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Original Article

Bath Ankylosing Spondylitis Disease Activity Index is Associated With the Quality of Sleep in Ankylosing Spondylitis Patients

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Objective. High disease activity of ankylosing spondylitis (AS) is associated with poor sleep quality. The purpose of this study was to identify which of the representative tools for evaluating the disease activity of AS best reflect the quality of sleep. **Methods.** A total of 107 AS patients were enrolled in the study and the sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI). Age, sex, concomitant medication, erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP) level, Beck Depression Inventory second edition (BDI-II), Bath ankylosing spondylitis disease activity index (BASDAI), ankylosing spondylitis disease activity score (ASDAS)-ESR, ASDAS-CRP, pain visual analog scale, Insomnia Severity Index (ISI), and Epworth Sleepiness Scale (ESS) were analyzed as covariates. **Results.** Overall, 65% (70/107) of subjects reported poor sleep quality (PSQI > 5). There was a positive correlation between the sleep quality and disease activity as measured by the BASDAI, ASDAS-ESR, and ASDAS-CRP. In addition, the BASDAI demonstrated good correlations with ISI, ESS, and BDI-II, respectively. However, only BASDAI showed reliable correlation with PSQI among the disease activity parameters of AS (adjusted odd ratio 5.36, p = 0.023). **Conclusion.** BASDAI is the most reliable parameter of disease activity associated with the sleep quality in patients with AS. **(J Rheum Dis 2021;28:143-149)**

Key Words. Ankylosing spondylitis, Bath ankylosing spondylitis disease activity index, Sleep quality

INTRODUCTION

Ankylosing spondylitis (AS) is a seronegative spondyloarthropathy with chronic inflammation around the spine and pelvis as the main symptom [1]. The disease onset is at a relatively young age, and the duration of the disease is relatively long. Hence, the patient's quality of life is greatly affected by the progression of the disease [1].

It is well known that the quality of sleep is poor among Koreans with rheumatic diseases such as rheumatoid arthritis, AS, and Behçet's disease [2-4]. Recent meta-analyses demonstrated that the quality of sleep in patients with AS is reduced by approximately 35%～90% compared to that in healthy individuals [5,6] and that higher disease activity has more impact on the sleep quality. In particular, back pain and stiffness are associated with

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sleep disturbances. Besides disease activity, pain, decline in body functions, and mood have been found to affect the sleep quality [5].

The use of biologic agents such as tumor necrosis factor-alpha (TNF-α) inhibitors has dramatically improved the treatment of AS. Biologic agents not only improve the quality of life but have also been recently found to prevent radiological progression [7]. It has not been established yet whether a biologic agent can improve the quality of sleep in patients with AS. However, it is crucial to find an indicator that reflects the disease activity and sleep quality accurately, and this can be used as an important assessment tool for optimal treatment of patients.

Tools for assessing the disease activity in AS patients include the Bath ankylosing spondylitis disease activity index (BASDAI), ankylosing spondylitis disease activity score-erythrocyte sedimentation rate (ASDAS-ESR), and ankylosing spondylitis disease activity score-C-reactive protein (ASDAS-CRP) [8]. The use of each of these indicators is associated with certain advantages and disadvantages. Therefore, we aimed to determine which of these indicators used for assessing the disease activity of AS best reflects the sleep quality.

MATERIALS AND METHODS

Study population

A total of 107 patients with AS who visited two tertiary rheumatology clinics in Korea were enrolled from September 2019 to October 2020.

Inclusion criteria for the patients were: age 19 years or older and meeting the 1984 modified New York criteria [9]. Exclusion criteria were: being uneducated and unable to answer the questionnaire; having low mental aptitude; having a history of medical diseases such as hypertension, diabetes mellitus, fibromyalgia, malignant tumor, or infection, which can affect the quality of sleep; or being suspected to be drug addicts (including sleeping pills or alcohol).

Ethics statement

This study was approved by the Institutional Review Board (IRB) at the university hospital where the study was conducted (IRB numbers: KUDH 2019-07-032 and GNAH 2019-10-014) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all study participants.

Assessment of clinical variables

Along with a questionnaire, face-to-face interviews were conducted with the patients with AS. Age, sex, body mass index (BMI), visual analogue scale (VAS) score for pain, and other associated disease history were recorded and analyzed. Sleep quality, depression, and disease activity of AS were also scrutinized. From the medical records, additional information was collected, such as blood test results for C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and human leukocyte antigen (HLA) B27 positivity; disease duration; and medical history associated with disease activity of AS.

Assessment of sleep quality

Quality of sleep was evaluated using the Korean version of the Pittsburgh Sleep Quality Index (PSQI) [10]. PSQI consists of a questionnaire regarding sleep habits over the past one month and is a useful test to evaluate the sleep quality. It contains seven subsections: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Each of these components has a range of 0～3 points, with the total adding up to 0～21 points. Higher scores indicate poor sleep quality; when the total score was over 5, patients were classified into the poor sleeper group.

Assessment of insomnia

Severity of insomnia was evaluated using the Korean version of Insomnia Severity Index (ISI) [11]. ISI consists of a questionnaire in which the respondents are asked to rate, on a range of 0～4 points, the nature and symptoms of their sleep problems. It contains five subsections: the severity of symptoms, the respondent's satisfaction with his or her sleep patterns, the degree to which insomnia interferes with daily functioning, how noticeable the respondent feels his or her insomnia is to others, and the overall level of distress created by the sleep problem. By adding the scores of each component, a total score from 0 to 28 points is achieved. A total score of 0～7 indicates no clinically significant insomnia, 8～14 means subthreshold insomnia, 15～21 is moderate severity clinical insomnia, and 22～28 indicates severe clinical insomnia [11].

Assessment of daytime sleepiness

Daytime sleepiness was measured using the Korean version of the Epworth Sleepiness Scale (ESS) [12]. ESS con-

sists of a questionnaire in which the respondents are asked to rate, on a range of 0～3 points, their usual chances of dozing off or falling asleep during eight different activities during the daytime. Higher ESS scores indicate an average person's higher sleep propensity in daily life; when the total score is more than 11, it is defined as excess daytime sleepiness [12].

Assessment of depression

The Korean version of the Beck Depression Inventory-second edition (BDI-II) was used to evaluate the degree of depression [13].

BDI-II consists of 21 multiple-choice self-report inventories, with points ranging from 0～3. By adding the scores of each component, a total score ranging from 0 to 63 points is achieved. Higher scores indicate severe depression, and 20 points has been defined as the cut-off point for depression [13].

Assessment of ankylosing spondylitis disease activity

The BASDAI [14] as well as ASDAS-CRP and ASDAS-ESR [15] were evaluated as indicators of AS disease activity. To assess the disease activity, we used the Korean versions of the BASDAI, ASDAS-CRP, and ASDAS-ESR.

The BASDAI questionnaire contains six questions regarding subjective symptoms during the week prior to answering the questions. Each question is scored on a scale of 0 to 10. According to the Assessment of Spondyloarthritis International Society criteria, a BASDAI score ≥4 was considered as high disease activity, while a score <2 was considered as remission [16].

The ASDAS-CRP and ASDAS-ESR take into an account both patient-perceived symptoms as well as acute-phase reactants. These composite indices take into account three questions of the BASDAI, patient's global assessment, as well as the CRP or ESR values. Scores range from 0 (no disease activity) to infinity (being determined by the level of CRP or ESR). The cutoffs between the disease activity states are: inactive disease ≤1.3, moderate: 1.3～2.0, high: 2.1～3.5, and very high ≥3.5 [17].

Statistical analysis

The statistical program SPSS for Windows, version 26.0 (IBM Co., Armonk, NY, USA), was used for data processing and statistical analysis. The continuous data were analyzed as means and standard deviations, while categorical data were assessed as frequencies and percentages. The independent t test was used to compare the means between the groups, while the chi-square test was used to compare the proportions. The correlation between variables was calculated with Pearson's correlation coefficient. The crude or adjusted odds ratios (ORs) were estimated using simple or multiple logistic regression analysis. All

Table 1. The demographic characteristics of the study population

Variable	Total population (n=107)
Sex, male	88 (82.2)
Age (yr)	35.81±11.78
BMI (kg/m^2)	24.66±4.09
ESR (mm/hr)	17.94±17.83
CRP (mg/dL)	0.32±0.77
HLA B27, positive	92 (86.0)
Disease duration (mo)	71.92±71.73
TNF-α inhibitor use	76 (71.0)
Pain (VAS) (cm)	2.48±1.84
Total BASDAI	3.10±1.68
Fatigue	5.28±2.37
Total back pain	3.44±2.37
Peripheral pain/swelling	2.30±2.21
Enthesitis	1.55±2.10
Level of morning stiffness	3.29±2.52
Duration of morning stiffness	2.55±2.36
ASDAS	
Total back pain	3.44±2.37
Duration of morning stiffness	2.55±2.36
Patient global assessment	3.10±1.94
Peripheral pain/swelling	2.30±2.21
Total ASDAS-ESR	2.11±0.88
Total ASDAS-CRP	1.83±0.74
ISI	8.42±5.49
ESS	6.50±3.88
PSQI	7.00±3.25
Subjective sleep quality	1.51±0.65
Sleep latency	1.50±1.05
Sleep duration	0.91±0.96
Habitual sleep efficiency	0.33±0.74
Sleep disturbance	1.17±0.50
Use of sleeping medicine	0.17±0.61
Daytime dysfunction	1.43±0.93
BDI-II	11.63±8.05

All values are numbers (%) or means±standard deviations. ASDAS: ankylosing spondylitis disease activity score, BASDAI: bath ankylosing spondylitis disease activity index, BDI: Beck Depression Inventory, BMI: body mass index, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, ESS: Epworth Sleepiness Scale, HLA B27: Human Leucocyte Antigen B27, ISI: insomnia severity index, PSQI: Pittsburgh Sleep Quality Index, TNF-α: tumor necrosis factor-alpha, VAS: Visual Analogue Scale.

the results with a p-value less than 0.05 were considered as significant.

RESULTS

Demographic and clinical characteristics of the patients with ankylosing spondylitis

A total of 107 patients were enrolled in this study and completed the questionnaire. Among them, 88 patients were men (82.2%), with mean age of 35.81±11.78 years and BMI of 24.66±4.09 kg/m^2. The average ESR was 17.94±17.83 mm/hr, and the CRP was 0.32±0.77 mg/dL. There were 92 (86%) patients with positive HLA B27, and the mean duration of the disease was 71.92±71.73 months. The mean VAS score was 2.48±1.84 cm. The mean BASDAI was 3.10±1.68, ASDAS-ESR was 2.11±0.88, and ASDAS-CRP was 1.83±0.74. The mean ISI was 8.42±5.49, mean ESS was 6.50±3.88, mean BDI-II was 11.63±8.05, and mean PSQI was 7.00±3.25 (Table 1).

Comparison between the good sleeper and poor sleeper groups

Out of the 107 patients in total, 37 (34.6%) were good sleepers and 70 (65.4%) were poor sleepers. There was no significant difference between men and women in both groups. Furthermore, there were no significant differences in the BMI, ESR, CRP, HLA status, duration of disease, and the use of TNF-α inhibitor. However, there was a significant difference in the mean age between the two groups. The mean ages of good sleepers and poor sleepers were 40.38±13.46 and 33.40±10.08 years, respectively ($p<0.05$). The VAS, BDI-II, BASDAI, ASDAS-ESR, and ASDAS-CRP scores also showed significant differences between the two groups ($p<0.05$) (Table 2).

Correlation between sleep quality parameters and the disease activity parameters

There were positive correlations between the tools for assessing the sleep quality (PSQI, ISI, ESS) and disease activity (BASDAI, ASDAS-ESR, ASDAS-CRP). The correlation of PSQI with BASDAI was the highest at 0.469, followed by ASDAS-CRP at 0.373, and ASDAS-ESR at 0.290. In addition, the ISI and ESS demonstrated correla-

Table 3. Correlation between the sleep quality indices and disease activity indices of ankylosing spondylitis

Parameters	PSQI	ISI	ESS
BASDAI	0.469**	0.523**	0.525**
ASDAS-ESR	0.290**	0.347**	0.366**
ASDAS-CRP	0.373**	0.429**	0.405**

ASDAS: ankylosing spondylitis disease activity score, BASDAI: bath ankylosing spondylitis disease activity index, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, ESS: Epworth Sleepiness Scale, ISI: insomnia severity index, PSQI: Pittsburgh Sleep Quality Index. **$p<0.01$.

Table 2. Comparison between the good sleeper and poor sleeper groups

Variable	Good sleeper (PSQI≤5)	Poor sleeper (PSQI >5)	p-value
Total	37 (34.6)	70 (65.4)	
Sex, male	31 (83.8)	57 (81.4)	0.970
Age (yr)	40.38±13.46	33.40±10.08	0.008
BMI (kg/m^2)	24.76±3.39	24.60±4.43	0.850
ESR (mm/hr)	15.49±13.96	19.24±19.54	0.254
CRP (mg/dL)	0.25±0.46	0.35±0.89	0.441
HLA B27, positive	30 (81.1)	62 (88.6)	0.384
Disease duration (mo)	87.30±81.15	63.79±65.39	0.107
TNF-α inhibitor use	27 (73.0)	49 (70.0)	0.922
Pain (VAS) (cm)	1.89±1.81	2.79±1.80	0.016
BDI-II	7.16±5.86	13.99±8.08	<0.001
BASDAI	2.09±1.34	3.63±1.60	<0.001
ASDAS-ESR	1.76±0.72	2.30±0.91	0.002
ASDAS-CRP	1.54±0.62	2.00±0.75	0.002

All values are numbers (%) or means±standard deviations. ASDAS: ankylosing spondylitis disease activity score, BASDAI: bath ankylosing spondylitis disease activity index, BDI: Beck Depression Inventory, BMI: body mass index, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, HLA B27: Human Leucocyte Antigen B27, PSQI: Pittsburgh Sleep Quality Index, TNF-α: tumor necrosis factor-alpha, VAS: Visual Analogue Scale.

tions with the BASDAI, ASDAS-ESR, and ASDAS-CRP scores (Table 3). Additionally, we analyzed the correlation between the detailed items constituting the PSQI and the detailed items of the disease activity evaluation indicators of AS (Supplementary Table 1). Among the detailed items of the disease activity evaluation indicators, fatigue was the most correlated with the total PSQI score ($r=0.465$, $p<0.01$).

Relationship between the sleep quality and disease activity

On comparing the odds ratios between the groups with well-controlled AS and poorly-controlled AS and between the poor sleepers and good sleepers, the crude OR was the highest for BASDAI at 4.27 (Table 4), followed by ASDAS-CRP at 2.56, and ASDAS-ESR at 2.46 ($p<0.05$). After adjustment for age, VAS, and BDI-II, which showed significant differences between the poor sleeper and good sleeper groups as shown in Table 2, the adjusted odds ratio was the highest for BASDAI at 5.36, followed by ASDAS-CRP at 2.74, and ASDAS-ESR at 2.61, but was significant only for BASDAI ($p=0.023$).

DISCUSSION

In the past, healthcare only focused on the treatment of acute diseases such as infections. However, with the development of medicine and emergence of an aging society, the focus is moving towards the treatment and management of chronic diseases. Consequently, modern medicine pays considerable attention to the improvement of the quality of life, sleep disorders, depression, and stress, which can be affected by diseases as well as the termination or alleviation of physical symptoms related to the diseases. Among them, sleep affects many functions such as memory, emotion control, recovery of body functions, metabolic regulation, immune function, and inflammation control [18,19]. Rheumatic diseases are mostly chronic inflammatory autoimmune diseases, and ensuring proper sleep can affect the control of the disease activity. An important goal of treatment of AS, which is a chronic inflammatory autoimmune disease occurring at a relatively young age, is the improvement of the sleep disorder or psychological factors in addition to simple pain relief since the duration of the disease is long. Consequently, we studied the relationship between disease activity and sleep quality in patients with AS.

Several previous studies, including a systematic literature review and meta-analysis, have shown that the factors influencing the sleep disorder in AS include demographic factors such as age, sex, and education; disease-related factors such as disease activity, fatigue, degree of body function, and pain; and psychological factors such as depression, anxiety, and quality of life. The strength of the correlations appears to be slightly different in each study [5,6,20-23]. In a meta-analysis of six studies that analyzed patients with AS and healthy controls using the PSQI as an index for the evaluation of sleep quality, the BASDAI score did not show a significant correlation with the total PSQI score [6]. Nevertheless, many studies have reported that the BASDAI, an evaluation index of disease activity, has a high correlation with sleep quality [5]. However, there has been no international study that has used ASDAS as an evaluation index for disease activity. Similar to previous studies that reported that high disease activity was correlated with poor sleep quality [3,5,6,21-24], our study also revealed that the group with low sleep quality (poor sleepers) demon-

Table 4. Relationship between the sleep quality and disease activity

Parameters		Crude		Adjusted*	
		OR (95% CI)	p-value	OR (95% CI)	p-value
BASDAI	<4	4.27 (1.48~12.28)	0.007	5.36 (1.26~22.69)	0.023
	≥4	1.00		1.00	
ASDAS-ESR	<2.1	2.46 (1.08~5.61)	0.032	2.61 (0.92~7.42)	0.073
	≥2.1	1.00		1.00	
ASDAS-CRP	<2.1	2.56 (1.03~6.41)	0.044	2.74 (0.87~8.67)	0.086
	≥2.1	1.00		1.00	

ASDAS: ankylosing spondylitis disease activity score, BASDAI: bath ankylosing spondylitis disease activity index, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, OR: odds ratio, CI: confidence intervals, VAS: Visual Analogue Scale, BDI-II: Beck Depression Inventory-II. *Adjusted for age, VAS, BDI-II.

strated higher disease activity, pain, and depression indices.

Between BASDAI and ASDAS, which are used as evaluation indices for disease activity in clinical practice, BASDAI showed a higher association with sleep quality. The possible reason that the BASDAI and ASDAS showed this difference, although they are disease activity indices with a high correlation between them, appears to be due to the difference in the items comprising each index. Among the items included in the BASDAI, fatigue, local tenderness, and level of morning stiffness are different from the ASDAS. The items included in the ASDAS but not in the BASDAI are patient global assessment and objective inflammatory markers such as ESR/CRP [14,15]. As can be seen from Supplementary Table 1, which shows the result of the correlation analysis between the detailed items of each of the disease activity indices and the PSQI, fatigue exhibited the highest correlation with the total PSQI, whereas local tenderness, level of morning stiffness, patient global assessment, and ESR/CRP did not show high correlations. This suggests that the BASDAI index has a greater association with the sleep quality compared to the ASDAS since fatigue affects sleep quality the most, and the BASDAI includes fatigue. This is a valid conjecture considering the result of previous studies: the worse the fatigue, the worse is the sleep quality in patients with AS [25-28].

The limitations of our study are as follows: First, we did not perform radiological evaluation of the joint deformities that may interfere with sleep, such as spinal deformities. Second, we did not investigate objective indicators related to sleep, such as polysomnography and sleep-related cytokines. Third, we did not follow up a large number of patients for a sufficient period of time to observe whether a decrease in the disease activity indicates an improvement in the sleep quality or whether a biological agent leads not only to a decrease in the disease activity but also an improvement in the sleep quality.

CONCLUSION

This study found that high disease activity in AS was associated with a decrease in the sleep quality and that the BASDAI reflects this the best among the disease activity indices. We can expect improvement in the sleep quality as well as pain through active control of the disease activity in patients with AS.

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CONFLIC OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Conceptualization: B.W.S., H.J.J., S.S.K., S.H.K., and C.N.S. Data curation: all authors. Formal analysis: B.W.S., H.J.J., S.S.K., B.Y.K., Y.W.C., S.H.K., and C.N.S. Funding acquisition: S.H.K., H.J.J., and C.N.S. Investigation: all authors. Methodology: Y.W.C., S.H.K., and C.N.S. Project administration: B.W.S., S.S.K., S.H.K., and C.N.S. Resources: all authors. Supervision: S.H.K., S.S.K., and C.N.S. Visualization: B.W.S., S.H.K., and C.N.S. Writing - original draft: B.W.S., H.J.J., S.S.K., S.H.K., and C.N.S. Writing - review and editing: all authors.

SUPPLEMENTARY DATA

Supplementary data can be found with this article online at https://doi.org/10.4078/jrd.2021.28.3.143.

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