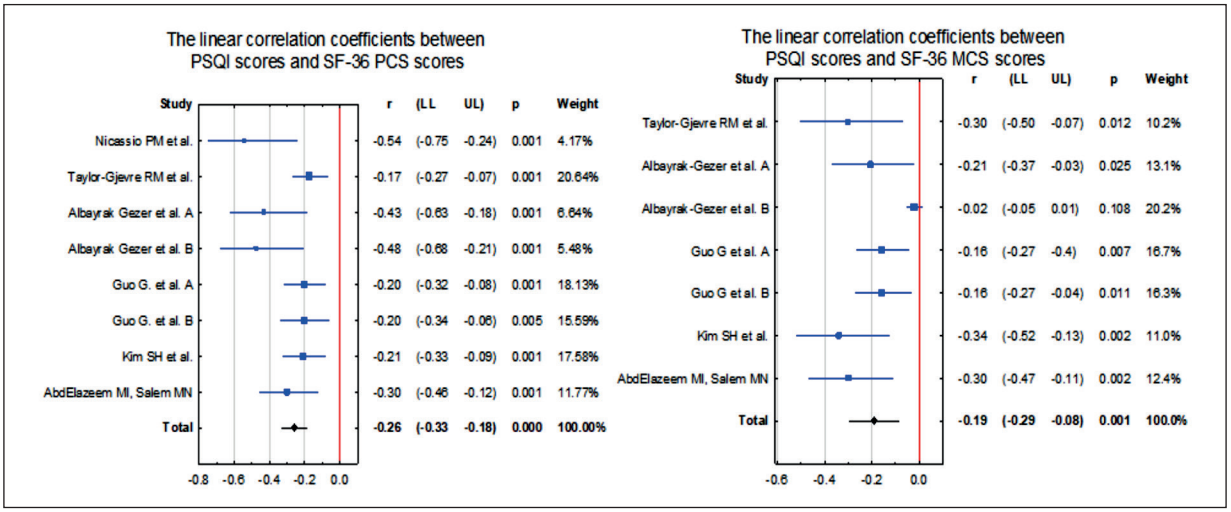

Figure 3. Correlation coefficient values between sleep quality (PSQI) and quality of life in the physical (SF-36 PCS) and mental domain (SF-36 MCS) and their 95% confidence intervals.
SF-36: Short Form Health Survey; PCS: physical domain; MCS: mental domain; PSQI: Pittsburgh Sleep Quality Index; LL: lower limit of the confidence interval; UL upper limit of the confidence interval.

Table III. Inclusion and exclusion criteria of the qualified studies.

	Criteria
Inclusion	Diagnosis of RA based on the ACR/EULAR 2010 criteria informed consent age ≥18 years not being pregnant currently being treated with disease-modifying anti-rheumatic drugs (DMARDs) or biologics female gender stable disease - modifying drug regimen for 3 months prior to entry into the study stable course of disease for 3 months sleep disturbances (the Pittsburgh Sleep Quality Index score ≥ 5) moderately or severely active RA [28-joint Disease Activity Score-erythrocyte sedimentation rate (DAS28-ESR) > 3.2] fulfilment of the center's predefined disease activity criteria ability to communicate, admission to the clinic during the study period
Exclusion	Current or previous history of other systemic diseases or psychiatric disorders chronic conditions that may affect sleep (such as diabetes mellitus, hypertension, COPD, obstructive sleep apnea, congestive heart failure, renal failure, cancer, angina, active malignancy, uncontrolled thyroid disease, stroke, serious infections, gastrointestinal disease concurrent diagnosis of fibromyalgia travelling through more than 3 time zones during the week before screening or during the study body mass index >35 sleep-related breathing disorders failure to complete the questionnaires use of sleep medications use of antidepressants, anxiolytics or antipsychotic drugs a lifestyle that placed the patient at serious risk of sleep disturbances (i.e. shift work or night work) other inflammatory rheumatic diseases absence of pain pain intensity measured using VAS≥8 use of anti-tumor necrosis factor (TNF)-α therapeutic agents restless legs syndrome lack of ability to understand Danish not speaking English substance abuse risk of falls past or present history of anti-histamine therapy non-adherence to RA drug therapy patients with a pathology that could lead to joint pain, such as a fracture, joint dislocation, acute strain or sprain use of drugs that could affect sleep quality not being independently mobile no ability to easily travel for assessments living farther than 1 h of travel time periodic limb movement disorder

studies conducted on the subject relate to small groups of patients. In addition, in the case of elderly patients with co-morbidities the latter may play a significant role as factors interfering with the assessment of both QoL and sleep disturbances[27,30]. A study by Gjeve et al[18] showed that RA patients had higher levels of sleep disturbances compared with the control group. The PSQI scores reported in the study were higher compared with those found in our meta-analysis[18]. Studies have shown that over 30% of RA patients take sleeping medication[35].

Low physical activity and sleep disorders are common in RA patients and contribute to lower quality of life. They are also predictors of poorer outcomes such as cardiovascular morbidity and mortality[4]. In the study by Katz et al[23], physical inactivity was correlated with poor sleep, depression, and obesity. This study suggests that fatigue may not be solely a result of RA disease activity but may result from a constellation of factors. These include RA disease activity or pain, but also inactivity, depression, obesity, and poor sleep. Physical activity and sleep quality are

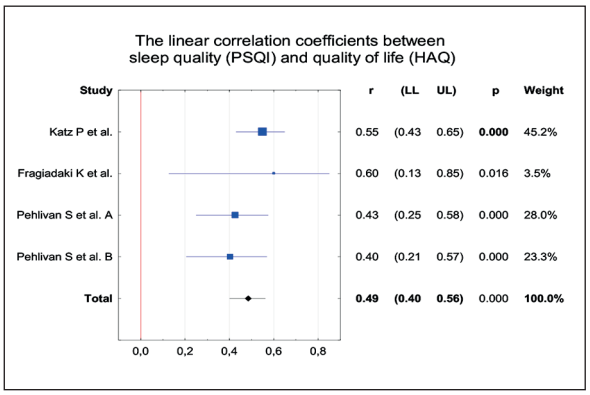

Figure 4. Correlation coefficient values between sleep quality (PSQI) and as assessed using the HAQ and their 95% confidence intervals.
HAQ: Health Assessment Questionnaire; PSQI: Pittsburgh Sleep Quality Index; LL: lower limit of the confidence interval; UL upper limit of the confidence interval.

consistently associated with QoL in many clinical and nonclinical populations. In the study by Gothe et al[36], physical activity and sleep quality were significantly correlated. Sleep quality indirectly influenced QoL through physical, mental, and social well-being. These relationships also persisted over time at month 6. However, neither physical activity nor sleep quality directly affected QoL[36]. In the study by Løppenthin et al[22], the use of physical activity showed that aerobic exercise is important in improving sleep in patients with RA. This, in turn, is considered important for the promotion of health and well-being[22].

As was the case with our meta-analysis, a study by Guo found a correlation between sleep disturbances and the physical and mental domains of quality of life[27]. According to Pehlivan et al[31], sleep disorders and fatigue may be important parameters in assessing clinical improvement. The authors found that the use of anti-TNF-α therapy in RA patients was associated with a better treatment effect (lower pain severity and higher quality of life), lower levels of sleep disturbances and improved sleep quality. However, a multivariate analysis did not show a statistically significant association between the treatment and sleep quality scores[31]. In that study, only HAQ scores were found to be strongly associated with sleep disorders[31]. In a study by Westhovens et al[25], the use of disease-modifying anti-rheumatic drugs (DMARDs) and concurrent medication was significantly associated with the quality of sleep in a univariate model. However, no such association was found in multivariate models[25]. The authors of the study suggest that the use of biological DMARDs may have similar effects as regards disease control. However, it may produce different effects as regards patients' reported outcomes. Depending on the type of the treatment used, the effects of treatment on sleep disturbances are interpreted differently[22]. It has been found that the administration of the IL-6 receptor antagonist tocilizumab in RA patients resulted in improved sleep quality and reduced disease activity[24,26]. However, no association has been found between changes in the PSQI scores and changes in disease activity as assessed using the DAS28[26].

Contrary to our meta-analysis, a study by Mustafa et al[37] did not find an association between sleep disturbances and quality of life. However, according to the authors of the study, this was due to the good clinical condition of the patients participating in the study and the fact that the majority of the patients were in remission from their underlying condition at the time of the study[37]. Moreover, it may be assumed that patients with severe sleep disturbances did not take part in the study concerned.

It is worth considering the relationship between sleep disorders and impairment of cognitive functions in RA patients. This aspect was addressed in some of the studies included in our meta-analysis[17,28]. While the issue was not part of our study, it is worth conducting further investigations due to the risks involved. According to Løppenthinet al[26], poor sleep may impair cognitive functions, particularly concentration, which may have a negative impact on physical and mental functioning, and well-being. The relationship between poor sleep and mental fatigue may be explained by the overlapping symptoms of fatigue and depression[26].

The authors of the available studies attempted to identify the determinants that may be linked to sleep disorders in RA patients. In addition to pain, fatigue and disease activity, the determinants reported include depression. In the case of chronic conditions, depression is often strongly linked to sleep disturbances and quality of life scores. However, due to the limited number of available studies, depression was not considered as a determinant of QoL in our meta-analysis. In other studies, fatigue, which affects almost 90% of patients[23], has been found to be associated with inflammation (CRP levels), depression, pain, low level of physical activity, as well as obesity and poor quality of sleep[23].

In a Belgian study, a negative relationship was found between DAS28-CRP scores and daytime sleepiness. This was explained by higher pain severity and inflammation levels leading to increased alertness[25]. Similarly, in a study by Woytala[38], the clinical and laboratory factors increasing the risk of sleep disorders in RA patients were elevated ESR and CRP values, as well as higher DAS28 scores. In that study, a particular association was found between high DAS28 scores and reduced sleep efficiency, decreased overall sleep duration, longer sleep latency, higher number of awakenings during the night and greater sleep fragmentation[38].

Sleep disorders have been identified as a determinant of low quality of life in RA patients. Therefore, it is important to implement preventive measures to improve the wellbeing of the patients, offer them an increased chance of normal functioning and thus improve their quality of life. A study by Durcan et al[29] showed that exercise programs significantly improve sleep quality and reduce fatigue in RA patients. The authors suggest that RA patients should be recommended to engage in long-term exercise, both during flare-ups and during remission[29]. Other treatment options include psychological interventions (cognitive behavioral therapy, training in pain-coping skills)[39].

The study has several limitations. One of them is the fact that the meta-analysis included studies in which the prevalence of sleep disturbances was assessed indirectly, using standardized questionnaires. This decreased the number of available studies that could be analyzed. Self-report measures may be limited by memory bias and by either over- or under-reporting of some information. The assessment of RA daily activity is mandatory in order to understand the weight of the findings. Moreover, steroid treatment, which can affect sleeping, was neglected. Another limitation of the study is the restriction of the inclusion criteria to studies from the last 10 years. Thus, the meta-analysis may not have included all of the relevant studies.

Practical Implications

The assessment of sleep disturbances in RA patients should be a diagnostic standard. Medical intervention should be initiated in RA patients with diagnosed sleep disorders to provide them with holistic clinical and behavioral care. The behavioral interventions intended to improve the quality of sleep that should be used in RA patients with sleep disorders include cognitive therapy and physical exercise. It seems that efforts to understand and improve the quality of sleep in RA patients are an important aspect of integrative treatment in rheumatoid arthritis. Special attention should be paid to the symptoms of fatigue, depression and the tendency to catastrophize, especially in those patients who feel that their disease is highly active, even though their test results show low inflammation levels[37].

Conclusions

This is the first analysis in the field of quality of life and sleep disturbances in a group of patients with RA. Sleep disturbances are very common between patients with RA and correlate negatively with daily activity and quality of life scores in the physical and mental domains. Identification of factors affecting sleep disturbances will make it possible to control and prevent them. It will also allow for taking measures aimed at preventing sleep disorders and improving quality of life. Sleep quality assessment of patients with rheumatoid arthritis should be performed routinely in clinical practice to develop and implement corrective strategies.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethics Approval and Consent to Participate

Not applicable. According to the regulations of the Bioethics Committee at the Wroclaw Medical University, only medical experiments and research projects are the subject of the committee's evaluation (https://www.umed.wroc.pl/bioetyka-regulamin).

Availability of Data and Materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' Contribution

All authors (WT, NŚL, AT, KD, BJP) contributed equally to this manuscript. All authors have read and approved the manuscript.

References

1) van den Hoek J, Boshuizen HC, Roorda LD, Tijhuis GJ, Nurmohamed MT, van den Bos GA, Dekker J. Mortality in patients with rheumatoid arthritis: a 15-year prospective cohort study. Rheumatol Int 2017; 37: 487-493.

2) Safiri S, Kolahi AA, Hoy D, Smith E, Bettampadi D, Mansournia MA, Almasi-Hashiani A, Ashrafi-Asgarabad A, Moradi-Lakeh M, Qorbani M, Collins G, Woolf AD, March L, Cross M. Global, regional and national burden of rheumatoid arthritis 1990-2017 a systematic analysis of the Global Burden of Disease study 2017. Ann Rheum Dis 2019; 78: 1463-1471.
3) Grabovac I, Haider S, Berner C, Lamprecht T, Fenzl KH, Erlacher L, Quittan M, Dorner TE. Sleep Quality in Patients with Rheumatoid arthritis and Associations with Pain, Disability, Disease Duration, and Activity. J Clin Med 2018; 7: 336.
4) Mohammad NS, Nazli R, Zafar H, Fatima S. Physical activity and Sleep differences between osteoarthritis, rheumatoid arthritis and non-arthritic people in China: objective versus self report comparisons. BMC Public Health 2021: 21: 1821.
5) Hughes M, Chalk A, Sharma P, Dahiya S, Galloway J. A cross-sectional study of sleep and depression in a rheumatoid arthritis population. Clin Rheumatol 2021; 40: 1299-1305.
6) Janiszewski ACG, Reis LAB, Silva MBG, Kahlow BS, Skare TL. Rheumatoid arthritis and sleep quality. Rev Bras Reumatol 2017; 57: 294-298.
7) Vgontzas AN, Zoumakis E, Bixler EO, Lin HM, Follett H, Kales A, Chrousos GP. Adverse effects of modest sleep restriction on sleepiness, performance, and inflammatory cytokines. J Clin Endocrinol Metab 2004; 89: 2119-2126.
8) Karatas G, Bal A, Yuceege M, Yalcin E, First H, Dulgeroglu D, Karataş F, Sahin S, Cakci A, Ardic S. The evaluation of sleep quality and response to anti-tumor necrosis factor α therapy in rheumatoid arthritis patients. Clin Rheumatol 2017; 36: 45-50.
9) Ng KJ, Huang KY, Tung CH, Hsu BB, Wu CH, Lu MC, Lai NS. Risk factors, including different biologics, associated with depression and anxiety in patients with rheumatoid arthritis: a cross-sectional observational study. Clin Rheumatol 2020; 39: 737-746.
10) Lisitsina TA, Vel'tishchev D, Krasnov VN, Nasonov EL. Clinical and pathogenetic relationships between immuno-inflammatory rheumatic diseases and psychic disorders. Klin Med 2014; 92: 12-21.
11) Yin J, Jin X, Shan Z, Li S, Huang H, Li P, Peng X, Peng Z, Yu K, Bao W, Yang W, Chen X, Liu L. Relationship of Sleep Duration With All-Cause Mortality and Cardiovascular Events: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies. J Am Heart Assoc 2017; 6: e005947.
12) Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009; 339: b2535.
13) Ware Jr JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992; 30: 473-483.
14) Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989; 28: 193-213.
15) Bruce B, Fries JF. The Health Assessment Questionnaire (HAQ). Clin Exp Rheumatol 2005; 23: S14-18.
16) Silva CR, Duarte C, Ferreira R, Santos E, da Silva JA. Multifactorial explanatory model of fatigue in patients with rheumatoid arthritis: a path analysis. Ann Rheum Dis 2018; 77: 117-118.
17) Taylor-Gjevre RM, Gjevre JA, Nair B, Skomro R, Lim HJ. Components of sleep quality and sleep fragmentation in rheumatoid arthritis and osteoarthritis. Musculoskeletal Care 2011; 9: 152-159.
18) Gjevre JA, Taylor-Gjevre RM, Nair BV, Lim HJ. Do sleepy rheumatoid arthritis patients have a sleep disorder? Musculoskeletal Care 2012; 10: 187-195.
19) Taylor-Gjevre RM, Gjevre JA, Nair B, Skomro R, Lim HJ. Hypersomnolence and sleep disorders in a rheumatic disease patient population. J Clin Rheumatol 2010; 16: 255-261.
20) Albayrak Gezer İ, Balkarli A, Can B, Bağçaci S, Küçükşen S, Küçük A. Pain, depression levels, fatigue, sleep quality, and quality of life in elderly patients with rheumatoid arthritis. Turk J Med Sci 2017; 47: 847-853.
21) Løppenthin K, Esbensen BA, Østergaard M, Jennum P, Tolver A, Aadahl M, Thomsen T, Midtgaard J. Physical activity and the association with fatigue and sleep in Danish patients with rheumatoid arthritis. Rheumatol Int 2015; 35: 1655-1664.
22) Katz P, Margaretten M, Trupin L, Schmajuk G, Yazdany J, Yelin E. Role of Sleep Disturbance, Depression, Obesity, and Physical Inactivity in Fatigue in Rheumatoid Arthritis. Arthritisc Care Res 2016; 68: 81-90.
23) Fragiadaki K, Tektonidou MG, Konsta M, Chrousos GP, Sfikakis PP. Sleep disturbances and interleukin 6 receptor inhibition in rheumatoid arthritis. J Rheumatol 2012; 39: 60-62.
24) Westhovens R, Van der Elst K, Matthys A, Tran M, Gilloteau I. Sleep problems in patients with rheumatoid arthritis. J Rheumatol 2014; 41: 31-40.
25) Løppenthin K, Esbensen BA, Jennum P, Østergaard M, Tolver A, Thomsen T, Midtgaard J. Sleep quality and correlates of poor sleep in patients with rheumatoid arthritis. Clin Rheumatol 2015; 34: 2029-2039.
26) Guo G, Fu T, Yin R, Zhang L, Zhang Q, Xia Y, Li L, Gu Z. Sleep quality in Chinese patients with rheumatoid arthritis: contributing factors and effects on health-related quality of life. Health Qual Life Outcomes 2016; 14: 151.
27) Kim SH, Kim H, Kim S, Paek S, Koh JH, Lee J, Cho YW, Park SH. Sleep Quality Independently Affects Health-related Quality of Life and Cognitive Function in Korean Female Patients with

Rheumatoid Arthritis: a Case-control Study. J Korean Med Sci 2018; 33: e216.

28) Durcan L, Wilson F, Cunnane G. The effect of exercise on sleep and fatigue in rheumatoid arthritis: a randomized controlled study. J Rheumatol 2014; 41: 1966-1973.

29) Elazeem MIA, Salem MN. Can rheumatoid arthritis affect sleep in Egyptian patients? The Egyptian Rheumatologist 2018; 40: 11-16.

30) Pehlivan S, Karadakovan A, Pehlivan Y, Onat AM. Sleep quality and factors affecting sleep in elderly patients with rheumatoid arthritis in Turkey. Turk J Med Sci 2016; 46: 1114-1121.

31) Nicassio PM, Ormseth SR, Custodio MK, Olmstead R, Weisman MH, Irwin MR. Confirmatory factor analysis of the Pittsburgh Sleep Quality Index in rheumatoid arthritis patients. Behav Sleep Med 2014; 12: 1-12.

32) Medic G, Wille M, Hemels ME. Short- and long-term health consequences of sleep disruption. Nat Sci Sleep 2017; 9: 151-161.

33) Kwiatkowska B, Kłak A, Raciborski F, Maślińska M. The prevalence of depression and insomnia symptoms among patients with rheumatoid arthritis and osteoarthritis in Poland: a case control study. Psychol Health Med 2019; 24: 333-343.

34) Belt NK, Kronholm E, Kauppi MJ. Sleep problems in fibromyalgia and rheumatoid arthritis compared with the general population. Clin Exp Rheumatol 2009; 27: 35-41.

35) Gothe NP, Ehlers DK, Salerno EA, Fanning J, Kramer AF, McAuley E. Physical Activity, Sleep and Quality of Life in Older Adults: Influence of Physical, Mental and Social Well-being. Behav Sleep Med 2020; 18: 797-808.

36) Mustafa M, Bawazir Y, Merdad L, Wali S, Attar S, Fathaldin O, Bahlas S, Alhejaili F, Aljohaney A, Jan A, Jadu F. Frequency of sleep disorders in patients with rheumatoid arthritis. Open Access Rheumatol 2019; 11: 163-171.

37) Woytala P. Zaburzenia snu u chorych na reumatoidalne zapalenie stawów [Eng. Sleep disorders in rheumatoid arthritis patients]. https: //www.umed.wroc.pl/sites/default/files/struktura/lekarski/dziekanat/przew_dokt/Patryk_Jerzy_Woytala_streszczenie.pdf.

38) Lindqvist J, Westerlind H, Klareskog L, Alfredsson L, Lampa J. Subgrouping of early ra-patients identified cluster of patients with high levels of pain, fatigue and psychosocial distress. Available at: https://ard.bmj.com/content/annrheumdis/76/Suppl_2/1038.2.full.pdf.