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Complete List of Authors:	Kim, Jae-Hyun; Ajou University, Preventive Medicine Park, Eun-Cheol; Yonsei University College of Medicine, Department of Preventive Medicine and Institute of Health Services Research Lee, Sang Gyu; Yonsei University, Graduate School of Public Health
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Relationship between Sleep Duration and Rheumatoid Arthritis in Korean Adults: Analysis of Seven Years of Aggregated Data from the National Health and Nutrition Examination Survey (KNHANES)

Jae-Hyun Kim[1,2], Eun-Cheol Park[2,3] , Sang-Gyu Lee[2,4],

[1]Department of Preventive Medicine, Ajou University School of Medicine, Suwon, Republic of Korea.

[2]Institute of Health Services Research; Yonsei University; Seoul, Korea

[3]Department of Preventive Medicine; Yonsei University College of Medicine; Seoul, Korea

[4]Department of Hospital Management; Graduate School of Public Health; Yonsei University; Seoul, Korea

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***Corresponding Author**

Sang Gyu Lee, MD, MBA, Ph.D.

Graduate School of Public Health and Institute of Health Services Research, Yonsei University

50 Yonsei-ro, Seodaemun-gu, Seoul, 120-752, Korea

Phone: +82 2 2228 1524, Fax: +82 2 392 7734

E-mail: LEEVAN@yuhs.ac

ABSTRACT

Objectives: To investigate the association between self-reported sleep duration and rheumatoid arthritis (RA).

Setting: The present study analyzed 7 years of aggregated cross-sectional data (2007-2013) from the Korea National Health and Nutrition Examination Surveys (KNHANES)

Participants: a total of 37,979 individuals were selected for the analyses.

Interventions: Sleep duration

Primary and secondary outcome measures: rheumatoid arthritis (RA)

Results: After adjusting for confounding factors, the odds of RA for short-duration sleepers (≤ 5 hours/day) and long-duration sleepers (≥ 9 hours/day) were 1.509-fold (95% confidence interval [CI]: 1.132-2.014) and 1.296-fold (95% CI: 0.838-2.003) higher, respectively, than those for subjects with a sleep duration of 7 hours/day. A subgroup analysis according to gender revealed that the U-shaped relationship between sleep disturbances and RA observed in the total population remained for both genders, although it was statistically significant only for females with a short sleep duration.

Conclusion: Individuals with RA may be at a higher risk for sleep disturbances compared with individuals without RA. This apparent difference may be attributed to the fatigue and pain reported by RA patients, because these factors can significantly affect the quality of life and risk of cardiovascular disease in this population. Therefore, the provision of comprehensive care for RA patients by health care professionals should include assessments of sleep duration, and patients with RA should be encouraged to report sleep problems.

Keywords: Sleep disturbance, rheumatoid arthritis, sleep

Strengths and limitations of this study

- This study used nationwide survey data of community dwelling people. A large population sample size was representative of the general population, so the results can be generalized to the general population in South Korea.
- The lack of validated questionnaires assessing sleep duration and RA was a major limitation of the present study, as more objective methods tend to yield more accurate results.
- Respondents' reports were subjective and were imperfect measures potentially affected by perception bias and adaptation of resources.
- We used cross-sectional nature data for our estimates. Therefore the results possibly reflected reverse causality and bidirectional.

INTRODUCTION

Arthritis is the most common cause of disability worldwide. Rheumatoid arthritis (RA) is characterized by persistent inflammatory symmetrical synovitis with pain, swelling, and a broad range of systemic manifestations in the peripheral joints [1]. This disease is also associated with sleep disturbances [2], which play an important role in the maintenance of an individual's health [3 4]. The sleep disturbances in RA patients are primarily caused by factors such as mental health conditions, including anxiety and depression, and physical health conditions, such as a frequent need to urinate. Additionally, sleep disorders such as sleep apnea or primary insomnia typically result in poor sleep quality in RA patients as well as exacerbate the patient's primary symptoms [5].

Sleep disturbances affect more than half of RA patients [6 7] and are thought to be more common among those with active inflammation [8] or physical health conditions such as associated pain, fatigue, and/or functional disabilities [9]. Although physicians often assume that inflammation is the stimulus for RA-related pain, many of these patients continue to experience pain following adequate suppression of inflammation [10]. Furthermore, sleep disturbances and inadequate sleep are related to serious outcomes such as reduced health-related quality of life [11], a higher risk of morbidities [12], and, ultimately, increased all-cause mortality [13]. Additionally, sleep disturbances are almost three-fold more frequent in females than males [14]. Thus, the quality and amount of sleep in patients with RA are important issues for rheumatologists, particularly after the finding that etanercept and infliximab reduce daytime sleepiness [15].

Therefore, the primary aim of the present study was to investigate the association between self-reported sleep duration and RA using 7 years of aggregated cross-sectional data (2007-2013) obtained from the National Health and Nutrition Examination Survey (KNHANES).

METHODS

Study Sample

To evaluate the relationship between sleep duration and RA, the present study analyzed data from the fourth (2007-2009), fifth (2010-2012), and sixth (2013) KNHANES assessments performed by the Korean Ministry of Health and Welfare. The KNHANES is a cross-sectional survey based on stratified multistage probability sampling units of Korean households that targets members of the civilian non-institutionalized South Korean population who are 1 year of age or older. The samples were determined by the household registries of the 2005 National Census Registry.

The total target population initially consisted of 24,871, 25,534, and 8,018 participants who completed the 2007-2009, 2010-2012, and 2013 KNHANES assessments, respectively, which had average response rates of 78.4%, 80.8% ,and 79.3%, respectively. The information from 14,305 individuals aged 1-18 years old were excluded from the present analyses while the information of 44,118 individuals aged 19 years and older were included. Additionally, the present study excluded 6,036 individuals with missing data regarding age, occupation, income, and/or marriage status and 103 individuals with missing data regarding smoking, drinking, perceived stress, exercise, sleep duration, RA, hypertension, and/or dyslipidemia. Thus, a total of 37,979 individuals were selected for the final analyses in the present study. Because all KNHANES data are available publicly, this study did not require approval from an institutional review board.

Variables

Independent Variables

In the present study, sleep duration was based on self-reported data acquired in response to the question “How many hours do you usually sleep?”. The responses were

classified into five categories (≤ 5 hours, 6 hours, 7 hours, 8 hours, and ≥ 9 hours) based on the sleep definitions of the International Classification of Sleep Disorders, 2nd edition, in which ≤ 5 hours is defined as a short sleep duration and ≥ 9 hours as a long sleep duration [16].

Dependent Variables

In the present study, DM2 cases were considered to be the participants who answered "Yes" to the question "Are you currently suffering from rheumatoid arthritis?" in the self-reported data. RA was categorized as either "Yes" or "No".

Sociodemographic Factors

The present analyses included age, gender, household income, marital status, occupation, and region of residency as sociodemographic factors; all of the covariates were categorical. Household income was calculated by dividing a participant's household monthly income by the square root of the household size, and the participants were ranked from lowest to highest income and then grouped into four household income quartiles. Predefined categories were used to categorize household incomes, similar to how the raw KNHANES data are processed. The residency regions were categorized into urban (administrative divisions of a city: Seoul, Daejeon, Daegu, Busan, Incheon, Kwangju, or Ulsan) and rural (not classified as administrative of a city), and occupational status was classified into the following three categories: white collar (administrative, engineering, scientific, teaching and related occupations, sales and related occupations, and service occupation), blue collar (farming, forestry, fishing and hunting, craft and repair, operators, fabricators, and laborers), and unemployed (including housewives and students).

Health Behavior Factors

Questions regarding alcohol use, smoking status, and the number of days of moderate exercise per week were assessed by a health interview survey and included as covariates in the present analyses. Alcohol use was further assessed by questioning the participants about their average frequency (days per week or month) of alcohol use during the last year.

Health Status Factors

Perceived stress, the extent of RA pain, body mass index (BMI), hypertension, and dyslipidemia were also included in the present model. The following were categorized into four groups for the present analyses: perceived stress (very high, high, low, and very low), the extent of RA pain (low or less, middle-low, middle-high, and high), and BMI (thin: < 18.5 kg/m^2, moderate: 18.5-23.9 kg/m^2, overweight: 24.0-26.9 kg/m^2, and obese: > 27.0 kg/m^2 [17]. Hypertension and dyslipidemia were considered to be present if a participant answered "Yes" to the question "Are you currently suffering from hypertension and/or dyslipidemia?", categorized as "Yes" or "No".

Statistical Analysis

The distributions of the general characteristics of the participants were assessed using Chi-square tests, and multivariate logistic regression analyses were used to determine whether the general characteristics, health statuses, and/or health risk behaviors of the participants had relationships with RA. All data were analyzed using SAS software, version 9.4 (SAS Institute; Inc., Cary, NC, USA).

RESULTS

Prevalence of Short Sleep and Long Sleep Durations

Of the 37,979 KNHANES participants included in the present study, 16,254 were male (42.8%), 21,735 were female (57.2%), and 670 were RA patients (1.8%). Of the 5,950 participants who reported a short sleep duration (≤ 5 hours), 209 had RA (3.5%), while of the 2,976 participants who reported a long sleep duration, 58 had RA (2.0%). Of the total sample, 119 (0.7%) of the males and 551 (2.5%) of the females were currently suffering from RA (Table 1).

Association between Sleep Duration and Rheumatoid Arthritis

Table 2 portrays the results of the logistic regression analyses after adjusting for age, gender, household income, marital status, occupation, region of residence, smoking status, frequency of alcohol use, number of days of moderate exercise per week, perceived stress, extent of RA pain, BMI, hypertension, dyslipidemia, and year of the survey. After adjusting for all of these confounding variables, the odds of RA were 1.509-fold higher (95% confidence interval [CI]: 1.132-2.014) for short-duration sleepers (≤ 5 hours/day) and 1.296-fold higher (95% CI: 0.838-2.003) for long-duration sleepers (≥ 9 hours/day) than for those with sleep durations of 7 hours/day (Table 2).

Table 3 depicts the results of a subgroup analysis according to gender after adjusting for age, household income, marital status, occupation, region of residence, smoking status, frequency of alcohol use, number of days of moderate exercise per week, perceived stress, extent of RA pain, BMI, hypertension, dyslipidemia, and year of the survey. Males who reported a short sleep duration were 45.9% more likely to have RA (odds ratio [OR]: 1.459, 95% CI: 0.713-2.984), while males who reported a long sleep duration were 64.3% more likely to have RA (OR: 1.64.3, 95% CI: 0.607-4.447), compared with males with reported

sleep durations of 7 hours. Females who reported a short sleep duration were 50.5% more likely to have RA (OR: 1.505, 95% CI: 1.104-2.051), while females who reported a long sleep duration were 22.1% more likely to have RA (OR: 1.221, 95% CI: 0.767-1.944), compared with females who reported sleep durations of 7 hours. Although the findings for the male subgroup were not statistically significant, the overall results showed a U-shaped curve for both genders (Fig. 1).

DISCUSSION

Because sleep disturbances may be an important clinical feature of patients with RA, this issue has recently received an increasing amount of attention [18 19]. Thus, the present study aimed to investigate sleep duration and its relationship with RA using 7 years of aggregated data from a large representative population-based survey conducted in Korea. The present study found an association between the reported symptoms of sleep duration and RA that was statistically significant (OR: 1.543, 95% CI: 1.158-2.057) even in the presence of perceived stress, which suggests that stress could be a trigger or signal for an inappropriate sleep duration in patients with RA. In general, there was a U-shaped association between short or long sleep duration and the risk of RA, and this U-shaped relationship remained in a subgroup analysis based on gender, although it was statistically significant only in females with short sleep duration. These associations were independent of sociodemographic variables, such as age, gender, household income level, marital status, occupation, and region of residence, health behavior variables, such as smoking status, frequency of alcohol use, and number of days of moderate exercise per week, and health status variables, such as perceived stress, the extent of RA pain, BMI, hypertension, and dyslipidemia, and year of the survey.

A nationwide study conducted in the United States found that sleep disturbances are associated with RA in approximately 10 million adults [20]. The presence of sleep disturbances in patients diagnosed with a range of rheumatological-related diseases including systemic lupus erythematosus, fibromyalgia, chronic fatigue syndrome, multiple sclerosis, and RA have also been assessed [21]. Additionally, recent studies have indicated that sleep disturbances such as difficulties with the onset of sleep and waking up early in the morning are also major complaints in RA patients, and that fatigue in RA patients is likely due to poor quality of sleep, a functional disability, joint pain, and/or depressive symptoms [21-25]. Poor quality of sleep and sleep disturbances can worsen physical and mental health conditions, including RA

symptoms and pain, in the general population [26]. Similarly, the pain and discomfort caused by RA with inflammation may result in a greater frequency of sleep disturbances, contributing to functional impairments such as poor sleep quality and lack of participation and social engagement, which have a significant negative impact on the health and well-being of individuals [27].

Along with a significantly higher prevalence of fatigue, there is also a greater risk of sleep disturbances such as obstructive sleep apnea (OSA) in patients with RA, because they are more likely to have chronic health issues, including high blood pressure and a high BMI, which can lead to increased risks of cardiovascular disease (CVD) and nocturnal sudden cardiac death [28]. Accordingly, the autonomic response is more severe in patients with chronic OSA than in individuals with a low risk of OSA [28-31].

In the present study, a multivariate logistic regression analysis revealed that the important factors influencing the relationship between sleep duration and RA include perceived stress and the extent of RA pain. Although the causes of sleep disturbances in patients with RA are likely multifactorial, only 30% of older Americans with sleep disturbances seek treatment at hospitals or treatment centers utilizing multidisciplinary approaches, relying on various self-care strategies instead [32 33]. Therefore, the provision of comprehensive care for RA patients requires encouragement of the patient to report sleep disturbances and timely diagnoses to reduce their symptoms. Additionally, the sleep disturbance symptoms of these patients should be monitored by physicians and health care professionals to detect them at an early stage. In this manner, the present data regarding the prevalence of sleep disturbances in RA patients will contribute to the awareness of physicians and health care professionals regarding this issue and may aid in the development of appropriate interventions to properly manage, minimize, or eliminate these symptoms.

There are several potential limitations that should be taken into consideration when

interpreting the present results. First, because this study utilized a cross-sectional design, the results may reflect reverse causality and a bidirectional relationship in the association between sleep duration and RA. Therefore, longitudinal studies using validated measures of RA and sleep duration are required to replicate these findings and to clarify the causality and mechanisms that underlie the association between sleep duration and RA. Second, although the use of self-reports is a valuable source of information in large-scale epidemiological studies, the lack of validated questionnaires assessing sleep duration and RA was a major limitation of the present study, as more objective methods tend to yield more accurate results. Controlling for socioeconomic status, health status, and behavior variables, as in the present study, may partially ameliorate these issues, but future in-depth studies are necessary to determine more accurately the relationship between RA and sleep disturbances, including difficulty falling asleep, difficulty maintaining sleep, time spent in bed, wake after sleep onset, sleep onset latency, sleep quality, time of going to bed in the evening, time of turning out the lights with the intention to sleep, wake time in the morning, time of getting out of bed in the morning, and insomnia.

Conclusions

The present study found that patients with RA may be at a higher risk for sleep disturbances than are individuals without RA. This apparent difference may be attributed to the fatigue and pain reported by RA patients who may also be associated with RA itself. The present findings suggest that health care professionals who treat RA patients in routine clinical practice should be aware of the relationship between sleep disturbances and RA and attempt to assess sleep duration, because it likely has a significant impact on quality of life and the risk of CVD. Future research that includes objective measures of sleep disturbances is necessary to fully characterize the extent to which sleep disturbances affect patients with RA.

Footnotes

Authors` contributions

JH Kim, EC Park, carried out the acquisition of data, performed the experiments and participated in drafted the manuscript. JH Kim, EC Park participated in the design of the study and performed the statistical analysis. JH Kim, SG Lee, conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Competing interests None.

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Table 1. Demographic characteristics of the study population

	Total		Rheumatoid arthritis (RA)				P-value
			No		Yes		
	N	%	N	%	N	%	
Sleep duration (hours)							< .0001
≤ 5	5,950	15.7	5,741	96.5	209	3.5	
6	9,905	26.1	9,767	98.6	138	1.4	
7	10,748	28.3	10,609	98.7	139	1.3	
8	8,400	22.1	8,274	98.5	126	1.5	
≥ 9	2,976	7.8	2,918	98.1	58	2.0	
Age (years)							< .0001
≤ 29	4,751	12.5	4,732	99.6	19	0.4	
30-39	7,290	19.2	7,258	99.6	32	0.4	
40-49	7,261	19.1	7,199	99.2	62	0.9	
50-59	6,941	18.3	6,804	98.0	137	2.0	
60-69	6,194	16.3	6,005	97.0	189	3.1	
70-79	4,547	12.0	4,352	95.7	195	4.3	
≥ 80	995	2.6	959	96.4	36	3.6	
Gender							< .0001
Male	16,254	42.8	16,135	99.3	119	0.7	
Female	21,725	57.2	21,174	97.5	551	2.5	
Household income level							< .0001
Low	7,633	20.1	7,340	96.2	293	3.8	
Lower-middle	9,685	25.5	9,536	98.5	149	1.5	
Upper-middle	10,216	26.9	10,096	98.8	120	1.2	
High	10,445	27.5	10,337	99.0	108	1.0	
Marital status							< .0001
Married	27,602	72.7	27,167	98.4	435	1.6	
Single	5,312	14.0	5,291	99.6	21	0.4	
Separated, divorced	5,065	13.3	4,851	95.8	214	4.2	
Occupation							< .0001
White-collar	12,635	33.3	12,541	99.3	94	0.7	
Blue-collar	10,340	27.2	10,136	98.0	204	2.0	
Unemployed	15,004	39.5	14,632	97.5	372	2.5	
Residential region							< .0001
Urban	17,032	44.9	16,806	98.7	226	1.3	
Rural	20,947	55.2	20,503	97.9	444	2.1	
Smoking status							< .0001
Current smoker	11,101	29.2	10,987	99.0	114	1.0	
Former smoker	4,552	12.0	4,498	98.8	54	1.2	
Never smoker	22,326	58.8	21,824	97.8	502	2.3	
Frequency of alcohol use							< .0001
Never drink	10,950	28.8	10,618	97.0	332	3.0	
0-1 times per month	10,786	28.4	10,609	98.4	177	1.6	
2-4 times per week	13,510	35.6	13,378	99.0	132	1.0	
4 times or more per week	2,733	7.2	2,704	98.9	29	1.1	
Number of days of moderate exercise per week							0.0018
Never	23,187	61.1	22,765	98.2	422	1.8	
1–3	9,145	24.1	9,016	98.6	129	1.4	
4–6	3,318	8.7	3,258	98.2	60	1.8	
Everyday	2,329	6.1	2,270	97.5	59	2.5	
Perceived stress							< .0001
Very high	1,749	4.6	1,687	96.5	62	3.5	
High	8,442	22.2	8,265	97.9	177	2.1	
Low	21,556	56.8	21,241	98.5	315	1.5	
Very low	6,232	16.4	6,116	98.1	116	1.9	
Extent of RA pain							< .0001
Low or less	35,482	93.4	34,947	98.5	535	1.5	
Middle-low	1,178	3.1	1,134	96.3	44	3.7	
Middle-high	739	2.0	702	95.0	37	5.0	
High	580	1.5	526	90.7	54	9.3	
Body mass index							0.0218
Thin (< 18.5 kg/m^2)	1,908	5.0	1,879	98.5	29	1.5	
Moderate (18.5-23.9 kg/m^2)	19,689	51.8	19,376	98.4	313	1.6	
Overweight (24.0-26.9 kg/m^2)	10,767	28.4	10,548	98.0	219	2.0	
Obese (≥ 27.0 kg/m^2)	5,615	14.8	5,506	98.1	109	1.9	
Hypertension							< .0001
No	30,297	79.8	29,862	98.6	435	1.4	
Yes	7,682	20.2	7,447	96.9	235	3.1	
Dyslipidemia							< .0001
No	35,427	93.3	34,830	98.3	597	1.7	
Yes	2,552	6.7	2,479	97.1	73	2.9	
Year							< .0001
2007	1,403	3.7	1,376	98.1	27	1.9	
2008	6,513	17.2	6,354	97.6	159	2.4	
2009	7,338	19.3	7,189	98.0	149	2.0	
2010	6,059	16.0	5,967	98.5	92	1.5	
2011	5,927	15.6	5,846	98.6	81	1.4	
2012	5,465	14.4	5,383	98.5	82	1.5	
2013	5,274	13.9	5,194	98.5	80	1.5	
Total	37,979	100.0	37,309	98.2	670	1.8	

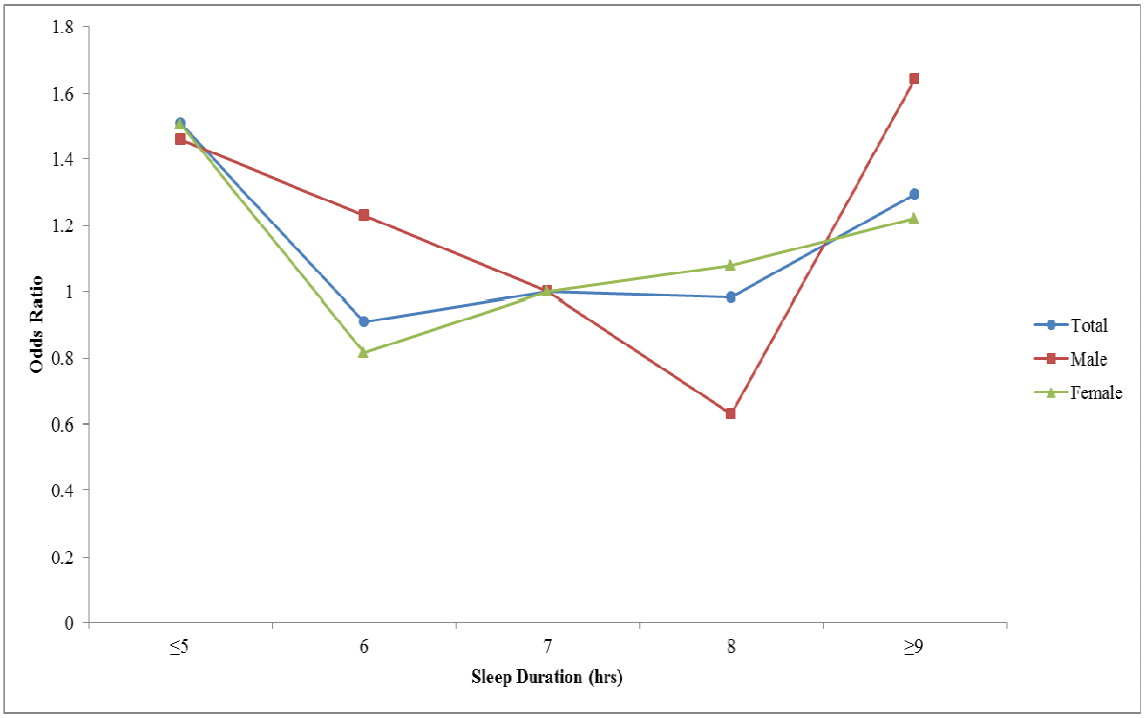
Table 2. Results of the logistic regression analysis assessing the relationships between the independent variables and rheumatoid arthritis

		Rheumatoid arthritis (RA)		
		OR	95% CI	
Sleep duration (hours)				
	≤5	1.509	1.132	2.014
	6	0.911	0.685	1.211
	7	1.000		
	8	0.982	0.726	1.329
	≥9	1.296	0.838	2.003
Age (years)				
	≤ 29	1.000		
	30-39	0.905	0.458	1.787
	40-49	1.845	0.991	3.436
	50-59	3.400	1.876	6.164
	60-69	4.196	2.279	7.726
	70-79	5.176	2.770	9.669
	≥ 80	3.847	1.847	8.012
Gender				
	Male	0.305	0.219	0.424
	Female	1.000		
Household income level				
	Low	1.442	1.081	1.924
	Lower-middle	0.961	0.709	1.303
	Upper-middle	1.142	0.844	1.545
	High	1.000		
Marital status				
	Married	1.000		
	Single	0.876	0.500	1.533
	Separated, divorced	1.071	0.843	1.362
Occupation				
	White-collar	1.000		
	Blue-collar	1.570	1.121	2.200
	Unemployed	1.494	1.087	2.054
Residential region				
	Urban	1.000		
	Rural	1.322	1.074	1.628
Smoking status				
	Current smoker	0.992	0.741	1.328
	Former smoker	1.309	0.889	1.928
	Never smoker	1.000		
Frequency of alcohol use				
	Never drink	1.279	0.769	2.129
	0-1 times per month	1.160	0.682	1.971
	2-4 times per week	1.256	0.735	2.146
	4 times or more per week	1.000		
Number of days of moderate exercise per week				
	Never	1.000		
	1–3	1.120	0.868	1.444
	4–6	0.970	0.706	1.331
	Everyday	1.157	0.786	1.704
Perceived stress				
	Very high	2.699	1.815	4.012
	High	1.643	1.222	2.208
	Low	1.311	1.011	1.701
	Very low	1.000		
Extent of pain of rheumatoid arthritis				
	Low or less	1.000		
	Middle-low	1.383	0.945	2.026
	Middle-high	1.567	1.006	2.441
	High	2.424	1.619	3.627
Body mass index				
	Thin (< 18.5 kg/m^2)	1.140	0.681	1.908
	Moderate (18.5-23.9 kg/m^2)	1.000		
	Overweight (24.0-26.9 kg/m^2)	1.048	0.842	1.306
	Obese (≥ 27.0 kg/m^2)	1.040	0.794	1.363
Hypertension				
	No	1.000		
	Yes	1.015	0.801	1.286
Dyslipidemia				
	No	1.000		
	Yes	0.978	0.698	1.369
Year				
	2007	1.000		
	2008	0.850	0.489	1.478
	2009	0.701	0.403	1.220
	2010	0.527	0.288	0.963
	2011	0.388	0.213	0.707
	2012	0.406	0.227	0.727
	2013	0.459	0.252	0.836

Table 3. Results of the logistic regression analysis assessing the relationships between the independent variables and rheumatoid arthritis by gender

	Rheumatoid arthritis (RA)					
	Male			Female		
	OR	95% CI		OR	95% CI	
Sleep duration (hours)						
≤5	1.459	0.713	2.984	1.505	1.104	2.051
6	1.231	0.626	2.420	0.816	0.600	1.108
7	1.000			1.000		
8	0.628	0.325	1.213	1.079	0.777	1.498
≥9	1.643	0.607	4.447	1.221	0.767	1.944
Age (years)						
≤ 29	1.000			1.000		
30-39	0.657	0.165	2.614	1.032	0.458	2.327
40-49	1.043	0.295	3.690	2.203	1.057	4.593
50-59	1.683	0.516	5.493	4.238	2.069	8.680
60-69	1.870	0.579	6.044	5.447	2.620	11.325
70-79	2.398	0.730	7.878	6.495	3.064	13.766
≥ 80	2.394	0.570	10.062	4.310	1.813	10.246
Household income level						
Low	1.782	0.946	3.357	1.354	0.981	1.867
Lower-middle	1.050	0.536	2.058	0.909	0.644	1.284
Upper-middle	1.066	0.499	2.277	1.146	0.815	1.612
High	1.000			1.000		
Marital status						
Married	1.000			1.000		
Single	0.618	0.203	1.878	0.876	0.438	1.753
Separated, divorced	0.690	0.310	1.534	1.140	0.879	1.478
Occupation						
White-collar	1.000			1.000		
Blue-collar	3.726	1.726	8.042	1.248	0.859	1.813
Unemployed	4.687	1.853	11.852	1.167	0.848	1.606
Residential region						
Urban	1.000			1.000		
Rural	1.535	0.951	2.476	1.276	1.013	1.606
Smoking status						
Current smoker	1.300	0.620	2.725	0.958	0.665	1.381
Former smoker	1.989	0.879	4.502	1.085	0.617	1.909
Never smoker	1.000			1.000		
Frequency of alcohol use						
Never drink	1.546	0.621	3.850	1.009	0.543	1.874
0-1 times per month	1.675	0.692	4.056	0.882	0.464	1.678
2-4 times per week	1.475	0.614	3.544	1.028	0.529	1.999
4 times or more per week	1.000			1.000		
Number of days of moderate exercise per week						
Never	1.000			1.000		
1–3	1.624	0.937	2.814	1.016	0.765	1.351
4–6	0.924	0.407	2.094	0.994	0.697	1.416
Everyday	1.520	0.654	3.534	1.085	0.719	1.639
Perceived stress						
Very high	4.203	1.717	10.294	2.456	1.591	3.790
High	1.993	0.922	4.308	1.601	1.169	2.193
Low	1.451	0.795	2.648	1.283	0.962	1.710
Very low	1.000			1.000		
Extent to pain of rheumatoid arthritis						
Low or less	1.000			1.000		
Middle-low	2.063	0.681	6.249	1.269	0.843	1.911
Middle-high	3.372	1.269	8.958	1.292	0.790	2.111
High	10.717	3.666	31.333	2.121	1.388	3.241
BMI						
Thin (< 18.5 kg/m^2)	1.004	0.335	3.008	1.186	0.670	2.099
Moderate (18.5-23.9 kg/m^2)	1.000			1.000		
Overweight (24.0-26.9 kg/m^2)	1.362	0.801	2.316	0.991	0.783	1.255
Obese (≥ 27.0 kg/m^2)	1.388	0.686	2.807	0.996	0.742	1.336
Hypertension						
No	1.000			1.000		
Yes	0.855	0.463	1.579	1.065	0.823	1.377
Dyslipidemia						
No	1.000			1.000		
Yes	1.199	0.399	3.604			
Year				0.955	0.682	1.336
2007	1.000			1.000		
2008	0.516	0.190	1.401	1.124	0.613	2.062
2009	0.318	0.111	0.908	0.993	0.540	1.825
2010	0.372	0.108	1.283	0.663	0.340	1.292
2011	0.122	0.037	0.403	0.589	0.302	1.148
2012	0.126	0.038	0.411	0.615	0.323	1.173
2013	0.216	0.067	0.695	0.643	0.329	1.254

Figure 1. Effects of the association between sleep duration and rheumatoid arthritis after adjusting for confounding factors



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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract(1P)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found(2p)
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported(4p)
Objectives	3	State specific objectives, including any prespecified hypotheses(5p)
Methods		
Study design	4	Present key elements of study design early in the paper(5p)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection(5-6p)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up(6p) *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable(6p)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group(7p)
Bias	9	Describe any efforts to address potential sources of bias(7-8p)
Study size	10	Explain how the study size was arrived at(6p)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why(6p)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding(7-8p)
		(*b*) Describe any methods used to examine subgroups and interactions(N/A)
		(*c*) Explain how missing data were addressed(6p)
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed(6p) *Case-control study*—If applicable, explain how matching of cases and controls was addressed(N/A) *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy(N/A)
		(*e*) Describe any sensitivity analyses(N/A)

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed(8p)
		(b) Give reasons for non-participation at each stage(N/A)
		(c) Consider use of a flow diagram(N/A)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders(5-7p)
		(b) Indicate number of participants with missing data for each variable of interest(5-7p)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) (5-7p)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time(5-7p)
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included(8-9p)
		(*b*) Report category boundaries when continuous variables were categorized(8-9p)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period(8-9p)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses(N/A)
Discussion		
Key results	18	Summarise key results with reference to study objectives(9-10p)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias(12p)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence(8-10p)
Generalisability	21	Discuss the generalisability (external validity) of the study results(12p)
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Association between Rheumatoid Arthritis and Sleep Duration in Korean Adults: Analysis of Seven Years of Aggregated Data from the National Health and Nutrition Examination Survey (KNHANES)

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Association between Rheumatoid Arthritis and Sleep Duration in Korean Adults: Analysis of Seven Years of Aggregated Data from the National Health and Nutrition Examination Survey (KNHANES)

Jae-Hyun Kim[1,2], Eun-Cheol Park[3,4], Yunhwan Lee[1,2], Sungkeun Shim[5], Jinhee Kim[1,2], Sang-Gyu Lee[4,6]

[1]Department of Preventive Medicine and Public Health, Ajou University School of Medicine, Suwon, Republic of Korea.

[2]Institute on Aging, Ajou University Medical Center, Suwon, Republic of Korea

[3]Preventive Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

[4]Institute of Health Services Research, Yonsei University, Seoul, Republic of Korea

[5]Department of Biostatistics, Graduate School of Public Health, Yonsei University, Seoul, Republic of Korea

[6]Department of Hospital management, Graduate School of Public Health, Yonsei University, Seoul, Republic of Korea

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***Corresponding Author**

Sang Gyu Lee, MD, MBA, Ph.D.

Graduate School of Public Health and Institute of Health Services Research, Yonsei University

50 Yonsei-ro, Seodaemun-gu, Seoul, 120-752, Korea

Phone: +82 2 2228 1524, Fax: +82 2 392 7734

E-mail: LEEVAN@yuhs.ac

ABSTRACT

Objectives: To investigate the association between rheumatoid arthritis (RA) and self-reported sleep duration

Setting: The present study analyzed 7 years of aggregated cross-sectional data (2007-2013) from the Korea National Health and Nutrition Examination Surveys (KNHANES)

Participants: a total of 37,979 individuals were selected for the analyses.

Interventions: rheumatoid arthritis (RA)

Primary and secondary outcome measures: sleep duration

Results: After adjusting for confounding factors, the odds of short-duration sleepers (≤ 6 hours/day) and long-duration sleepers (≥ 9 hours/day) for RA were 1.23-fold (95% confidence interval [CI]: 1.101-1.51) and 1.27-fold (95% CI: 0.85-1.88) higher, respectively, than those for subjects with a sleep duration of 7-8 hours/day. A subgroup analysis according to extent to pain of RA revealed that the strong relationship between RA and sleep disturbances was observed in those with high pain of RA (OR: 1.28 CI: 1.04-1.58).

Conclusion: Individuals with RA may be at a higher risk for sleep disturbances compared with individuals without RA. This apparent difference may be attributed to the pain reported by RA patients, because these factors may significantly affect the self-rated health and risk of cardiovascular disease in this population. Therefore, the provision of comprehensive care for RA patients by health care professionals should include assessments of sleep duration, and patients with RA should be encouraged to report sleep problems.

Keywords: Sleep disturbance, rheumatoid arthritis, sleep

Strengths and limitations of this study

- This study used nationwide survey data of community dwelling people. A large population sample size was representative of the general population, so the results can be generalized to the general population in South Korea.
- The lack of validated questionnaires assessing RA and sleep duration was a major limitation of the present study, as more objective methods tend to yield more accurate results.
- Respondents' reports were subjective and were imperfect measures potentially affected by perception bias and adaptation of resources.
- We used cross-sectional nature data for our estimates. Therefore the results possibly reflected reverse causality and bidirectional.

INTRODUCTION

Arthritis is the most common cause of disability worldwide. Rheumatoid arthritis (RA) is characterized by persistent inflammatory symmetrical synovitis with pain, swelling, and a broad range of systemic manifestations in the peripheral joints [1]. This disease is also associated with sleep disturbances [2], which play an important role in the maintenance of an individual's health [3 4]. Importantly, poor sleep in RA patients may be by pain or may contribute to increase pain and fatigue[5 6]. Additionally, sleep disorders such as sleep apnea or primary insomnia typically result in poor sleep quality in RA patients as well as exacerbate the patient's primary symptoms [7].

Sleep disturbances were affected by more than half of RA patients [8 9] and are thought to be more common among those with active inflammation [10] or physical health conditions such as associated pain, fatigue, and/or functional disabilities [11]. Although physicians often assume that inflammation is the stimulus for RA-related pain, many of these patients continue to experience pain following adequate suppression of inflammation [12]. Furthermore, sleep disturbances and inadequate sleep are related to serious outcomes such as reduced health-related quality of life [13], a higher risk of morbidities [14], and, ultimately, increased all-cause mortality [15]. Additionally, sleep disturbances are almost three-fold more frequent in females than males [16]. Thus, the quality and amount of sleep in patients with RA are important issues for rheumatologists, particularly after the finding that etanercept and infliximab reduce daytime sleepiness [17].

Therefore, the primary aim of the present study was to investigate the association between RA and self-reported sleep duration using 7 years of aggregated cross-sectional data (2007-2013) obtained from the National Health and Nutrition Examination Survey (KNHANES).

METHODS

Study Sample

To evaluate the relationship between sleep duration and RA, the present study analyzed data from the fourth (2007-2009), fifth (2010-2012), and sixth (2013) KNHANES assessments performed by the Korean Ministry of Health and Welfare. The KNHANES is a cross-sectional survey based on stratified multistage probability sampling units of Korean households that targets members of the civilian non-institutionalized South Korean population who are 1 year of age or older. The samples were determined by the household registries of the 2005 National Census Registry.

The total target population initially consisted of 24,871, 25,534, and 8,018 participants who completed the 2007-2009, 2010-2012, and 2013 KNHANES assessments, respectively, which had average response rates of 78.4%, 80.8% ,and 79.3%, respectively. The information from 14,305 individuals aged 1-18 years old were excluded from the present analyses while the information of 44,118 individuals aged 19 years and older were included. Additionally, the present study excluded 6,036 individuals with missing data regarding age, occupation, income, and/or marriage status and 103 individuals with missing data regarding smoking, drinking, perceived stress, exercise, sleep duration, RA, hypertension, and/or dyslipidemia. Thus, a total of 37,979 individuals were selected for the final analyses in the present study. Because all KNHANES data are available publicly, this study did not require approval from an institutional review board.

Variables

Dependent Variables

In the present study, sleep duration was based on self-reported data acquired in response to the question “How many hours do you usually sleep?”. The responses were

classified into three categories (≤ 6 hours, 7-8 hours, and ≥ 9 hours) based on the sleep definitions of the International Classification of Sleep Disorders, 2nd edition, in which ≤ 6 hours is defined as a short sleeper and ≥ 9 hours as a long sleeper [18].

Independent Variables

In the present study, DM2 cases were considered to be the participants who answered "Yes" to the question "Are you currently suffering from rheumatoid arthritis?" in the self-reported data. RA was categorized as either "Yes" or "No".

Sociodemographic Factors

The present analyses included age, gender, household income, marital status, occupation, and region of residency as sociodemographic factors; all of the covariates were categorical. Household income was calculated by dividing a participant's household monthly income by the square root of the household size, and the participants were ranked from lowest to highest income and then grouped into four household income quartiles. Predefined categories were used to categorize household incomes, similar to how the raw KNHANES data are processed. The residency regions were categorized into urban (administrative divisions of a city: Seoul, Daejeon, Daegu, Busan, Incheon, Kwangju, or Ulsan) and rural (not classified as administrative of a city), and occupational status was classified into the following three categories: white collar (administrative, engineering, scientific, teaching and related occupations, sales and related occupations, and service occupation), blue collar (farming, forestry, fishing and hunting, craft and repair, operators, fabricators, and laborers), and unpaid employment (including housewives and students).

Health Behavior Factors

Questions regarding alcohol use, smoking status, and the number of days of moderate exercise per week were assessed by a health interview survey and included as covariates in the present analyses. Alcohol use was further assessed by questioning the participants about their average frequency (days per week or month) of alcohol use during the last year.

Health Status Factors

Perceived stress, the extent of RA pain, and body mass index (BMI) were also included in the present model. The following were categorized into four groups for the present analyses: perceived stress (very high, high, low, and very low), and BMI (thin: < 18.5 kg/m^2, moderate: 18.5-23.9 kg/m^2, overweight: 24.0-26.9 kg/m^2, and obese: > 27.0 kg/m^2 [19] and categorized into two groups for the present analyses: the extent of RA pain (high and low),

Statistical Analysis

The distributions of the general characteristics of the participants were assessed using Chi-square tests, and multinomial logistic regression analyses were used to determine whether the general characteristics, health statuses, and/or health risk behaviors of the participants had relationships with RA. All data were analyzed using SAS software, version 9.4 (SAS Institute; Inc., Cary, NC, USA).

RESULTS

Prevalence of Short Sleep and Long Sleep Durations

Of the 37,979 KNHANES participants included in the present study, 16,254 were male (42.8%), 21,735 were female (57.2%), and 670 were RA patients (1.8%). Of the 15,855 participants who reported a short sleeper(≤ 6 hours), 347 had RA (51.8%), while of the 2,976 participants who reported a long sleeper, 265 had RA (39.6%) (Table 1).

Association between Sleep Duration and Rheumatoid Arthritis

Table 2 portrays the results of the logistic regression analyses after adjusting for age, gender, household income, marital status, occupation, region of residence, smoking status, frequency of alcohol use, number of days of moderate exercise per week, perceived stress, extent of RA pain, BMI, and year of the survey. After adjusting for all of these confounding variables, in terms of RA, the odds of short sleep (≤ 6 hours/day) were 1.23-fold higher (95% confidence interval [CI]: 1.01-1.51) and the odds of long sleep (≥ 9 hours/day) were 1.27-fold higher (95% CI: 0.85-1.88) than for those with sleep durations of 7-8 hours/day (Table 2).

Table 3 depicts the results of a subgroup analysis according to extent of RA painafter adjusting for age, household income, marital status, occupation, region of residence, smoking status, frequency of alcohol use, number of days of moderate exercise per week, perceived stress, BMI, and year of the survey. Those who reported RA were 28% more likely to have short sleep (odds ratio [OR]: 1.28, 95% CI: 1.04 -1.58), while those who not reported RA were not more likely to have short sleep (OR: 0.84, 95% CI: 0.49-1.46), compared with those with reported sleep durations of 7-8 hours (Table 3).

DISCUSSION

Because sleep disturbances may be an important clinical feature of patients with RA, this issue has recently received an increasing amount of attention [20 21]. Thus, the present study aimed to investigate RA and its relationship with sleep duration using 7 years of aggregated data from a large representative population-based survey conducted in Korea. The present study found an association between RA and the reported symptoms of short sleep duration that was statistically significant (OR: 1.23, 95% CI: 1.01-1.51) even in the presence of perceived stress, which suggests that stress could be a trigger or signal for an inappropriate sleep duration in patients with RA. In general, there was a U-shaped association between RA and short or long sleep duration, and this U-shaped relationship remained in this study. in addition, in a subgroup analysis based on extent to pain of RA, these association was statistically significant only in those with high pain of RA. These associations were independent of sociodemographic variables, such as age, gender, household income level, marital status, occupation, and region of residence, health behavior variables, such as smoking status, frequency of alcohol use, and number of days of moderate exercise per week, and health status variables, such as perceived stress, the extent of RA pain, BMI, and year of the survey.

A nationwide study conducted in the United States found that RA are associated with sleep disturbances in approximately 10 million adults [22]. The presence of sleep disturbances in patients diagnosed with a range of rheumatological-related diseases including systemic lupus erythematosus, fibromyalgia, chronic fatigue syndrome, multiple sclerosis, and RA have also been assessed [23]. Additionally, recent studies have indicated that sleep disturbances such as difficulties with the onset of sleep and waking up early in the morning are also major complaints in RA patients, and that fatigue in RA patients is likely due to poor quality of sleep, a functional disability, joint pain, and/or depressive symptoms [23-27]. Poor quality of

sleep and sleep disturbances can worsen physical and mental health conditions, including RA symptoms and pain, in the general population [28]. Similarly, the pain and discomfort caused by RA with inflammation may result in a greater frequency of sleep disturbances, contributing to functional impairments such as poor sleep quality and lack of participation and social engagement, which have a significant negative impact on the health and well-being of individuals [29].

Along with a significantly higher prevalence of fatigue, there is also a greater risk of sleep disturbances such as obstructive sleep apnea (OSA) in patients with RA, because they are more likely to have chronic health issues, including high blood pressure and a high BMI, which can lead to increased risks of cardiovascular disease (CVD) and nocturnal sudden cardiac death [30]. Accordingly, the autonomic response is more severe in patients with chronic OSA than in individuals with a low risk of OSA [30-33].

In the present study, a multinomial logistic regression analysis revealed that the important factors influencing the relationship between RA and sleep duration include perceived stress and the extent of RA pain. Although the causes of sleep disturbances in patients with RA are likely multifactorial, only 30% of older Americans with sleep disturbances seek treatment at hospitals or treatment centers utilizing multidisciplinary approaches, relying on various self-care strategies instead [34 35]. Therefore, the provision of comprehensive care for RA patients requires encouragement of the patient to report sleep disturbances and timely diagnoses to reduce their symptoms. In this manner, the present data regarding the prevalence of sleep disturbances in RA patients will contribute to the awareness of physicians and health care professionals regarding this issue and may aid in the development of appropriate interventions to properly manage, minimize, or eliminate these symptoms.

There are several potential limitations that should be taken into consideration when

interpreting the present results. First, because this study utilized a cross-sectional design, the results may reflect reverse causality and a bidirectional relationship in the association between RA and sleep duration. Therefore, longitudinal studies using validated measures of RA and sleep duration are required to replicate these findings and to clarify the causality and mechanisms that underlie the association between RA and sleep duration. Second, although the use of self-reports is a valuable source of information in large-scale epidemiological studies, the lack of validated questionnaires assessing RA and sleep duration was a major limitation of the present study, as more objective methods tend to yield more accurate results. Controlling for socioeconomic status, health status, and behavior variables, as in the present study, may partially ameliorate these issues, but future in-depth studies are necessary to determine more accurately the relationship between RA and sleep disturbances, including difficulty falling asleep, difficulty maintaining sleep, time spent in bed, wake after sleep onset, sleep onset latency, sleep quality, time of going to bed in the evening, time of turning out the lights with the intention to sleep, wake time in the morning, time of getting out of bed in the morning, and insomnia.

Conclusions

The present study found that patients with RA may be at a higher risk for sleep disturbances than are individuals without RA. This apparent difference may be attributed to pain reported by RA patients which may also be associated with RA itself. The present findings suggest that health care professionals who treat RA patients in routine clinical practice should be aware of the relationship between RA and sleep disturbances and attempt to assess sleep duration, because it may have a significant impact on self-rated health and the risk of CVD[30 36]. Future research that includes objective measures of sleep disturbances is necessary to fully characterize the extent to which sleep disturbances affect patients with RA.

Footnotes

Authors` contributions

JH Kim, EC Park, carried out the acquisition of data, performed the experiments and participated in drafted the manuscript. JH Kim, EC Park, YH Lee participated in the design of the study and performed the statistical analysis. JH Kim, SG Lee, SK Shim, JH Kim conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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Table 1. Demographic Characteristics of the Study Population

	Total		Sleep duration						P-value
			Short sleeper (≤6h)		Appropriate sleeper (7-8h)		Long sleeper (≥9h)		
	N	%	N	%	N	%	N	%	
Rheumatoid arthritis (RA)									<.0001
No	37,309	98.2	15,508	40.8	18,883	49.7	2,918	7.7	
Yes	670	1.8	347	51.8	58	8.7	265	39.6	
Age (yr)									<.0001
≤29	4,751	12.5	1,566	33.0	2,569	54.1	616	13.0	
30-49	14,551	38.3	5,476	37.6	8,259	56.8	816	5.6	
50-69	13,135	34.6	6,001	45.7	6,253	47.6	881	6.7	
≥79	5,542	14.6	2,812	50.7	2,067	37.3	663	12.0	
Gender									<.0001
Male	16,254	42.8	6,732	41.4	8,357	51.4	1,165	7.2	
Female	21,725	57.2	9,123	42.0	10,791	49.7	1,811	8.3	
Household income level									<.0001
Low	7,633	20.1	3,592	47.1	3,226	42.3	815	10.7	
Lower middle	9,685	25.5	4,102	42.4	4,790	49.5	793	8.2	
Upper middle	10,216	26.9	3,980	39.0	5,462	53.5	774	7.6	
High	10,445	27.5	4,181	40.0	5,670	54.3	594	5.7	
Marital status									<.0001
Married	27,602	72.7	11,246	40.7	14,338	52.0	2,018	7.3	
Single	5,312	14.0	1,889	35.6	2,876	54.1	547	10.3	
Separated, divorced	5,065	13.3	2,720	53.7	1,934	38.2	411	8.1	
Occupation									<.0001
White-collar	12,635	33.3	5,171	40.9	6,846	54.2	618	4.9	
Blue-collar	10,340	27.2	4,488	43.4	5,073	49.1	779	7.5	
Unpaid employment	15,004	39.5	6,196	41.3	7,229	48.2	1,579	10.5	
Residential region									<.0001
Urban	17,032	44.9	7,363	43.2	8,517	50.0	1,152	6.8	
Rural	20,947	55.2	8,492	40.5	10,631	50.8	1,824	8.7	
Smoking status									0.402
Current smoker	11,101	29.2	4,564	41.1	5,633	50.7	904	8.1	
Former smoker	4,552	12.0	1,927	42.3	2,280	50.1	345	7.6	
Never smoked	22,326	58.8	9,364	41.9	11,235	50.3	1,727	7.7	
Frequency of alcohol use									<.0001
Never drink	10,950	28.8	4,947	45.2	5,018	45.8	985	9.0	
1 times or less per month	10,786	28.4	4,238	39.3	5,734	53.2	814	7.6	
2-4 times per week	13,510	35.6	5,462	40.4	7,122	52.7	926	6.9	
4 times or more per week	2,733	7.2	1,208	44.2	1,274	46.6	251	9.2	
Number of days of moderate exercise per week									<.0001
Never	23,187	61.1	9,718	41.9	11,457	49.4	2,012	8.7	
1–3	9,145	24.1	3,741	40.9	4,829	52.8	575	6.3	
4–6	3,318	8.7	1,361	41.0	1,761	53.1	196	5.9	
Everyday	2,329	6.1	1,035	44.4	1,101	47.3	193	8.3	
Perceived stress									<.0001
Very high	1,749	4.6	920	52.6	685	39.2	144	8.2	
High	8,442	22.2	3,960	46.9	3,887	46.0	595	7.1	
Low	21,556	56.8	8,495	39.4	11,480	53.3	1,581	7.3	
Very low	6,232	16.4	2,480	39.8	3,096	49.7	656	10.5	
Extent to pain of rheumatoid arthritis									<.0001
Low	36,660	96.5	15,099	41.2	18,708	51.0	2,853	7.8	
High	1,319	3.5	756	57.3	440	33.4	123	9.3	
BMI									<.0001
Thin (<18.5 kg/m2)	1,908	5.0	656	34.4	1,010	52.9	242	12.7	
Moderate (18.5kg/m-23.9kg/m2)	19,689	51.8	7,970	40.5	10,153	51.6	1,566	8.0	
Overweight (24.0kg/m-26.9kg/m2)	10,767	28.4	4,649	43.2	5,351	49.7	767	7.1	
Obese (≥27.0 kg/m2)	5,615	14.8	2,580	46.0	2,634	46.9	401	7.1	
Year									<.0001
2007	1,403	3.7	576	41.1	747	53.2	80	5.7	
2008	6,513	17.2	2,672	41.0	3,258	50.0	583	9.0	
2009	7,338	19.3	2,922	39.8	3,796	51.7	620	8.5	
2010	6,059	16.0	2,461	40.6	3,114	51.4	484	8.0	
2011	5,927	15.6	2,535	42.8	2,947	49.7	445	7.5	
2012	5,465	14.4	2,303	42.1	2,762	50.5	400	7.3	
2013	5,274	13.9	2,386	45.2	14	47.9	364	6.9	
Total	37,979	100.0	15,855	41.8	2,524	50.4	2,976	7.8	

Table 2. Results of logistic regression between rheumatoid arthritis and sleep duration

	Rheumatoid Arthritis (RA)							
	Appropriate sleeper (7-8h)	Short sleeper (≤6h)			Long sleeper (≥9h)			
	Ref	OR	95% CI		OR	95% CI		
Rheumatoid arthritis (RA)								
No	1.00							
Yes		1.23	1.01	1.51	1.27	0.85	1.88	
Age (yr)								
≤29	1.00							
30-49		1.16	1.04	1.31	0.45	0.37	0.55	
50-69		1.49	1.32	1.69	0.51	0.42	0.63	
≥79		2.15	1.85	2.50	0.84	0.65	1.08	
Gender								
Male		1.02	0.95	1.10	0.64	0.55	0.74	
Female	1.00							
Household income level								
Low		1.04	0.95	1.14	1.50	1.27	1.77	
Lower middle		1.01	0.93	1.09	1.25	1.09	1.44	
Upper middle		0.95	0.89	1.02	1.25	1.08	1.44	
High	1.00							
Marital status								
Married	1.00							
Single		1.11	1.00	1.23	0.99	0.82	1.21	
Separated, divorced		1.49	1.37	1.62	0.90	0.77	1.06	
Occupation								
White-collar	1.00							
Blue-collar		1.05	0.97	1.12	1.32	1.14	1.54	
Unpaid employment		0.87	0.81	0.93	1.78	1.55	2.04	
Residential region								
Urban	1.00							
Rural		0.88	0.83	0.94	1.24	1.12	1.38	
Smoking status								
Current smoker		0.99	0.92	1.08	1.51	1.31	1.75	
Former smoker		0.95	0.85	1.05	1.51	1.26	1.81	
Never smoked	1.00							
Frequency of alcohol use								
Never drink		0.96	0.85	1.09	0.88	0.71	1.09	
1 times or less per month		0.89	0.79	1.01	0.81	0.65	1.00	
2-4 times per week		0.93	0.83	1.04	0.79	0.65	0.96	
4 times or more per week	1.00							
Number of days of moderate exercise per week								
Never	1.00							
1–3		0.98	0.92	1.05	0.75	0.66	0.86	
4–6		0.99	0.90	1.09	0.70	0.57	0.85	
Everyday		1.09	0.98	1.22	1.04	0.84	1.28	
Perceived stress								
Very high		1.88	1.64	2.16	1.19	0.93	1.51	
High		1.57	1.44	1.71	0.86	0.74	1.01	
Low		1.12	1.04	1.21	0.85	0.75	0.97	
Very low	1.00							
Extent to pain of rheumatoid arthritis								
Low	1.00							
High		1.39	1.19	1.63	1.22	0.93	1.58	
BMI								
Thin (<18.5 kg/m2)		0.79	0.70	0.90	1.26	1.04	1.53	
Moderate (18.5kg/m-23.9kg/m2)	1.00							
Overweight (24.0kg/m-26.9kg/m2)		1.05	0.99	1.11	0.95	0.84	1.07	
Obese (≥27.0 kg/m2)		1.20	1.11	1.29	1.00	0.86	1.17	
Year								
2007	1.00							
2008		1.05	0.89	1.24	1.30	0.98	1.73	
2009		0.95	0.80	1.12	1.19	0.90	1.57	
2010		1.00	0.84	1.19	1.22	0.91	1.64	
2011		1.03	0.86	1.23	1.10	0.82	1.47	
2012		1.00	0.84	1.19	1.14	0.85	1.54	
2013		1.16	0.98	1.38	1.04	0.78	1.40	

Table 3. Results of logistic regression between rheumatoid arthritis and sleep duration by extent to pain of rheumatoid arthritis

	Rheumatoid Arthritis (RA)						
	Appropriate sleeper (7-8h)	Short sleeper (≤6h)			Long sleeper (≥9h)		
	Ref	OR	95% CI		OR	95% CI	
Extent to pain of rheumatoid arthritis (High)							
Rheumatoid arthritis (RA)							
No	1.00						
Yes		1.28	1.04	1.58	1.40	0.93	2.12
Extent to pain of rheumatoid arthritis (Low)							
Rheumatoid arthritis (RA)							
No	1.00						
Yes		0.84	0.49	1.46	0.52	0.18	1.45

***Adjusted for all variables**

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract(1P)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found(2p)
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported(4p)
Objectives	3	State specific objectives, including any prespecified hypotheses(5p)
Methods		
Study design	4	Present key elements of study design early in the paper(5p)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection(5-6p)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up(6p) *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable(6p)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group(7p)
Bias	9	Describe any efforts to address potential sources of bias(7-8p)
Study size	10	Explain how the study size was arrived at(6p)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why(6p)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding(7-8p)
		(*b*) Describe any methods used to examine subgroups and interactions(N/A)
		(*c*) Explain how missing data were addressed(6p)
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed(6p) *Case-control study*—If applicable, explain how matching of cases and controls was addressed(N/A) *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy(N/A)
		(*e*) Describe any sensitivity analyses(N/A)

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed(8p)
		(b) Give reasons for non-participation at each stage(N/A)
		(c) Consider use of a flow diagram(N/A)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders(5-7p)
		(b) Indicate number of participants with missing data for each variable of interest(5-7p)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) (5-7p)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time(5-7p)
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included(8-9p)
		(*b*) Report category boundaries when continuous variables were categorized(8-9p)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period(8-9p)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses(N/A)
Discussion		
Key results	18	Summarise key results with reference to study objectives(9-10p)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias(12p)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence(8-10p)
Generalisability	21	Discuss the generalisability (external validity) of the study results(12p)
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

The Association of Sleep Duration with Rheumatoid Arthritis in Korean Adults: Analysis of Seven Years of Aggregated Data from the National Health and Nutrition Examination Survey (KNHANES)

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The Association of Sleep Duration with Rheumatoid Arthritis in Korean Adults: Analysis of Seven Years of Aggregated Data from the National Health and Nutrition Examination Survey (KNHANES)

Jae-Hyun Kim[1,2], Eun-Cheol Park[3,4], Kwang Soo Lee[5], Yunhwan Lee[1,2], Sungkeun Shim[6], Jinhee Kim[1,2], Doukyoung Chon[1,2,] Sang-Gyu Lee[4,7]

[1]Department of Preventive Medicine and Public Health, Ajou University School of Medicine, Suwon, Republic of Korea.

[2]Institute on Aging, Ajou University Medical Center, Suwon, Republic of Korea

[3]Preventive Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

[4]Institute of Health Services Research, Yonsei University, Seoul, Republic of Korea

[5]Department of Health Administration, College of Health Sciences, Yonsei University, Wonju, gwangwondo, South Korea

[6]Department of Biostatistics, Graduate School of Public Health, Yonsei University, Seoul, Republic of Korea

[7]Department of Hospital management, Graduate School of Public Health, Yonsei University, Seoul, Republic of Korea

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***Corresponding Author**

Sang Gyu Lee, MD, MBA, Ph.D.

Graduate School of Public Health and Institute of Health Services Research, Yonsei University

50 Yonsei-ro, Seodaemun-gu, Seoul, 120-752, Korea

Phone: +82 2 2228 1524, Fax: +82 2 392 7734

E-mail: LEEVAN@yuhs.ac

ABSTRACT

Objectives: To investigate the association between rheumatoid arthritis (RA) and self-reported sleep duration

Setting: The present study analyzed 7 years of aggregated cross-sectional data (2007-2013) from the Korea National Health and Nutrition Examination Surveys (KNHANES)

Participants: a total of 37,979 individuals were selected for the analyses.

Interventions: rheumatoid arthritis (RA)

Primary and secondary outcome measures: sleep duration

Results: After adjusting for confounding factors, the odds of short-duration sleepers (≤ 6 hours/day) and long-duration sleepers (≥ 9 hours/day) for RA were 1.23-fold (95% confidence interval [CI]: 1.101-1.51) and 1.27-fold (95% CI: 0.85-1.88) higher, respectively, than those for subjects with a sleep duration of 7-8 hours/day. A subgroup analysis according to extent to pain of RA revealed that the strong relationship between RA and sleep disturbances was observed in those with high pain of RA (OR: 1.28 CI: 1.04-1.58).

Conclusion: Individuals with RA may be at a higher risk for sleep disturbances compared with individuals without RA. This apparent difference may be attributed to the pain reported by RA patients, because these factors may significantly affect the self-rated health and risk of cardiovascular disease in this population. Therefore, the provision of comprehensive care for RA patients by health care professionals should include assessments of sleep duration, and patients with RA should be encouraged to report sleep problems.

Keywords: Sleep disturbance, rheumatoid arthritis, sleep

Strengths and limitations of this study

- This study used nationwide survey data of community dwelling people. A large population sample size was representative of the general population, so the results can be generalized to the general population in South Korea.
- The lack of validated questionnaires assessing RA and sleep duration was a major limitation of the present study, as more objective methods tend to yield more accurate results.
- Respondents' reports were subjective and were imperfect measures potentially affected by perception bias and adaptation of resources.
- We used cross-sectional nature data for our estimates. Therefore the results possibly reflected reverse causality and bidirectional.

INTRODUCTION

Arthritis is the most common cause of disability worldwide. Rheumatoid arthritis (RA) is characterized by persistent inflammatory symmetrical synovitis with pain, swelling, and a broad range of systemic manifestations in the peripheral joints [1]. This disease is also associated with sleep disturbances [2], which play an important role in the maintenance of an individual's health [3 4]. Importantly, poor sleep in RA patients could originate from pain or may contribute to increased or increase in pain and fatigue[5 6]. Additionally, sleep disorders such as sleep apnea or primary insomnia typically result in poor sleep quality in RA patients as well as exacerbating the patient's primary symptoms [7].

Sleep disturbances affect more than half of RA patients [8 9] and are thought to be more common among those with active inflammation [10] or physical health conditions such as associated pain, fatigue, and/or functional disabilities [11]. Although physicians often assume that inflammation is the stimulus for RA-related pain, many of these patients continue to experience pain following adequate suppression of inflammation [12]. Furthermore, sleep disturbances and inadequate sleep are related to serious outcomes such as reduced health-related quality of life [13], a higher risk of morbidities [14], and, ultimately, increased all-cause mortality [15]. Additionally, sleep disturbances are almost three-fold more frequent in females than males [16]. Thus, the quality and amount of sleep in patients with RA are important issues for rheumatologists, particularly after the finding that illustrated etanercept and infliximab's ability to reduce daytime sleepiness [17].

Therefore, the primary aim of the present study was to investigate the association between RA and self-reported sleep duration using 7 years of aggregated cross-sectional data (2007-2013) obtained from the National Health and Nutrition Examination Survey (KNHANES).

METHODS

Study Sample

To evaluate the relationship between sleep duration and RA, the present study analyzed data from the fourth (2007-2009), fifth (2010-2012), and sixth (2013) KNHANES assessments performed by the Korean Ministry of Health and Welfare. The KNHANES is a cross-sectional survey based on stratified multistage probability sampling units of Korean households that targets members of the civilian non-institutionalized South Korean population who are 1 year of age or older. The samples were determined by the household registries of the 2005 National Census Registry.

The total target population initially consisted of 24,871, 25,534, and 8,018 participants who completed the 2007-2009, 2010-2012, and 2013 KNHANES assessments, respectively, which had average response rates of 78.4%, 80.8% ,and 79.3%, respectively. The information from 14,305 individuals aged 1-18 years old were excluded from the present analyses while the information of 44,118 individuals aged 19 years and older were included. Additionally, the present study excluded 6,036 individuals with missing data regarding age, occupation, income, and/or marriage status and 103 individuals with missing data regarding smoking, drinking, perceived stress, exercise, sleep duration, RA, hypertension, and/or dyslipidemia. Thus, a total of 37,979 individuals were selected for the final analyses in the present study. Because all KNHANES data are available publicly, this study did not require approval from an institutional review board.

Variables

Dependent Variables

In the present study, sleep duration was based on self-reported data acquired in response to the question “How many hours do you usually sleep?”. The responses were

classified into three categories (≤ 6 hours, 7-8 hours, and ≥ 9 hours) based on the sleep definitions of the International Classification of Sleep Disorders, 2nd edition, in which ≤ 6 hours is defined as a short sleeper and ≥ 9 hours as a long sleeper [18].

Independent Variables

In the present study, DM2 cases were considered to be the participants who answered "Yes" to the question "Are you currently suffering from rheumatoid arthritis?" in the self-reported data. RA was categorized as either "Yes" or "No".

Sociodemographic Factors

The present analyses included age, gender, household income, marital status, occupation, and region of residency as sociodemographic factors; all of the covariates were categorical. Household income was calculated by dividing a participant's household monthly income by the square root of the household size, and the participants were ranked from lowest to highest income and then grouped into four household income quartiles. Predefined categories were used to categorize household incomes, similar to how the raw KNHANES data are processed. The residency regions were categorized into urban (administrative divisions of a city: Seoul, Daejeon, Daegu, Busan, Incheon, Kwangju, or Ulsan) and rural (not classified as administrative of a city), and occupational status was classified into the following three categories: white collar (administrative, engineering, scientific, teaching and related occupations, sales and related occupations, and service occupation), blue collar (farming, forestry, fishing and hunting, craft and repair, operators, fabricators, and laborers), and unpaid employment (including housewives and students).

Health Behavior Factors

Questions regarding alcohol use, smoking status, and the number of days of moderate exercise per week were assessed by a health interview survey and included as covariates in the present analyses. Alcohol use was further assessed by questioning the participants about their average frequency (days per week or month) of alcohol use during the last year.

Health Status Factors

Perceived stress, the extent of RA pain, and body mass index (BMI) were also included in the present model. The following were categorized into four groups for the present analyses: perceived stress (very high, high, low, and very low), and BMI (thin: < 18.5 kg/m^2, moderate: 18.5-23.9 kg/m^2, overweight: 24.0-26.9 kg/m^2, and obese: > 27.0 kg/m^2 [19]. Extent of RA pain was measured by asking the respondents to assess extent suffering from RA using a pictorial representation of 0-10 scores. Extent of RA pain was categorized into two groups: Low (0-5) or High (6-10).

Statistical Analysis

The distributions of the general characteristics of the participants were assessed using Chi-square tests, and multinomial logistic regression analyses were used to determine whether the general characteristics, health statuses, and/or health risk behaviors of the participants had relationships with RA. All data were analyzed using SAS software, version 9.4 (SAS Institute; Inc., Cary, NC, USA).

RESULTS

Prevalence of Short Sleep and Long Sleep Durations

Of the 37,979 KNHANES participants included in the present study, 16,254 were male (42.8%), 21,735 were female (57.2%), and 670 were RA patients (1.8%). Of the 15,855 participants who reported a short sleeper(≤ 6 hours), 347 had RA (51.8%), while of the 2,976 participants who reported a long sleeper, 265 had RA (39.6%) (Table 1).

Association between Sleep Duration and Rheumatoid Arthritis

Table 2 portrays the results of the logistic regression analyses after adjusting for age, gender, household income, marital status, occupation, region of residence, smoking status, frequency of alcohol use, number of days of moderate exercise per week, perceived stress, extent of RA pain, BMI, and year of the survey. After adjusting for all of these confounding variables, in terms of RA, the odds of short sleep (≤ 6 hours/day) were 1.23-fold higher (95% confidence interval [CI]: 1.01-1.51) and the odds of long sleep (≥ 9 hours/day) were 1.27-fold higher (95% CI: 0.85-1.88) than for those with sleep durations of 7-8 hours/day (Table 2).

Table 3 depicts the results of a subgroup analysis according to extent of RA painafter adjusting for age, household income, marital status, occupation, region of residence, smoking status, frequency of alcohol use, number of days of moderate exercise per week, perceived stress, BMI, and year of the survey. Those who reported RA were 28% more likely to have short sleep (odds ratio [OR]: 1.28, 95% CI: 1.04 -1.58), while those who not reported RA were not more likely to have short sleep (OR: 0.84, 95% CI: 0.49-1.46), compared with those with reported sleep durations of 7-8 hours (Table 3).

DISCUSSION

Because sleep disturbances may be an important clinical feature of patients with RA, this issue has recently received an increasing amount of attention [20 21]. Thus, the present study aimed to investigate RA and its relationship with sleep duration using 7 years of aggregated data from a large representative population-based survey conducted in Korea. The present study found an association between RA and the reported symptoms of short sleep duration that was statistically significant (OR: 1.23, 95% CI: 1.01-1.51) even in the presence of perceived stress, which suggests that stress could be a trigger or signal for an inappropriate sleep duration in patients with RA. In general, there is a U-shaped association between RA and short or long sleep duration, and this a similarly shaped relationship was evident in this study. In addition, in a subgroup analysis based on extent to pain of RA, these association were statistically significant only in those with high pain of RA. These associations were independent of sociodemographic variables, such as age, gender, household income level, marital status, occupation, and region of residence, health behavior variables, such as smoking status, frequency of alcohol use, and number of days of moderate exercise per week, and health status variables, such as perceived stress, the extent of RA pain, BMI, and year of the survey.

A nationwide study conducted in the United States found that RA is associated with sleep disturbances in approximately 10 million adults [22]. The presence of sleep disturbances in patients diagnosed with a range of rheumatological-related diseases including systemic lupus erythematosus, fibromyalgia, chronic fatigue syndrome, multiple sclerosis, and RA have also been assessed [23]. Additionally, recent studies have indicated that sleep disturbances such as difficulties with the onset of sleep and waking up early in the morning are also major complaints in RA patients, and that fatigue in RA patients is likely due to poor quality of sleep, a functional disability, joint pain, and/or depressive symptoms [23-27]. Poor quality of

sleep and sleep disturbances can worsen physical and mental health conditions, including RA symptoms and pain, in the general population [28]. Similarly, the pain and discomfort caused by RA with inflammation may result in a greater frequency of sleep disturbances, contributing to functional impairments such as poor sleep quality and lack of participation in and social engagement, which have a significantly negative impact on the health and well-being of individuals [29].

Along with a significantly higher prevalence of fatigue, there is also a greater risk of sleep disturbances such as obstructive sleep apnea (OSA) in patients with RA, because they are more likely to have chronic health issues, including high blood pressure and a high BMI, which can lead to increased risks of cardiovascular disease (CVD) and nocturnal sudden cardiac death [30]. Accordingly, the autonomic response is more severe in patients with chronic OSA than in individuals with a low risk of OSA [30-33].

In the present study, a multinomial logistic regression analysis revealed that the important factors influencing the relationship between RA and sleep duration include perceived stress and the extent of RA pain. Although the causes of sleep disturbances in patients with RA are likely multifactorial, only 30% of older Americans with sleep disturbances seek treatment at hospitals or treatment centers utilizing multidisciplinary approaches, relying on various self-care strategies instead [34 35]. Therefore, the provision of comprehensive care for RA patients requires encouraging the patient to report sleep disturbances as well as conducting timely diagnoses to reduce their symptoms. In this manner, the present data regarding the prevalence of sleep disturbances in RA patients will contribute to the awareness of physicians and health care professionals regarding this issue and may aid in the development of appropriate interventions to properly manage, minimize, or eliminate these symptoms.

There are several potential limitations that should be taken into consideration when

interpreting the present results. First, because this study utilized a cross-sectional design, the results may reflect reverse causality and a bidirectional relationship in the association between RA and sleep duration. Therefore, longitudinal studies using validated measures of RA and sleep duration are required to replicate these findings and to clarify the causality and mechanisms that underlie the association between RA and sleep duration. Second, although the use of self-reports is a valuable source of information in large-scale epidemiological studies, the lack of validated questionnaires assessing RA and sleep duration was a major limitation of the present study, as more objective methods tend to yield more accurate results. Controlling for socioeconomic status, health status, and behavior variables, as in the present study, may partially ameliorate these issues, but future in-depth studies are necessary to determine more accurately the relationship between RA and sleep disturbances (more accurately), including difficulty falling asleep, difficulty maintaining sleep, time spent in bed, wakeing after sleep onset, sleep onset latency, sleep quality, time of going to bed in the evening, time of turning out the lights with the intention to sleep, wake time in the morning, time of getting out of bed in the morning, and insomnia.

Conclusions

The present study found that patients with RA may be at a higher risk for sleep disturbances than are individuals without RA. This apparent difference may be attributed to pain reported by RA patients which may also be associated with RA itself. The present findings suggest that health care professionals who treat RA patients in routine clinical practice should be aware of the relationship between RA and sleep disturbances and attempt to assess sleep duration, because it may have a significant impact on self-rated health and the risk of CVD[30 36]. Future research that includes objective measures of sleep disturbances is necessary to fully characterize the extent to which sleep disturbances affect patients with RA.

Footnotes

Authors` contributions

JH Kim, EC Park, carried out the acquisition of data, performed the experiments and participated in drafted the manuscript. JH Kim, EC Park, YH Lee participated in the design of the study and performed the statistical analysis. JH Kim, SG Lee, SK Shim, JH Kim conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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Table 1. Demographic Characteristics of the Study Population

	Total		Sleep duration						P-value
			Short sleeper (≤6h)		Appropriate sleeper (7-8h)		Long sleeper (≥9h)		
	N	%	N	%	N	%	N	%	
Rheumatoid arthritis (RA)									<.0001
No	37,309	98.2	15,508	40.8	18,883	49.7	2,918	7.7	
Yes	670	1.8	347	51.8	58	8.7	265	39.6	
Age (yr)									<.0001
≤29	4,751	12.5	1,566	33.0	2,569	54.1	616	13.0	
30-49	14,551	38.3	5,476	37.6	8,259	56.8	816	5.6	
50-69	13,135	34.6	6,001	45.7	6,253	47.6	881	6.7	
≥79	5,542	14.6	2,812	50.7	2,067	37.3	663	12.0	
Gender									<.0001
Male	16,254	42.8	6,732	41.4	8,357	51.4	1,165	7.2	
Female	21,725	57.2	9,123	42.0	10,791	49.7	1,811	8.3	
Household income level									<.0001
Low	7,633	20.1	3,592	47.1	3,226	42.3	815	10.7	
Lower middle	9,685	25.5	4,102	42.4	4,790	49.5	793	8.2	
Upper middle	10,216	26.9	3,980	39.0	5,462	53.5	774	7.6	
High	10,445	27.5	4,181	40.0	5,670	54.3	594	5.7	
Marital status									<.0001
Married	27,602	72.7	11,246	40.7	14,338	52.0	2,018	7.3	
Single	5,312	14.0	1,889	35.6	2,876	54.1	547	10.3	
Separated, divorced	5,065	13.3	2,720	53.7	1,934	38.2	411	8.1	
Occupation									<.0001
White-collar	12,635	33.3	5,171	40.9	6,846	54.2	618	4.9	
Blue-collar	10,340	27.2	4,488	43.4	5,073	49.1	779	7.5	
Unpaid employment	15,004	39.5	6,196	41.3	7,229	48.2	1,579	10.5	
Residential region									<.0001
Urban	17,032	44.9	7,363	43.2	8,517	50.0	1,152	6.8	
Rural	20,947	55.2	8,492	40.5	10,631	50.8	1,824	8.7	
Smoking status									0.402
Current smoker	11,101	29.2	4,564	41.1	5,633	50.7	904	8.1	
Former smoker	4,552	12.0	1,927	42.3	2,280	50.1	345	7.6	
Never smoked	22,326	58.8	9,364	41.9	11,235	50.3	1,727	7.7	
Frequency of alcohol use									<.0001
Never drink	10,950	28.8	4,947	45.2	5,018	45.8	985	9.0	
1 times or less per month	10,786	28.4	4,238	39.3	5,734	53.2	814	7.6	
2-4 times per week	13,510	35.6	5,462	40.4	7,122	52.7	926	6.9	
4 times or more per week	2,733	7.2	1,208	44.2	1,274	46.6	251	9.2	
Number of days of moderate exercise per week									<.0001
Never	23,187	61.1	9,718	41.9	11,457	49.4	2,012	8.7	
1–3	9,145	24.1	3,741	40.9	4,829	52.8	575	6.3	
4–6	3,318	8.7	1,361	41.0	1,761	53.1	196	5.9	
Everyday	2,329	6.1	1,035	44.4	1,101	47.3	193	8.3	
Perceived stress									<.0001
Very high	1,749	4.6	920	52.6	685	39.2	144	8.2	
High	8,442	22.2	3,960	46.9	3,887	46.0	595	7.1	
Low	21,556	56.8	8,495	39.4	11,480	53.3	1,581	7.3	
Very low	6,232	16.4	2,480	39.8	3,096	49.7	656	10.5	
Extent to pain of rheumatoid arthritis									<.0001
Low	36,660	96.5	15,099	41.2	18,708	51.0	2,853	7.8	
High	1,319	3.5	756	57.3	440	33.4	123	9.3	
BMI									<.0001
Thin (<18.5 kg/m2)	1,908	5.0	656	34.4	1,010	52.9	242	12.7	
Moderate (18.5kg/m-23.9kg/m2)	19,689	51.8	7,970	40.5	10,153	51.6	1,566	8.0	
Overweight (24.0kg/m-26.9kg/m2)	10,767	28.4	4,649	43.2	5,351	49.7	767	7.1	
Obese (≥27.0 kg/m2)	5,615	14.8	2,580	46.0	2,634	46.9	401	7.1	
Year									<.0001
2007	1,403	3.7	576	41.1	747	53.2	80	5.7	
2008	6,513	17.2	2,672	41.0	3,258	50.0	583	9.0	
2009	7,338	19.3	2,922	39.8	3,796	51.7	620	8.5	
2010	6,059	16.0	2,461	40.6	3,114	51.4	484	8.0	
2011	5,927	15.6	2,535	42.8	2,947	49.7	445	7.5	
2012	5,465	14.4	2,303	42.1	2,762	50.5	400	7.3	
2013	5,274	13.9	2,386	45.2	14	47.9	364	6.9	
Total	37,979	100.0	15,855	41.8	2,524	50.4	2,976	7.8	

Table 2. Results of logistic regression between rheumatoid arthritis and sleep duration

	Rheumatoid Arthritis (RA)					
	Appropriate sleeper (7-8h)	Short sleeper (≤6h)		Long sleeper (≥9h)		
	Ref	OR	95% CI	OR	95% CI	
Rheumatoid arthritis (RA)						
No	1.00					
Yes		1.23	1.01 1.51	1.27	0.85	1.88
Age (yr)						
≤29	1.00					
30-49		1.16	1.04 1.31	0.45	0.37	0.55
50-69		1.49	1.32 1.69	0.51	0.42	0.63
≥79		2.15	1.85 2.50	0.84	0.65	1.08
Gender						
Male		1.02	0.95 1.10	0.64	0.55	0.74
Female	1.00					
Household income level						
Low		1.04	0.95 1.14	1.50	1.27	1.77
Lower middle		1.01	0.93 1.09	1.25	1.09	1.44
Upper middle		0.95	0.89 1.02	1.25	1.08	1.44
High	1.00					
Marital status						
Married	1.00					
Single		1.11	1.00 1.23	0.99	0.82	1.21
Separated, divorced		1.49	1.37 1.62	0.90	0.77	1.06
Occupation						
White-collar	1.00					
Blue-collar		1.05	0.97 1.12	1.32	1.14	1.54
Unpaid employment		0.87	0.81 0.93	1.78	1.55	2.04
Residential region						
Urban	1.00					
Rural		0.88	0.83 0.94	1.24	1.12	1.38
Smoking status						
Current smoker		0.99	0.92 1.08	1.51	1.31	1.75
Former smoker		0.95	0.85 1.05	1.51	1.26	1.81
Never smoked	1.00					
Frequency of alcohol use						
Never drink		0.96	0.85 1.09	0.88	0.71	1.09
1 times or less per month		0.89	0.79 1.01	0.81	0.65	1.00
2-4 times per week		0.93	0.83 1.04	0.79	0.65	0.96
4 times or more per week	1.00					
Number of days of moderate exercise per week						
Never	1.00					
1–3		0.98	0.92 1.05	0.75	0.66	0.86
4–6		0.99	0.90 1.09	0.70	0.57	0.85
Everyday		1.09	0.98 1.22	1.04	0.84	1.28
Perceived stress						
Very high		1.88	1.64 2.16	1.19	0.93	1.51
High		1.57	1.44 1.71	0.86	0.74	1.01
Low		1.12	1.04 1.21	0.85	0.75	0.97
Very low	1.00					
Extent to pain of rheumatoid arthritis						
Low	1.00					
High		1.39	1.19 1.63	1.22	0.93	1.58
BMI						
Thin (<18.5 kg/m2)		0.79	0.70 0.90	1.26	1.04	1.53
Moderate (18.5kg/m-23.9kg/m2)	1.00					
Overweight (24.0kg/m-26.9kg/m2)		1.05	0.99 1.11	0.95	0.84	1.07
Obese (≥27.0 kg/m2)		1.20	1.11 1.29	1.00	0.86	1.17
Year						
2007	1.00					
2008		1.05	0.89 1.24	1.30	0.98	1.73
2009		0.95	0.80 1.12	1.19	0.90	1.57
2010		1.00	0.84 1.19	1.22	0.91	1.64
2011		1.03	0.86 1.23	1.10	0.82	1.47
2012		1.00	0.84 1.19	1.14	0.85	1.54
2013		1.16	0.98 1.38	1.04	0.78	1.40

Table 3. Results of logistic regression between rheumatoid arthritis and sleep duration by extent to pain of rheumatoid arthritis

	Rheumatoid Arthritis (RA)						
	Appropriate sleeper (7-8h)	Short sleeper (≤6h)			Long sleeper (≥9h)		
	Ref	OR	95% CI		OR	95% CI	
Extent to pain of rheumatoid arthritis (High)							
Rheumatoid arthritis (RA)							
No	1.00						
Yes		1.28	1.04	1.58	1.40	0.93	2.12
Extent to pain of rheumatoid arthritis (Low)							
Rheumatoid arthritis (RA)							
No	1.00						
Yes		0.84	0.49	1.46	0.52	0.18	1.45

***Adjusted for all variables**

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract(1P)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found(2p)
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported(4p)
Objectives	3	State specific objectives, including any prespecified hypotheses(5p)
Methods		
Study design	4	Present key elements of study design early in the paper(5p)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection(5-6p)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up(6p) *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable(6p)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group(7p)
Bias	9	Describe any efforts to address potential sources of bias(7-8p)
Study size	10	Explain how the study size was arrived at(6p)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why(6p)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding(7-8p)
		(*b*) Describe any methods used to examine subgroups and interactions(N/A)
		(*c*) Explain how missing data were addressed(6p)
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed(6p) *Case-control study*—If applicable, explain how matching of cases and controls was addressed(N/A) *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy(N/A)
		(*e*) Describe any sensitivity analyses(N/A)

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed(8p)
		(b) Give reasons for non-participation at each stage(N/A)
		(c) Consider use of a flow diagram(N/A)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders(5-7p)
		(b) Indicate number of participants with missing data for each variable of interest(5-7p)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) (5-7p)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time(5-7p)
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included(8-9p)
		(*b*) Report category boundaries when continuous variables were categorized(8-9p)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period(8-9p)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses(N/A)
Discussion		
Key results	18	Summarise key results with reference to study objectives(9-10p)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias(12p)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence(8-10p)
Generalisability	21	Discuss the generalisability (external validity) of the study results(12p)
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The Association of Sleep Duration with Rheumatoid Arthritis in Korean Adults: Analysis of Seven Years of Aggregated Data from the National Health and Nutrition Examination Survey (KNHANES)

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The Association of Sleep Duration with Rheumatoid Arthritis in Korean Adults: Analysis of Seven Years of Aggregated Data from the National Health and Nutrition Examination Survey (KNHANES)

Jae-Hyun Kim[1,2], Eun-Cheol Park[3,4], Kwang Soo Lee[5], Yunhwan Lee[1,2], Sungkeun Shim[6], Jinhee Kim[1,2], Doukyoung Chon[1,2,] Sang-Gyu Lee[4,7]

[1]Department of Preventive Medicine and Public Health, Ajou University School of Medicine, Suwon, Republic of Korea.

[2]Institute on Aging, Ajou University Medical Center, Suwon, Republic of Korea

[3]Preventive Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

[4]Institute of Health Services Research, Yonsei University, Seoul, Republic of Korea

[5]Department of Health Administration, College of Health Sciences, Yonsei University, Wonju, gwangwondo, South Korea

[6]Department of Biostatistics, Graduate School of Public Health, Yonsei University, Seoul, Republic of Korea

[7]Department of Hospital management, Graduate School of Public Health, Yonsei University, Seoul, Republic of Korea

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***Corresponding Author**

Sang Gyu Lee, MD, MBA, Ph.D.

Graduate School of Public Health and Institute of Health Services Research, Yonsei University

50 Yonsei-ro, Seodaemun-gu, Seoul, 120-752, Korea

Phone: +82 2 2228 1524, Fax: +82 2 392 7734

E-mail: LEEVAN@yuhs.ac

ABSTRACT

Objectives: To investigate the association between rheumatoid arthritis (RA) and self-reported sleep duration

Setting: The present study analyzed 7 years of aggregated cross-sectional data (2007-2013) from the Korea National Health and Nutrition Examination Surveys (KNHANES)

Participants: a total of 37,979 individuals were selected for the analyses.

Interventions: rheumatoid arthritis (RA)

Primary and secondary outcome measures: sleep duration

Results: After adjusting for confounding factors, the odds of short-duration sleepers (≤ 6 hours/day) and long-duration sleepers (≥ 9 hours/day) for RA were 1.23-fold (95% confidence interval [CI]: 1.101-1.51) and 1.27-fold (95% CI: 0.85-1.88) higher, respectively, than those for subjects with a sleep duration of 7-8 hours/day. A subgroup analysis according to the extent of pain in RA revealed that the strong relationship between RA and sleep disturbances was observed in those with high pain from RA (OR: 1.28 CI: 1.04-1.58).

Conclusion: Individuals with RA may be at a higher risk for sleep disturbances compared with individuals without RA. Therefore, the provision of comprehensive care for RA patients by health care professionals should include assessments of sleep duration, and patients with RA should be encouraged to report sleep problems.

Keywords: Sleep disturbance, rheumatoid arthritis, sleep

Strengths and limitations of this study

- This study used nationwide survey data of community dwelling people. A large population sample size was representative of the general population, so the results can be generalized to the general population in South Korea.
- The lack of validated questionnaires assessing RA and sleep duration was a major limitation of the present study, as more objective methods tend to yield more accurate results.
- Respondents' reports were subjective and were imperfect measures potentially affected by perception bias and adaptation of resources.
- We used cross-sectional nature data for our estimates. Therefore the results possibly reflected reverse causality and bidirectional.

INTRODUCTION

Arthritis is the most common cause of disability worldwide. Rheumatoid arthritis (RA) is characterized by persistent inflammatory symmetrical synovitis with pain, swelling, and a broad range of systemic manifestations in the peripheral joints [1]. This disease is also associated with sleep disturbances [2], which play an important role in the maintenance of an individual's health [3 4]. **Importantly, poor sleep in RA patients could originate from pain or may contribute to increased level of pain and fatigue[5 6].** Additionally, sleep disorders such as sleep apnea or primary insomnia typically result in poor sleep quality in RA patients as well as exacerbating the patient's primary symptoms [7].

Sleep disturbances affect more than half of RA patients [8 9] and are thought to be more common among those with active inflammation [10] or physical health conditions such as associated pain, fatigue, and/or functional disabilities [11]. Although physicians often assume that inflammation is the stimulus for RA-related pain, many of these patients continue to experience pain following adequate suppression of inflammation [12]. Furthermore, sleep disturbances and inadequate sleep are related to serious outcomes such as reduced health-related quality of life [13], a higher risk of morbidities [14], and, ultimately, increase in all-cause mortality [15]. Additionally, sleep disturbances are almost three-fold more frequent in females than males [16]. Thus, the quality and amount of sleep in patients with RA are important issues for rheumatologists, particularly after the finding that illustrated etanercept and infliximab's ability to reduce daytime sleepiness [17].

Therefore, the primary aim of the present study was to investigate the association between RA and self-reported sleep duration using 7 years of aggregated cross-sectional data (2007-2013) obtained from the National Health and Nutrition Examination Survey (KNHANES).

METHODS

Study Sample

To evaluate the relationship between sleep duration and RA, the present study analyzed data from the fourth (2007-2009), fifth (2010-2012), and sixth (2013) KNHANES assessments performed by the Korean Ministry of Health and Welfare. The KNHANES is a cross-sectional survey based on stratified multistage probability sampling units of Korean households that targets members of the civilian non-institutionalized South Korean population who are 1 year of age or older. The samples were determined by the household registries of the 2005 National Census Registry.

The total target population initially consisted of 24,871, 25,534, and 8,018 participants who completed the 2007-2009, 2010-2012, and 2013 KNHANES assessments, which had average response rates of 78.4%, 80.8% ,and 79.3%, respectively. The information from 14,305 individuals aged 1-18 years old were excluded from the present analyses while the information of 44,118 individuals aged 19 years and older were included. Additionally, the present study excluded 6,036 individuals with missing data regarding age, occupation, income, and/or marriage status and 103 individuals with missing data regarding smoking, drinking, perceived stress, exercise, sleep duration, RA, hypertension, and/or dyslipidemia. Thus, a total of 37,979 individuals were selected for the final analyses in the present study. Because all KNHANES data are available publicly, this study did not require approval from an institutional review board.

Variables

Dependent Variables

In the present study, sleep duration was based on self-reported data acquired in response to the question “How many hours do you usually sleep?”. The responses were

classified into three categories (≤ 6 hours, 7-8 hours, and ≥ 9 hours) based on the sleep definitions of the International Classification of Sleep Disorders, 2nd edition, in which ≤ 6 hours is defined as a short sleeper and ≥ 9 hours as a long sleeper [18].

Independent Variables

In the present study, DM2 cases were considered to be the participants who answered "Yes" to the question "Are you currently suffering from rheumatoid arthritis?" in the self-reported data. RA was categorized as either "Yes" or "No".

Sociodemographic Factors

The present analyses included age, gender, household income, marital status, occupation, and region of residency as sociodemographic factors; all of the covariates were categorical. **Individual income was calculated by dividing a participant's household monthly income by the square root of the household size**, and the participants were ranked from lowest to highest income and then grouped into four household income quartiles. Predefined categories were used to categorize household incomes, similar to how the raw KNHANES data are processed. The residency regions were categorized into urban (administrative divisions of a city: Seoul, Daejeon, Daegu, Busan, Incheon, Kwangju, or Ulsan) and rural (not classified as administrative of a city), and occupational status was classified into the following three categories: white collar (administrative, engineering, scientific, teaching and related occupations, sales and related occupations, and service occupation), blue collar (farming, forestry, fishing and hunting, craft and repair, operators, fabricators, and laborers), and unpaid employment (including housewives and students).

Health Behavior Factors

Questions regarding alcohol use, smoking status, and the number of days of moderate exercise per week were assessed by a health interview survey and included as covariates in the present analyses. Alcohol use was further assessed by questioning the participants about their average frequency (days per week or month) of alcohol use during the last year.

Health Status Factors

Perceived stress, the extent of RA pain, and body mass index (BMI) were also included in the present model. The following were categorized into four groups for the present analyses: perceived stress (very high, high, low, and very low), and BMI (thin: < 18.5 kg/m^2, moderate: 18.5-23.9 kg/m^2, overweight: 24.0-26.9 kg/m^2, and obese: > 27.0 kg/m)^2 [19]. Extent of RA pain was measured by asking the respondents to assess the extent suffering from RA using a pictorial representation of 0-10 scores. Extent of RA pain was categorized into two groups: Low (0-5) or High (6-10).

Statistical Analysis

The distributions of the general characteristics of the participants were assessed using Chi-square tests, and multinomial logistic regression analyses were used to determine whether the general characteristics, health statuses, and/or health risk behaviors of the participants had relationships with RA. All data were analyzed using SAS software, version 9.4 (SAS Institute; Inc., Cary, NC, USA).

RESULTS

Prevalence of Short Sleep and Long Sleep Durations

Of the 37,979 KNHANES participants included in the present study, 16,254 were male (42.8%), 21,735 were female (57.2%), and 670 were RA patients (1.8%). Of the 15,855 participants who reported a short sleeper(≤ 6 hours), 347 had RA (51.8%), while of the 2,976 participants who reported a long sleeper (≥ 9 hours), 265 had RA (39.6%) (Table 1).

Association between Sleep Duration and Rheumatoid Arthritis

Table 2 portrays the results of the logistic regression analyses after adjusting for age, gender, household income, marital status, occupation, region of residence, smoking status, frequency of alcohol use, number of days of moderate exercise per week, perceived stress, extent of RA pain, BMI, and year of the survey. After adjusting for all of these confounding variables, in terms of RA, the odds of short sleep (≤ 6 hours/day) were 1.23-fold higher (95% confidence interval [CI]: 1.01-1.51) and the odds of long sleep (≥ 9 hours/day) were 1.27-fold higher (95% CI: 0.85-1.88) than for those with sleep durations of 7-8 hours/day (Table 2).

Table 3 depicts the results of a subgroup analysis according to the extent of RA pain after adjusting for age, household income, marital status, occupation, region of residence, smoking status, frequency of alcohol use, number of days of moderate exercise per week, perceived stress, BMI, and year of the survey. Those who reported RA were 28% more likely to have short sleep (odds ratio [OR]: 1.28, 95% CI: 1.04 -1.58), while those who did not report RA were not more likely to have short sleep (OR: 0.84, 95% CI: 0.49-1.46), compared with those with reported sleep durations of 7-8 hours (Table 3).

DISCUSSION

Because sleep disturbances may be an important clinical feature for patients with RA, this issue has recently received an increasing amount of attention [20 21]. Thus, the present study aimed to investigate RA and its relationship with sleep duration using 7 years of aggregated data from a large representative population-based survey conducted in Korea. The present study found an association between RA and the reported symptoms of short sleep duration that was statistically significant (OR: 1.23, 95% CI: 1.01-1.51) even in the presence of perceived stress, which suggests that stress could be a trigger or signal for an inappropriate sleep duration in patients with RA. In general, there is a U-shaped association between RA and short or long sleep duration, and this a similarly shaped relationship was evident in this study. In addition, in a subgroup analysis based on the extent of pain in RA, these associations were statistically significant only in those with high pain from RA. These associations were independent of sociodemographic variables, (e.g., age, gender, household income level, marital status, occupation, and region of residence), health behavior variables (e.g., smoking status, frequency of alcohol use, and number of days of moderate exercise per week), and health status variables (e.g., perceived stress, the extent of RA pain, BMI), and year of the survey.

A nationwide study conducted in the United States found that RA is associated with sleep disturbances in approximately 10 million adults [22]. The presence of sleep disturbances in patients diagnosed with a range of rheumatological-related diseases including systemic lupus erythematosus, fibromyalgia, chronic fatigue syndrome, multiple sclerosis, and RA have also been assessed [23]. Additionally, recent studies have indicated that sleep disturbances from other causes such as difficulties with the onset of sleep and waking up early in the morning are also major complaints in RA patients, and that fatigue in RA patients is likely due to poor quality of sleep, a functional disability, joint pain, and/or depressive symptoms [23-

[27]. Poor quality of sleep and sleep disturbances can worsen physical and mental health conditions, including RA symptoms and pain, in the general population [28]. Similarly, the pain and discomfort caused by RA with inflammation may result in a greater frequency of sleep disturbances, contributing to functional impairments such as poor sleep quality which have a significantly negative impact on the health and well-being of individuals [29].

Along with a significantly higher prevalence of fatigue, there is also a greater risk of sleep disturbances from causes such as obstructive sleep apnea (OSA) in patients with RA, because they are more likely to have chronic health issues, including high blood pressure and high BMI. This consequently leads to increased risks of cardiovascular disease (CVD) and nocturnal sudden cardiac death [30]. Accordingly, the autonomic response is more severe in patients with chronic OSA than in individuals with a low risk of OSA [30-33].

In the present study, a multinomial logistic regression analysis revealed that the important factors influencing the relationship between RA and sleep duration include perceived stress and the extent of RA pain. Although the causes of sleep disturbances in patients with RA are likely multifactorial, only 30% of older Americans with sleep disturbances seek treatment at hospitals or treatment centers utilizing multidisciplinary approaches, relying on various self-care strategies instead [34 35]. Therefore, the provision of comprehensive care for RA patients requires encouraging the patient to report sleep disturbances as well as conducting timely diagnoses to reduce their symptoms. In this manner, the present data regarding the prevalence of sleep disturbances in RA patients will contribute to the awareness of physicians and health care professionals regarding this issue and may aid in the development of appropriate interventions to properly manage, minimize, or eliminate these symptoms.

There are several potential limitations that should be taken into consideration when interpreting the present results. First, because this study utilized a cross-sectional design, the

results may reflect reverse causality and a bidirectional relationship in the association between RA and sleep duration. Therefore, longitudinal studies using validated measures of RA and sleep duration are required to see if these findings can be replicated and to clarify the causality and mechanisms that underlie the association between RA and sleep duration. Second, although the use of self-reports is a valuable source of information in large-scale epidemiological studies, the lack of validated questionnaires assessing RA and sleep duration was a major limitation of the present study, as more objective methods tend to yield more accurate results. Controlling for socioeconomic status, health status, and behavior variables, as in the present study, may partially ameliorate these issues, but future in-depth studies are necessary to determine more accurately the relationship between RA and sleep disturbances, including difficulty falling asleep, difficulty maintaining sleep, time spent in bed, waking after sleep onset, sleep onset latency, sleep quality, time of going to bed in the evening, time of turning out the lights with the intention to sleep, wake time in the morning, time of getting out of bed in the morning, and insomnia.

Conclusions

The present study found that patients with RA may be at a higher risk for sleep disturbances than are individuals without RA. This apparent difference may be attributed to pain reported by RA patients which may also be associated with RA itself. The present findings suggest that health care professionals who treat RA patients in routine clinical practice should be aware of the relationship between RA and sleep disturbances. Future research that includes objective measures of sleep disturbances is necessary to fully characterize the extent to which sleep disturbances affect patients with RA.

Footnotes

Authors` contributions

JH Kim, EC Park, carried out the acquisition of data, performed the experiments and participated in drafted the manuscript. JH Kim, EC Park, YH Lee participated in the design of the study and performed the statistical analysis. JH Kim, SG Lee, SK Shim, JH Kim conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

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Table 1. Demographic Characteristics of the Study Population

	Total		Sleep duration						P-value
			Short sleeper (≤6h)		Appropriate sleeper (7-8h)		Long sleeper (≥9h)		
	N	%	N	%	N	%	N	%	
Rheumatoid arthritis (RA)									<.0001
No	37,309	98.2	15,508	40.8	18,883	49.7	2,918	7.7	
Yes	670	1.8	347	51.8	58	8.7	265	39.6	
Age (yr)									<.0001
≤29	4,751	12.5	1,566	33.0	2,569	54.1	616	13.0	
30-49	14,551	38.3	5,476	37.6	8,259	56.8	816	5.6	
50-69	13,135	34.6	6,001	45.7	6,253	47.6	881	6.7	
≥79	5,542	14.6	2,812	50.7	2,067	37.3	663	12.0	
Gender									<.0001
Male	16,254	42.8	6,732	41.4	8,357	51.4	1,165	7.2	
Female	21,725	57.2	9,123	42.0	10,791	49.7	1,811	8.3	
Household income level									<.0001
Low	7,633	20.1	3,592	47.1	3,226	42.3	815	10.7	
Lower middle	9,685	25.5	4,102	42.4	4,790	49.5	793	8.2	
Upper middle	10,216	26.9	3,980	39.0	5,462	53.5	774	7.6	
High	10,445	27.5	4,181	40.0	5,670	54.3	594	5.7	
Marital status									<.0001
Married	27,602	72.7	11,246	40.7	14,338	52.0	2,018	7.3	
Single	5,312	14.0	1,889	35.6	2,876	54.1	547	10.3	
Separated, divorced	5,065	13.3	2,720	53.7	1,934	38.2	411	8.1	
Occupation									<.0001
White-collar	12,635	33.3	5,171	40.9	6,846	54.2	618	4.9	
Blue-collar	10,340	27.2	4,488	43.4	5,073	49.1	779	7.5	
Unpaid employment	15,004	39.5	6,196	41.3	7,229	48.2	1,579	10.5	
Residential region									<.0001
Urban	17,032	44.9	7,363	43.2	8,517	50.0	1,152	6.8	
Rural	20,947	55.2	8,492	40.5	10,631	50.8	1,824	8.7	
Smoking status									0.402
Current smoker	11,101	29.2	4,564	41.1	5,633	50.7	904	8.1	
Former smoker	4,552	12.0	1,927	42.3	2,280	50.1	345	7.6	
Never smoked	22,326	58.8	9,364	41.9	11,235	50.3	1,727	7.7	
Frequency of alcohol use									<.0001
Never drink	10,950	28.8	4,947	45.2	5,018	45.8	985	9.0	
1 times or less per month	10,786	28.4	4,238	39.3	5,734	53.2	814	7.6	
2-4 times per week	13,510	35.6	5,462	40.4	7,122	52.7	926	6.9	
4 times or more per week	2,733	7.2	1,208	44.2	1,274	46.6	251	9.2	
Number of days of moderate exercise per week									<.0001
Never	23,187	61.1	9,718	41.9	11,457	49.4	2,012	8.7	
1–3	9,145	24.1	3,741	40.9	4,829	52.8	575	6.3	
4–6	3,318	8.7	1,361	41.0	1,761	53.1	196	5.9	
Everyday	2,329	6.1	1,035	44.4	1,101	47.3	193	8.3	
Perceived stress									<.0001
Very high	1,749	4.6	920	52.6	685	39.2	144	8.2	
High	8,442	22.2	3,960	46.9	3,887	46.0	595	7.1	
Low	21,556	56.8	8,495	39.4	11,480	53.3	1,581	7.3	
Very low	6,232	16.4	2,480	39.8	3,096	49.7	656	10.5	
Extent of pain from rheumatoid arthritis									<.0001
Low	36,660	96.5	15,099	41.2	18,708	51.0	2,853	7.8	
High	1,319	3.5	756	57.3	440	33.4	123	9.3	
BMI									<.0001
Thin (<18.5 kg/m2)	1,908	5.0	656	34.4	1,010	52.9	242	12.7	
Moderate (18.5kg/m-23.9kg/m2)	19,689	51.8	7,970	40.5	10,153	51.6	1,566	8.0	
Overweight (24.0kg/m-26.9kg/m2)	10,767	28.4	4,649	43.2	5,351	49.7	767	7.1	
Obese (≥27.0 kg/m2)	5,615	14.8	2,580	46.0	2,634	46.9	401	7.1	
Year									<.0001
2007	1,403	3.7	576	41.1	747	53.2	80	5.7	
2008	6,513	17.2	2,672	41.0	3,258	50.0	583	9.0	
2009	7,338	19.3	2,922	39.8	3,796	51.7	620	8.5	
2010	6,059	16.0	2,461	40.6	3,114	51.4	484	8.0	
2011	5,927	15.6	2,535	42.8	2,947	49.7	445	7.5	
2012	5,465	14.4	2,303	42.1	2,762	50.5	400	7.3	
2013	5,274	13.9	2,386	45.2	2,524	47.9	364	6.9	
Total	37,979	100.0	15,855	41.8	19,148	50.4	2,976	7.8	

Table 2. Results of logistic regression between rheumatoid arthritis and sleep duration

	Rheumatoid Arthritis (RA)								
	Appropriate sleeper (7-8h)	Short sleeper (≤6h)			Long sleeper (≥9h)				
	Ref	OR	95% CI		OR	95% CI			
Rheumatoid arthritis (RA)									
No	1.00								
Yes		1.23	1.01	1.51	1.27	0.85	1.88		
Age (yr)									
≤29	1.00								
30-49		1.16	1.04	1.31	0.45	0.37	0.55		
50-69		1.49	1.32	1.69	0.51	0.42	0.63		
≥79		2.15	1.85	2.50	0.84	0.65	1.08		
Gender									
Male		1.02	0.95	1.10	0.64	0.55	0.74		
Female	1.00								
Household income level									
Low		1.04	0.95	1.14	1.50	1.27	1.77		
Lower middle		1.01	0.93	1.09	1.25	1.09	1.44		
Upper middle		0.95	0.89	1.02	1.25	1.08	1.44		
High	1.00								
Marital status									
Married	1.00								
Single		1.11	1.00	1.23	0.99	0.82	1.21		
Separated, divorced		1.49	1.37	1.62	0.90	0.77	1.06		
Occupation									
White-collar	1.00								
Blue-collar		1.05	0.97	1.12	1.32	1.14	1.54		
Unpaid employment		0.87	0.81	0.93	1.78	1.55	2.04		
Residential region									
Urban	1.00								
Rural		0.88	0.83	0.94	1.24	1.12	1.38		
Smoking status									
Current smoker		0.99	0.92	1.08	1.51	1.31	1.75		
Former smoker		0.95	0.85	1.05	1.51	1.26	1.81		
Never smoked	1.00								
Frequency of alcohol use									
Never drink		0.96	0.85	1.09	0.88	0.71	1.09		
1 times or less per month		0.89	0.79	1.01	0.81	0.65	1.00		
2-4 times per week		0.93	0.83	1.04	0.79	0.65	0.96		
4 times or more per week	1.00								
Number of days of moderate exercise per week									
Never	1.00								
1–3		0.98	0.92	1.05	0.75	0.66	0.86		
4–6		0.99	0.90	1.09	0.70	0.57	0.85		
Everyday		1.09	0.98	1.22	1.04	0.84	1.28		
Perceived stress									
Very high		1.88	1.64	2.16	1.19	0.93	1.51		
High		1.57	1.44	1.71	0.86	0.74	1.01		
Low		1.12	1.04	1.21	0.85	0.75	0.97		
Very low	1.00								
Extent of pain from rheumatoid arthritis									
Low	1.00								
High		1.39	1.19	1.63	1.22	0.93	1.58		
BMI									
Thin (<18.5 kg/m2)		0.79	0.70	0.90	1.26	1.04	1.53		
Moderate (18.5kg/m-23.9kg/m2)	1.00								
Overweight (24.0kg/m-26.9kg/m2)		1.05	0.99	1.11	0.95	0.84	1.07		
Obese (≥27.0 kg/m2)		1.20	1.11	1.29	1.00	0.86	1.17		
Year									
2007	1.00								
2008		1.05	0.89	1.24	1.30	0.98	1.73		
2009		0.95	0.80	1.12	1.19	0.90	1.57		
2010		1.00	0.84	1.19	1.22	0.91	1.64		
2011		1.03	0.86	1.23	1.10	0.82	1.47		
2012		1.00	0.84	1.19	1.14	0.85	1.54		
2013		1.16	0.98	1.38	1.04	0.78	1.40		

Table 3. Results of logistic regression between rheumatoid arthritis and sleep duration by extent to pain of rheumatoid arthritis

	Rheumatoid Arthritis (RA)						
	Appropriate sleeper (7-8h)	Short sleeper (≤6h)			Long sleeper (≥9h)		
	Ref	OR	95% CI		OR	95% CI	
Extent to pain of rheumatoid arthritis (High)							
Rheumatoid arthritis (RA)							
No	1.00						
Yes		1.28	1.04	1.58	1.40	0.93	2.12
Extent to pain of rheumatoid arthritis (Low)							
Rheumatoid arthritis (RA)							
No	1.00						
Yes		0.84	0.49	1.46	0.52	0.18	1.45

***Adjusted for all variables**

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract(1P)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found(2p)
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported(4p)
Objectives	3	State specific objectives, including any prespecified hypotheses(5p)
Methods		
Study design	4	Present key elements of study design early in the paper(5p)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection(5-6p)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up(6p) *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable(6p)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group(7p)
Bias	9	Describe any efforts to address potential sources of bias(7-8p)
Study size	10	Explain how the study size was arrived at(6p)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why(6p)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding(7-8p)
		(*b*) Describe any methods used to examine subgroups and interactions(N/A)
		(*c*) Explain how missing data were addressed(6p)
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed(6p) *Case-control study*—If applicable, explain how matching of cases and controls was addressed(N/A) *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy(N/A)
		(*e*) Describe any sensitivity analyses(N/A)

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed(8p)
		(b) Give reasons for non-participation at each stage(N/A)
		(c) Consider use of a flow diagram(N/A)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders(5-7p)
		(b) Indicate number of participants with missing data for each variable of interest(5-7p)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) (5-7p)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time(5-7p)
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included(8-9p)
		(*b*) Report category boundaries when continuous variables were categorized(8-9p)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period(8-9p)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses(N/A)
Discussion		
Key results	18	Summarise key results with reference to study objectives(9-10p)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias(12p)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence(8-10p)
Generalisability	21	Discuss the generalisability (external validity) of the study results(12p)
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.