

## Association between cold–heat symptoms and sleep disturbances according to the Sasang constitution: a cross–sectional community study

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### Abstract

**Objectives :** Evidence supporting the cold–heat symptom and sasang constitution type, which are diagnostic items of traditional Korean medicine, is needed to manage sleep disturbances, which is a typical symptom of mibyeong (subhealth). This study examined the association between each cold–heat symptom and sleep disturbances according to each sasang constitution type.

**Methods :** This research was a cross–sectional study of 5,793 subjects from the Korean Medicine Data Center (KDC) community cohort survey. The association between each cold–heat symptom and sleep disturbances was analyzed by logistic regression analysis adjusted for several demographic variables. Subgroup analysis was then performed for each type of sasang constitution.

**Results :** The soeum and soyang types were 1.53 and 1.26 times more likely to have sleep disturbances than the taeum type. Sleep disturbances were associated with ‘coldness of the abdomen’, ‘watery mouth’ in the cold domain items, and ‘body feverishness’, ‘flushed face and eye’, ‘thirst’, and ‘scanty dark urine’ in the heat domain items. The soeum and soyang types were 1.55 and 1.39 times more likely to sleep less than five hours per night than the taeum type. In addition, the associations of those showed a different pattern for each sasang constitution type.

**Conclusions :** Sleep disturbances are associated with specific cold–heat symptoms, and the associated cold–heat symptoms differ according to the sasang constitution type. These results may help traditional medicine specialists select customized interventions for patients with sleep disturbances.

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**Key words :** Sleep–Wake Disorders; Cold–heat symptoms, Sasang constitution; Diagnosis; Medicine, East Asian Traditional; Cross–Sectional Studies

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## I. Introduction

Sleep disorders, including insomnia and sleep-related breathing disorders, are classified into seven categories according to the third edition of the International Classification of Sleep Disorders (ICSD)(1). The prevalence of insomnia and short sleep duration is 18.8% and 29.1%, respectively, according to the 2012 National Health Interview Survey in the United States (US). The prevalence of general sleep disturbances is 32.1%, and insufficient sleep is 43.2%, and insomnia is 8.2% in the Netherlands (2). On the other hand, although previous studies estimated that more than a quarter of the general population suffers from sleep disorders, the low clinical diagnosis rate makes it difficult to measure the prevalence of sleep disorders accurately (3). Nevertheless, the diagnosis of sleep disorders is worthwhile because insufficient sleep and sleep disorders are associated with unhealthy outcomes, such as inflammation and metabolism problems (4). The expansion of self-diagnosis may assist in the early detection of sleep disorders. Moreover, with the recent advances of smart healthcare, sleep tracking wearable devices and applications worn on the limbs are being used to diagnose sleep problems (5). Despite this, the clinical practice guidelines of the American Academy of Sleep Medicine highlight the need for reliable evidence on actigraphy to judge the benefits and patient values (6, 7).

Many patients complain of sleep disturbances and request treatments by traditional or complementary medicine. Therefore, several attempts have been made to treat sleep disturbances with interventions of traditional medicine in Asia (TM: Traditional Chinese Medicine (TCM), Traditional Korean Medicine (TKM), and Kampo Medicine). At this time, the evidence for a TM diagnosis is

important. The core of a diagnosis of TM is dialectic. Moreover, syndrome differentiation, also called pattern differentiation, involves the comprehensive analysis of clinical information obtained through four major diagnostic procedures (inspection, listening (and smelling), inquiry, and palpation) of TM to determine the location, cause, and nature of the disease in patients (8). In addition, it is a standard process for TM healthcare professionals to decide which interventions in TM are appropriate for patients based on the results of syndrome differentiation. Among them, cold-heat pattern Identification (CHPI) is one of the most frequent pattern identifications among the eight-principal syndrome differentiation in clinical practice: yin-yang, exterior-interior, cold-heat, and deficiency-excess. Therefore, some types of questionnaire survey tools for CHPI have been developed and verified to measure the CHPI accurately (9–12).

Some studies on the difference in symptoms or diseases according to the results of CHPI have been performed, such as the body mass index (BMI), hypertension, dysfunctional breathing, dysmenorrhea, cough, rhinitis, asthma, rheumatoid arthritis (RA), acute myocardial infarction (MI), and dementia, but few studies have examined the relationship between CHPI and sleep disturbances (9, 11, 13–22).

Therefore, this study examined the association between CHPI and sleep disturbances to generate evidence for a TM diagnosis and treatment using large-scale community-based data. In addition, the differences according to the type of *asang* constitution were also examined.

## II. Methods

### 1. Study design and data source

This study performed a cross-sectional analysis

of 5,793 subjects who completed the Pittsburgh Sleep Quality Index (PSQI) and the CHPI questionnaire in a community cohort survey of the Korean Medicine Data Center (KDC) from June 2012 to December 2014 (23, 24).

## 2. Variables Definition

### 1) Sleep disturbances

The categorical variable, sleep disturbance, was developed from scores calculated from the survey results of the Pittsburgh Sleep Quality Index (PSQI), a self-administered questionnaire used worldwide to evaluate sleep quality (25, 26). The individual items of the PSQI generate seven component scores, the sum of which ranges from 0 to 21 (25). The cutoff score of the Korean version of PSQI was 8.5, so this study defined a PSQI of 8.5 or higher as a sleep disturbance (26).

### 2) Sleep time

The PSQI item, “During the past month, how many hours of actual sleep did you have at night? (This may be different from the number of hours spent in bed.)” was used to identify the subject’s sleep time per night (25). Originally, the sleep time was set as a categorical variable based on seven hours according to the recommendations of a joint consensus statement of the American Academy of Sleep Medicine (AASM) and Sleep Research Society. On the other hand, considering that the total sleep time of Koreans is short, categorical variables for sleep time between five and seven hours were added by referring to an analysis of the frequency of sleep time per night and the results of ROC analysis of sleep disturbances. Finally, five hours of sleep time, which showed a difference between groups, was determined as a sleep time variable, and factor analysis was performed.

### 3) Cold-heat pattern Identification (CHPI)

Several versions of the questionnaire of CHPI have been developed and used in diagnosis to determine the treatment options for various diseases in the Republic of Korea (ROK) and China (9, 13, 27–29). The CHPI questionnaire used to collect data in this study contained 12 questions, consisting of six questions each in two domains: the cold domain and the heat domain (30, 31). The items of the cold domain were composed of a desire for heat (喜暖), coldness of the abdomen (腹冷), coldness of the limbs (手足冷), pale face (面色蒼白), profuse clear urine (小便清長), and watery mouth (口淡). The items of the heat domain were composed of a desire for cold (喜涼), body feverishness (身熱), feverishness of the limbs (手足煩熱), flushed face and eye (面紅目赤), thirst (口渴), and scanty dark urine (小便短赤). Each item was classified on a three-point Likert scale of rarely, sometimes, and often (Table S1). This study used the survey results for each cold-heat symptom item as the categorical variables. The total scores of the CHPI questionnaire, cold domain, and heat domain were used as the continuous variables. The scores ranged from one to three points per item. The total score for each domain ranged from six to 18 points, and the total score of CHPI ranged from six to 36 points.

### 4) Sasang constitution classified by KS-15

The Korea Sasang Constitutional Diagnostic Questionnaire (KS-15) is a “shortened Sasang Constitutional Diagnosis Questionnaire,” which is a survey tool that classifies a patient’s constitution using 15 items corresponding to personality, evidence, and body type (Table S2) (32, 33). The KS-15 is classified into one of Taeumin (太陰人), Soeumin (少陰人), and Soyangin (少陽人) according to the weighted calculation formula that reflects the characteristics of each constitution.

The result of the sasang constitution calculated by KDC was used in this study. No subject was judged to be Taeyangin (太陽人) from the data. This result is reasonable because sasang medicine founder Lee Je-ma stated that Taeyangin accounted for only 0.03 to 0.1% of the population (34).

#### 5) Other covariates

The following demographic variables were selected: gender, age, marital status, education period, economic activity, and behavioral variables, such as current smoker, current drinker, physical activity, and obesity.

### 3. Statistical Analysis

The demographic and behavioral variables were summarized using descriptive statistics, such as the proportion, mean, and standard deviation. The association between each cold-heat symptom and sleep disturbances was analyzed using logistic regression analysis that adjusted for several factors, such as gender, age group, marital status, education period, economic activity, current smoker, current drinker, physical activity, and obesity.

Subgroup analysis according to the sasang constitution was performed. In addition, the association between each cold-heat sleep duration of fewer than five hours per night was analyzed.

A two-sided p-value  $< 0.05$  was considered significant. All data manipulations and statistical analyses were conducted using Stata/MP version 16 (StataCorp LP, College Station, TX, USA).

## III. Results

### 1. Univariate descriptive analysis of subjects

A significant difference was observed between the sleep disturbances and the sasang constitution type, and between those who slept less than five hours per night and the sasang constitution type (Figure 1). The sasang constitution of sleep disturbances was highest in taeum (444, 52.61% of the total sleep disturbances), but the proportion of sleep disturbances within each sasang constitution type was the highest in soeum (205, 18.34% of the total soeum constitution type) (Figure 1). Significant differences were observed between the sleep disturbances and each of the

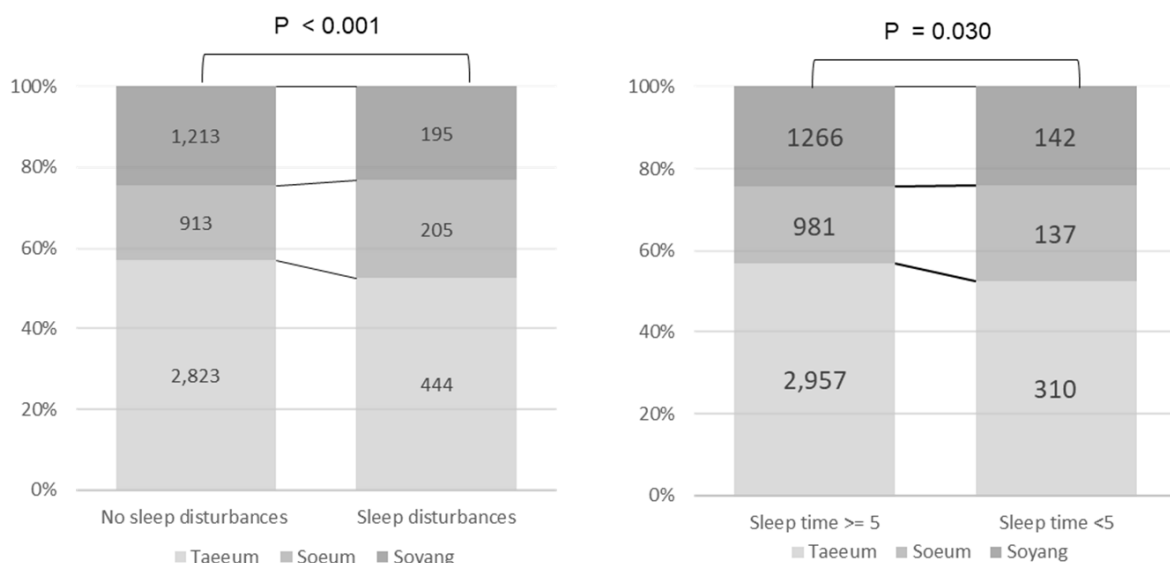


Figure 1. Sasang constitutions of subjects

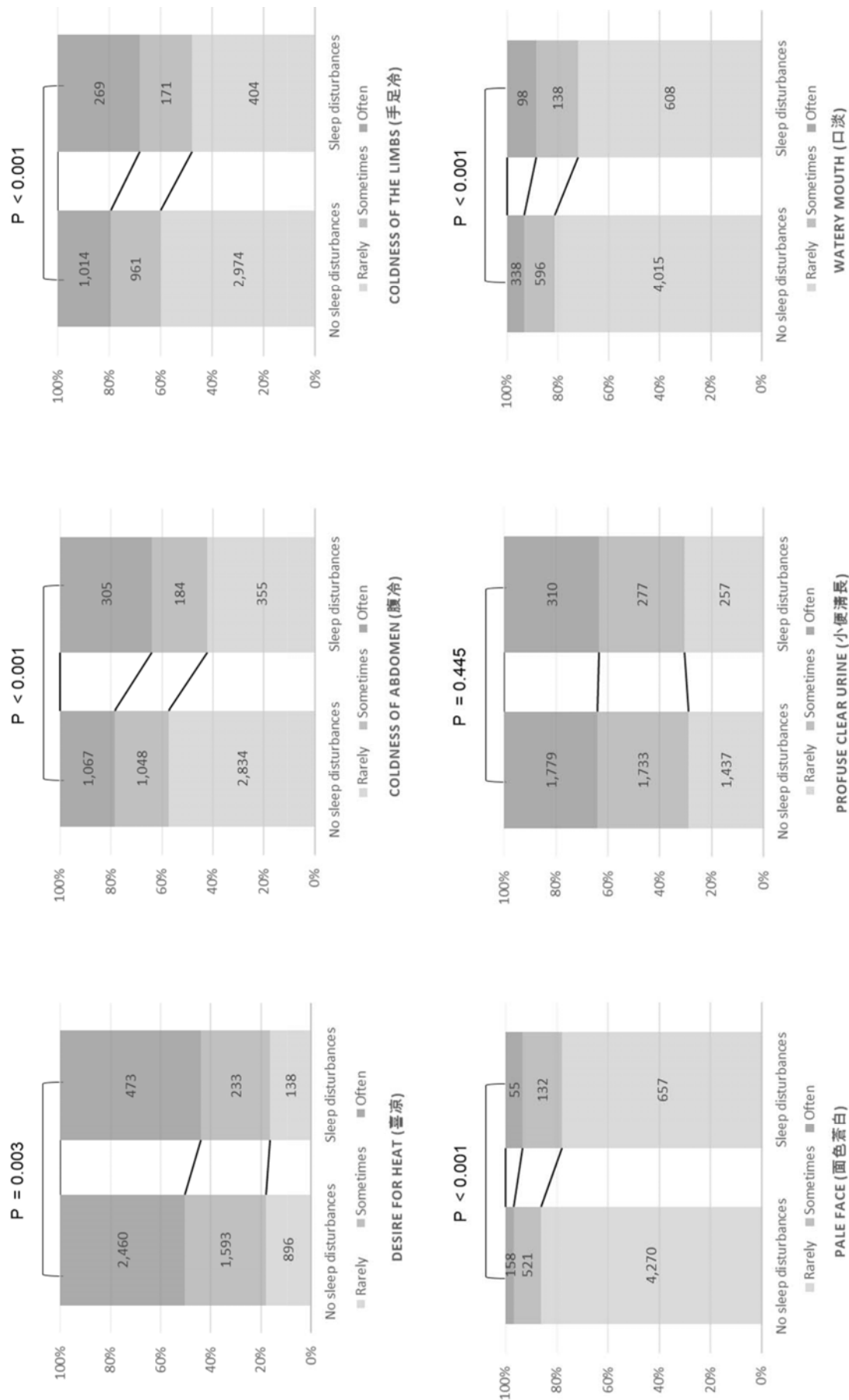


Figure 2. Cold-heat symptoms of subjects (A. Cold domain)

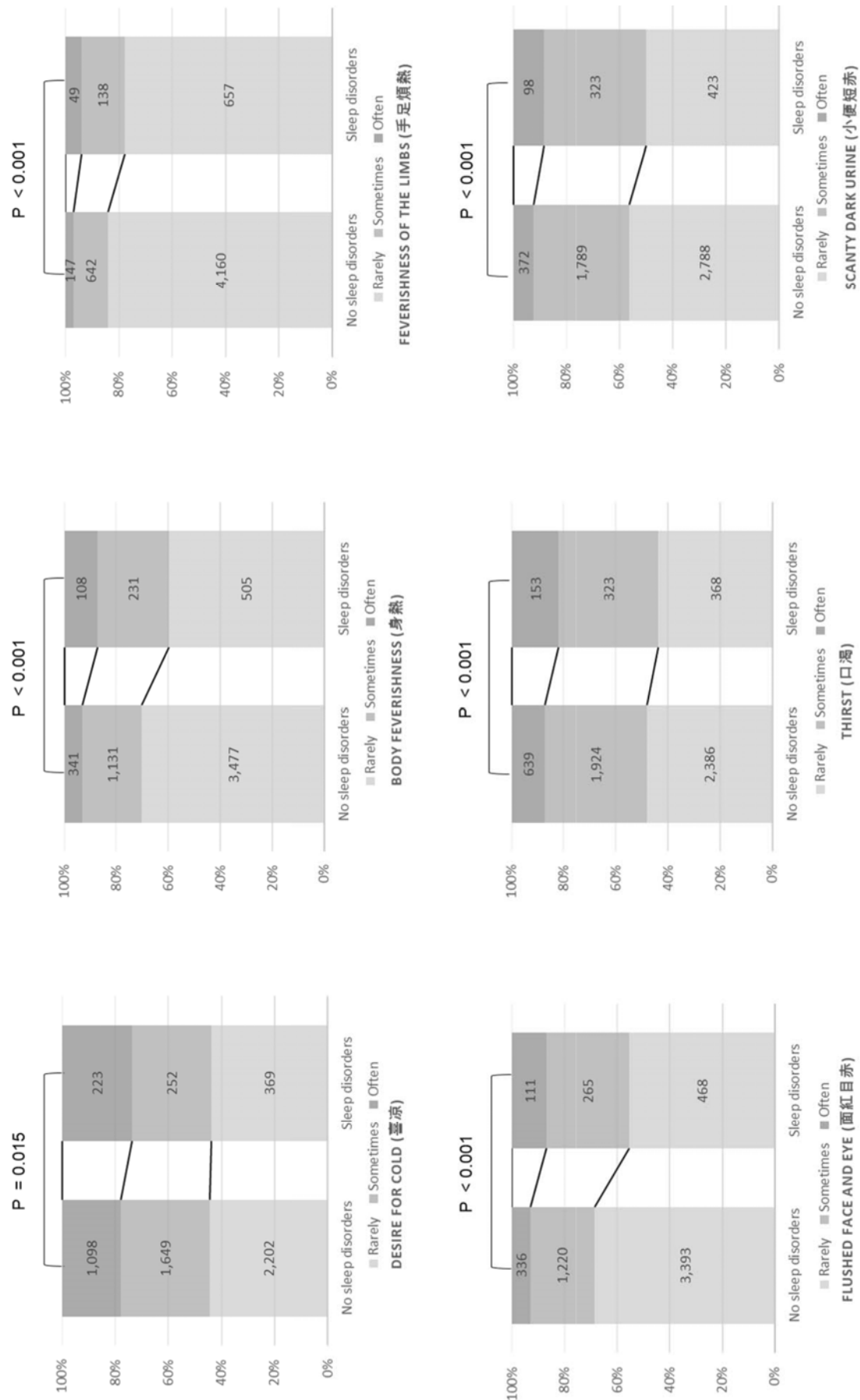


Figure 2. Cold-heat symptoms of subjects (B. Heat domain)

Table 1. Sleep quality and average CHPI scores of the subjects

Variables	No sleep disturbances (n=4,949, 85.43%)		Sleep disturbances (n=844, 14.57%)		<i>p</i>	Sleep time ≥ 5h (n=5,204, 89.83%)		Sleep time < 5h (n= 589, 10.17%)		<i>p</i>
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
PSQI	3.92	2.14	11.18	2.17	<0.001	4.40	2.78	10.15	3.45	<0.001
CHPI										
Total score	18.93	3.17	20.50	3.36	<0.001	19.04	3.23	20.18	3.27	<0.001
Cold score	10.06	2.34	10.92	2.45	<0.001	10.11	2.36	10.83	2.46	<0.001
Heat score	8.87	2.16	9.57	2.36	<0.001	8.93	2.19	9.35	2.30	<0.001

Abbreviations: PSQI, the Pittsburgh Sleep Quality Index; CHPI, Cold-heat pattern Identification; SD, Standard Deviation

11 items in the cold and heat domains, except for 'profuse clear urine' (Figure 2). The mean total CHPI score was 20.50 and 20.18 in the sleep disturbances and less than five hours sleep groups, respectively. The mean total scores for the cold and heat domains were 10.92 and 9.57 in the sleep disturbances group, and 10.83 and 9.35 in the less than five hours sleep group, respectively (Table 1).

## 2. Factors associated with sleep disturbances by sasang constitution

The soeum and soyang types were 1.53 and 1.26 times more likely to have a sleep disorder, respectively, than the taeum type. Sleep disturbances were associated with 'coldness of the abdomen' (often: aOR=1.54, 95% CI=1.27–1.91) and 'watery mouth' (often: aOR=1.30, 95% CI=1.004–1.68) in the cold domain, and 'body feverishness' (sometimes: aOR=1.23, 95% CI=1.01–1.50, often: aOR=1.61, 95% CI=1.21–2.14), 'flushed face and eye' (sometimes: aOR=1.39, 95% CI=1.16–1.67, often: aOR=1.58, 95% CI=1.22–2.05), 'thirst' (often: aOR=1.28, 95% CI=1.01–1.62), and 'scanty dark urine' (often: aOR=1.47, 95% CI=1.11–1.95) in the heat domain. Among them, the taeum constitution type was associated with 'coldness of the abdomen' (often: aOR=1.83, 95% CI=1.39–2.41), and 'watery mouth' (often: aOR=1.50, 95% CI=1.05–2.14) in the

cold domain, and 'body feverishness' (often: aOR=1.75, 95% CI=1.21–2.52), 'flushed face and eye' (sometimes: aOR=1.43, 95% CI=1.12–1.83), and 'scanty dark urine' (often: aOR=1.48, 95% CI=1.001–1.63) in the heat domain. The soeum constitution type was associated with 'coldness of the abdomen' (often: aOR=1.81, 95% CI=1.16–2.81) in the cold domain, and 'body feverishness' (often: aOR=2.78, 95% CI=1.38–5.60), and 'flushed face and eye' (often: aOR=2.84, 95% CI=1.68–4.80) in the heat domain. The soyang constitution type was only associated with 'scanty dark urine' (often: aOR=1.95, 95% CI=1.13–3.36) in the CHPI items (Table 2).

For each one-unit increase in the total CHPI score, the odds of having a sleep disturbance increased by 1.15 times. For each one-unit increase in the cold and heat domain scores, the odds of having a sleep disturbance increased by 1.12 and 1.17 times, respectively (Figure 3). In addition, the results were different within each sasang constitution group (Figure 3).

## 3. Factors associated with less than five hours of sleep time per night

The soeum and soyang types were 1.55 and 1.39 times more likely to sleep less than five hours per night, respectively, than the taeum type. Sleeping less than five hours was associated with

Table 2. Factors associated with sleep disturbances by sasang constitution

Variables	Total (n=844, 14.5%)			Taeum (n=444, 13.59%)			Soeum (n=205, 18.34%)			Soyang (n=195, 13.85%)		
	aOR	95%CI	p	aOR	95%CI	p	aOR	95%CI	p	aOR	95%CI	p
<b>Sasang constitution</b>												
Taeum	1.00											
Soeum	1.53	1.19–1.96	0.001									
Soyang	1.26	1.001–1.60	0.049									
<b>Cold domain</b>												
Coldness of abdomen												
Rarely	1.00			1.00			1.00					–
Sometimes	1.15	0.93–1.42	0.188	1.03	0.76–1.39	0.842	1.23	0.77–1.96	0.393			
Often	1.54	1.27–1.91	<0.001	1.83	1.39–2.41	<0.001	1.81	1.16–2.81	0.009			
Watery mouth												
Rarely	1.00			1.00			–					
Sometimes	1.19	0.96–1.48	0.114	1.18	0.87–1.61	0.279						
Often	1.30	1.004–1.68	0.047	1.50	1.05–2.14	0.026						
<b>Heat domain</b>												
Body feverishness												
Rarely	1.00			1.00			1.00					–
Sometimes	1.23	1.01–1.50	0.039	1.16	0.88–1.52	0.289	1.33	0.87–2.03	0.187			
Often	1.61	1.21–2.14	0.001	1.75	1.21–2.52	0.003	2.78	1.38–5.60	0.004			
Flushed face and eye												
Rarely	1.00			1.00			1.00					
Sometimes	1.39	1.16–1.67	<0.001	1.43	1.12–1.83	0.004	1.23	0.82–1.85	0.307			–
Often	1.58	1.22–2.05	0.001	1.17	0.81–1.70	0.398	2.84	1.68–4.80	<0.001			
Thirst												
Rarely	1.00			–			–					–
Sometimes	1.06	0.88–1.27	0.534									
Often	1.28	1.01–1.62	0.040									
Scanty dark urine												
Rarely	1.00			1.00			–			1.00		
Sometimes	1.18	0.99–1.40	0.068	1.27	0.999–1.62	0.051				0.96	0.66–1.38	0.815
Often	1.47	1.11–1.95	0.007	1.48	1.001–2.19	0.049				1.95	1.13–3.36	0.016

\* Adjusted for gender, age group, marital status, education period, economic activity, current smoker, current drinker, physical activity, obesity



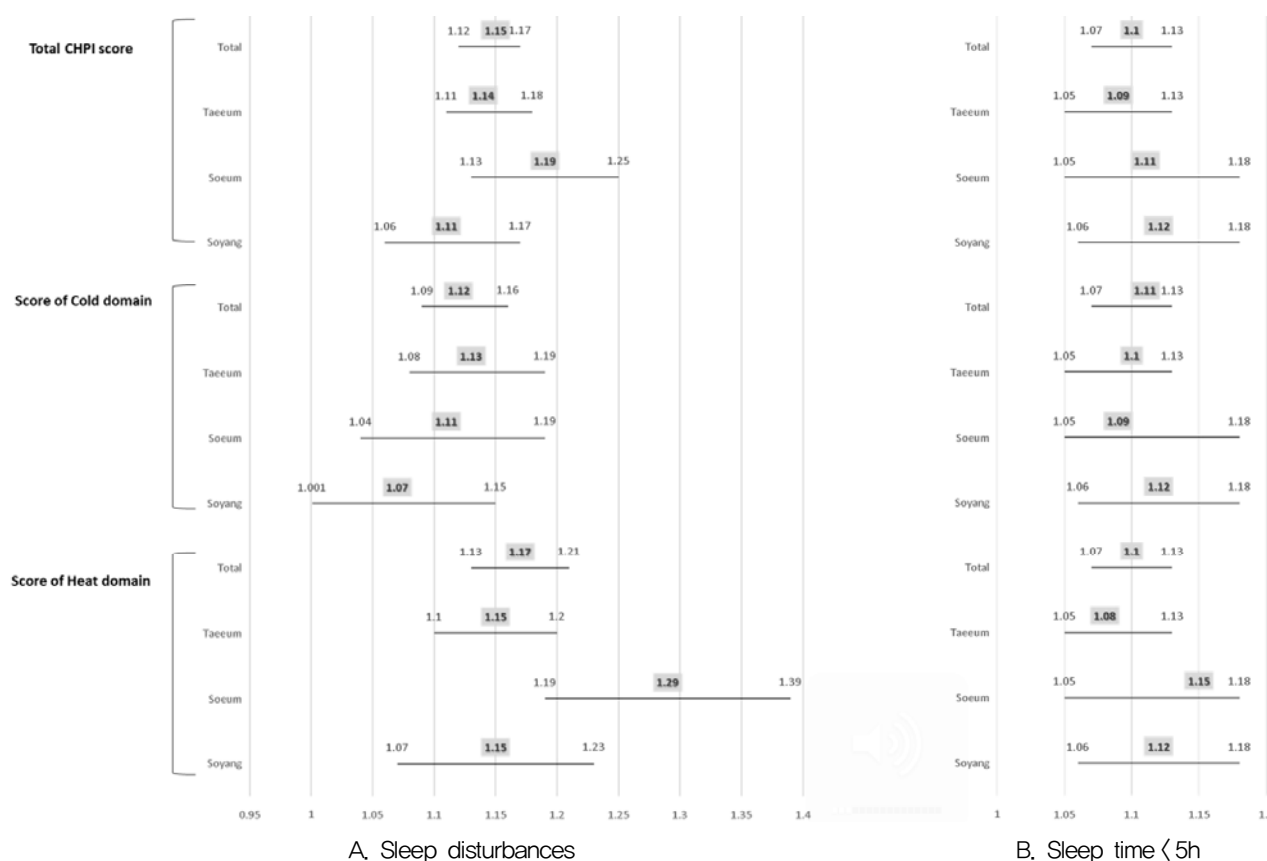


Figure 3. The association with CHPI score (A. Sleep disturbances, B. Sleep time < 5h)

\* Adjusted for gender, age group, marital status, education period, economic activity, current smoker, current drinker, physical activity, obesity

‘coldness of the abdomen’ (often: aOR=1.29, 95% CI=1.01–1.63) and ‘watery mouth’ (often: aOR=1.62, 95% CI=1.22–2.16) in the cold domain. Among them, the taeum constitution type was associated with ‘watery mouth’ (often: aOR=1.64, 95% CI=1.10–2.45) in the cold domain and ‘body feverishness’ (often: aOR=1.61, 95% CI=1.05–2.45) in the heat domain. The soeum constitution type was only associated with ‘flushed face and eye’ (often: aOR=2.12, 95% CI=1.19–3.78) in the CHPI items. The soyang constitution type was associated with ‘coldness of the abdomen’ (sometimes: aOR=2.24, 95% CI=1.40–3.57), and ‘watery mouth’ (often: aOR=2.23, 95% CI=1.22–4.06) in the cold domain, and a ‘desire for cold’ (sometimes: aOR=1.61, 95% CI=1.02–2.56) in the heat domain (Table 3).

For each one-unit increase in the total CHPI score, the odds of sleeping less than five hours

increased by 1.10 times. For each one-unit increase in the cold and heat domain scores, the odds of sleeping less than five hours increased by 1.11 and 1.10 times, respectively (Figure 3). In addition, the results were different within each sasang constitution group (Figure 3).

## IV. Discussion

In this study, sleep disturbances were associated with cold-heat symptoms, and each CHPI item was different for each sasang constitution. Previous studies reporting associations between other diseases and CHPI showed that patients with a cold pattern might be an exacerbating factor for the clinical course and prognosis of dysmenorrhea and AMI (13, 14). In contrast, pa-

Table 3. Factors associated with less than five hours of sleep time per night

Variables	sleeping time < 5h (n=589, 10.17%)			Taeum (n=310, 9.49%)			Soeum (n=137, 12.25%)			Soyang (n=142, 10.09%)		
	aOR	95%CI	p	aOR	95%CI	p	aOR	95%CI	p	aOR	95%CI	p
<b>Sasang constitution</b>												
Taeum	1.00											
Soeum	1.55	1.16–2.08	0.003									
Soyang	1.39	1.06–1.82	0.017									
<b>Cold domain</b>												
Coldness of abdomen				–			–			1.00		
Rarely	1.00											
Sometimes	1.25	0.98–1.59	0.067							2.24	1.40–3.57	0.001
Often	1.29	1.01–1.63	0.038							1.54	0.92–2.58	0.101
Watery mouth				1.00			–			1.00		
Rarely	1.00											
Sometimes	1.28	0.997–1.65	0.053	1.29	0.91–1.83	0.157				0.97	0.54–1.75	0.927
Often	1.62	1.22–2.16	0.001	1.64	1.10–2.45	0.015				2.23	1.22–4.06	0.009
<b>Heat domain</b>												
Desire for cold				–			–			1.00		
Rarely	–											
Sometimes										1.61	1.02–2.56	0.043
Often										1.60	0.95–2.71	0.080
Body feverishness				1.00			–			–		
Rarely	–											
Sometimes				1.09	0.79–1.51	0.588						
Often				1.61	1.05–2.45	0.027						
Flushed face and eye				–			1.00			–		
Rarely	–											
Sometimes							1.08	0.68–1.74	0.737			
Often							2.12	1.19–3.78	0.011			

\* Adjusted for gender, age group, marital status, education period, economic activity, current smoker, current drinker, physical activity, obesity

tients with a heat pattern might be an exacerbating factor for rhinitis and RA (15, 21). On the other hand, previous studies on the association with specific symptoms or diseases and CHPI were insufficient for TM practitioners to use them appropriately for clinical diagnosis, so the findings of this study may have clinical utility.

On the other hand, several versions of the CHPI questionnaire have been published, but there are no studies on the cutoff values of CHPI. Therefore, most researchers have usually compared the sum of the scores from cold or heat pattern questionnaires to determine the tendency of cold or heat. That is, a higher total score of each cold or heat indicates a more severe degree of cold or heat. In this study, the total score of CHPI and scores in the cold and heat domains were significantly higher in patients with sleep disturbances. On the other hand, comparative analysis with the results of this study is difficult because there are no reports of an association of each CHPI question with a specific disease. In addition to the CHPI scores, each item of cold and heat domain may also be helpful for a TM diagnosis process. Items of the CHPI significantly related to sleep disturbances were derived in this study, so a follow-up study using other data can compare with the present results. Because this study used secondary data, it was impossible to select the type of CHPI questionnaire. Hence, it was necessary to study which CHPI questionnaires were most effective for diagnosing TM. Most studies of TM focused on the effectiveness and safety of interventions, but research on TM diagnosis is needed to determine the differences in treatment methods for an individual pattern.

Korean medicine doctors (KMD) generally use clinical diagnosis information derived from modern medical devices and input the patient's disease code with the Korean Standard Classification of Diseases (KCD), which is the Korean International Classification of Diseases (ICD), when claiming

national health insurance. In other words, the frequency of clinical information derived from modern diagnostic devices is high, and KMD aim to use modern medical devices legally (35). Accordingly, studies on the diagnosis of TM are relatively scarce. The 11<sup>th</sup> version of the ICD (ICD-11) was adopted by the World Health Assembly in May 2019 and came into effect on 1 January 2022 (36). ICD-11 consists of 26 chapters and two supplementary chapters, and the traditional medical condition is newly established as the 26<sup>th</sup> chapter, enabling dual coding of conventional medicine and TM (36-38). One of the two traditional medical conditions is the traditional medicine patterns (TM1); hence, related research is expected to increase. In addition, the sleep-wake disorders chapter was also newly established in the ICD-11, and research in the sleep disorder area is expected to expand. At that time, these results provide fundamental data for conducting future studies. This is because sleep disturbance is one of the subjective symptoms of mibyeong (or subhealth), and related evidence is needed to systematize the diagnosis of KM (39).

There are reports that the same disease shows different symptoms according to the sasang constitution (40). This suggests that one diagnosis by biomedical medicine could require a different and personalized treatment approach in view of TM. Regarding the risk of disease prevalence, the taeum type was reported to have a 2.4 and 3.96 times higher risk of obstructive sleep apnea and diabetes, respectively, than the soeum type (41, 42). In contrast, although there were differences in the adjusted variables and disease type, the soeum type was more likely to have sleep disturbances than the taeum type. Further studies will be needed to draw definitive conclusions.

Several limitations need to be considered while interpreting the results. First, CHPI is one of the most frequent pattern identifications in clinics among the eight-principal syndrome differentiation,

but there have been few relevant studies in terms of the completeness of the measurement tool. In addition, several versions of the CHPI measurement tool exist in the ROK, and there may be other versions in China and Japan that share the CHPI diagnostic method. In the future, it will be helpful to develop the diagnostic area of TM if researchers can develop a CHPI diagnosis measurement tool composed of common items and country-specific items through collaborative research between the ROK, China, and Japan. Second, CHPI, sasang constitution, and sleep disturbances were all based on the subjective symptoms of the subjects who responded to the subjects' self-report questionnaires, not biomedical tests, such as diagnostic images or genetic tests. Several studies have tried to identify an objective measurement of these classifications, and future studies should include them (43–45). In addition, these classifications do not consider the variance of the subjects' total number of symptoms. In other words, there should be subjects who are sensitive to their discomfort or tend to overexpress it. Third, it was difficult to analyze and interpret the minimum seven hours recommended by the AASM because Koreans' sleep time tends to fall short of international standards. Indeed, 844 participants (14.5% out of 5,803 participants) were classified as having a sleep disturbance according to a PSQI score  $\geq 8.5$ , whereas 3,513 (60.64%) had  $<7$  hours sleep time per night. Therefore, through descriptive analysis, a sleep time of fewer than five hours per night suitable for Koreans was set as a categorical variable and analyzed. In the future, it will be necessary to consider the cultural and economic conditions of each country and various fundamental studies that can be referenced for sleep time studies. Fourth, because the results of this study were derived from observational data, it cannot be concluded that there is a causal relationship between sleep disturbances, CHPI, and the sasang constitution. Therefore, it is

necessary to perform well-designed randomized controlled trials (RCT) in the future.

## V. Conclusions

Considering clinical practice, as the number of patients belonging to the mibyeong (or subhealth) category increases, it will be necessary to manage them. Hence, there is a need for research on the diagnosis of TM. Sleep disturbances appear to be associated with specific cold-heat symptoms, and the association pattern was different for each sasang constitution type. Moreover, it is important to identify the cold-heat pattern in the management and treatment of diseases because cold-heat are symptoms to be considered in the diagnosis of TM and the overall TM treatment process, such as herbs or herbal formulas. Therefore, the accumulation of some related evidence for CHPI and sasang constitution is one of the implications of this study. Furthermore, subsequent studies using comprehensive longitudinal data will be needed to confirm the results.

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### Conflicts of Interest

The authors have no conflicts of interest to declare with respect to the authorship and publication of this article

### Author statement

M.K.Hyun conceptualized the study and performed the analysis, while M. K. Hyun and T. Yoshino interpreted the results, wrote the original

draft, and read and approved the final manuscript.

### Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Dongguk University, Gyeongju s (DRG IRB 20200021-01). Patient consent was exempted because of the total anonymity of all research data used in this study.

### Data Availability

Applications for the use of data can be submitted on the website of the Korean Medicine Data Center (KDC) of the Korea Institute of Oriental Medicine. Data will be provided after an application has been reviewed and approved. Researchers can only analyze submitted topics, and the given dataset must be discarded after use. (E-mail: kdc@kiom.re.kr, Website: <https://kdc.kiom.re.kr/html/>).

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