

RESEARCH ARTICLE

A possible association between dysphonia and sleep duration: A cross-sectional study based on the Korean National Health and nutrition examination surveys from 2010 to 2012

Jung-Hae Cho¹, Christian Guilminault², Young-Hoon Joo¹, Sang-Kyun Jin¹, Kyung-Do Han³, Chan-Soon Park^{1*}

1 Department of Otolaryngology-Head and Neck Surgery, College of Medicine, The Catholic university of Korea, Seoul, Republic of Korea, **2** Center for Sleep Medicine, Department of Psychiatry and behavioral science, Stanford University, Redwood City, CA, United States of America, **3** Department of Biostatistics, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

* pcs012@catholic.ac.kr



OPEN ACCESS

Citation: Cho J-H, Guilminault C, Joo Y-H, Jin S-K, Han K-D, Park C-S (2017) A possible association between dysphonia and sleep duration: A cross-sectional study based on the Korean National Health and nutrition examination surveys from 2010 to 2012. PLoS ONE 12(8): e0182286. <https://doi.org/10.1371/journal.pone.0182286>

Editor: Thomas Penzel, Charité - Universitätsmedizin Berlin, GERMANY

Received: April 10, 2017

Accepted: July 14, 2017

Published: August 4, 2017

Copyright: © 2017 Cho et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: The database for all data files can be accessed via <https://knhanes.cdc.go.kr/knhanes/eng/index.do>. The data of the respective year are available to everyone free of charge. If the applicant completes a simple subscription process for the official website (in Korean) of Korean National Health and Nutrition Examination Survey (KNHANES), the data of the respective years can be download free of charge.

Abstract

Background

Sleep is important in terms of good general health and appropriate sleep duration has been linked to quality-of-life. Dysphonia may impair communication and social relationships, and is thus also closely related to quality-of-life. No large-scale, cross-sectional epidemiological study of a sample representative of the population of an entire country has yet assessed the possible existence of a relationship between sleep duration and dysphonia.

Methods

We investigated a possible association between subjective voice problems and self-reported sleep duration in South Korean subjects using 2010–2012 data from the Korean National Health and Nutrition Examination Survey (KNHANES). Cross-sectional data on 17,806 adults (7,578 males and 10,228 females) over the age of 19 years who completed the KNHANES were analyzed. All participants reported voice problems (if present) and their daily average sleep duration using a self-reporting questionnaire. Sleep duration was classified into five categories as follows: ≤ 5 , 6, 7, 8, and ≥ 9 h/day.

Results

The overall prevalence of dysphonia was 6.8%; 5.7% in males and 7.7% in females. The prevalence for dysphonia by sleep duration exhibited a U-shape, with the lowest point being at sleep duration of 7–8h. After adjustment for covariates (age, sex, smoking status, alcohol consumption, regular exercise, low income, high-level education), a sleep duration of ≤ 5 h (OR = 1.454; 95% CI, 1.153–1.832) and a sleep duration of ≥ 9 h (OR = 1.365; 95% CI, 1.017–1.832) were significantly associated with dysphonia, compared to a sleep duration of

Funding: The authors received no specific funding for this work.

Competing interests: The authors have declared that no competing interests exist.

7 h. In terms of gender, males who slept for ≥ 9 h were at a 2-fold (OR = 2.028; 95% CI, 1.22–3.35) higher odds for dysphonia ($p < 0.05$) compared to those who slept for 7 h. A sleep duration ≤ 5 h was associated with a 1.6-fold (OR = 1.574; 95% CI, 1.203–2.247) higher odds of dysphonia ≥ 3 weeks in duration (long-term dysphonia).

Conclusions

This is the first study to show that both short and long sleep duration were significantly associated with the development of dysphonia. The association between sleep duration and dysphonia was more marked in males than females. A sleep duration ≤ 5 h had a significant impact on the prevalence of long-term dysphonia.

Introduction

Sleep duration is associated with quality-of-life and general health outcomes [1, 2]. Previous studies have shown that unusually short or long sleep durations are associated with mortality from cardiovascular disease, hypertension, obesity, and cancer [2–6]. As extreme sleep durations (abnormally long or short) affect health and morbidity, the ideal sleep duration is considered to be 6–8 h per day. Recent studies performed in Korea and Spain have suggested that a sleep duration of 7–8 h should be recommended to maintain a generally healthy lifestyle [7, 8]. In addition, Chinese studies have found relationships between sleep duration and quality-of-life in adolescents and adults, and between sleep deprivation and health-related quality-of-life in older adults [9, 10]. These studies showed that sleep was closely related to quality-of-life, as is voice.

A national health survey conducted in the USA found that about 7.6% of adults reported a voice problem annually [11]. The cumulative frequency of such problems over a life-span is thought to be much higher. Risk factors for dysphonia have been extensively investigated [12, 13]. Well-known common causes of voice problems are: voice overuse or misuse, lifestyle choice or occupation, environmental pollution, pharmacological agents or alcohol, laryngitis or laryngopharyngeal reflux, and a neural disorder of the larynx. These factors, alone or in combination, affect the voice. In addition, dysphonia may be either temporary or persistent, depending on the etiology. In particular, dysphonia that lasts for > 3 weeks (long-term dysphonia) is often caused by laryngeal pathologies and must be thoroughly evaluated [14].

It is generally considered that the voice changes when sleep duration is inadequate; fatigue affects voice. Sleep deprivation may affect the ability to voice feeling and emotion, emphasizing the importance of sleep in terms of healthy adult emotional functioning [15]. Moreover, patients with dysphonia had a lower voice-specific quality-of-life and higher depression scores [13]. Therefore, maintenance of good voice quality is an important component of good general health.

Based on previous studies, we hypothesized that inappropriate sleep duration, either too short or too long, would be associated with poor voice quality. However, to the best of our knowledge, no population-based study has yet examined the relationship between dysphonia and sleep duration in adults. Therefore, our aim was to investigate the relationship between self-reported sleep duration and dysphonia in Korean subjects using the extensive data available on the national prevalences of various diseases.

Materials and methods

Ethic statement

Written informed consent was obtained from all participants prior to the survey, and approval was obtained from the Institutional Review Board of the Catholic University of Korea in Seoul, South Korea.

Study population

Data were obtained from the Korean National Health and Nutrition Examination Survey (KNHANES); this is a cross-sectional survey designed to measure the health and nutritional status of the non-institutionalized Korean population from 2010 to 2012. KNHANES is a government-sponsored survey conducted by the Korean Center for Disease Control and Prevention, and commenced in 1998. Individuals were selected annually and complete questionnaires exploring health status, health behavior, nutrition, and attendance at health examinations. Participating households were selected with the aid of a stratified, multistage probability sampling design. The survey featured a health interview, nutritional assessment, and a health examination. Demographic data and information on health-related behaviors were collected by self-reported questionnaire and during personal interviews. Medical staff conducted physical examinations and blood and urine sampling using standard procedures. All participants provided written informed consent.

Subjective voice problems and sleep duration

Participants aged ≥ 19 years were studied; they were asked about subjective vocal problems and attended otolaryngological interviews. Self-reported vocal problems were classified as “present” or “absent” depending on the response to the question: “Do you currently experience voice pain and/or discomfort?” Participants who responded positively were then asked: “Have you had this problem for 3 weeks or longer?” Long-term dysponia was defined as dysponia persisting for ≥ 3 weeks. Question for self-reported voice problems was designed by the Epidemiologic Survey Committee of the Korean Otolaryngologic Society. In addition, the Korea centers for disease control and prevention verified the quality of the survey. Sleep duration was self-reported. All participants were asked: “How long do you usually sleep every night?” The responses were classified as ≤ 5 , 6, 7, 8, and ≥ 9 h.

Demographic variables

Medical histories and lifestyle habits were self-reported. Smoking history was categorized as current smoker, ex-smoker, and nonsmoker. Based on the amount of alcohol consumed per day during the 1-month period prior to the interview, all subjects were classified into three groups: nondrinkers, mild-to-moderate drinkers (< 15 g alcohol/day), and heavy drinkers (≥ 15 g/day). Regular exercise was defined as strenuous physical activity performed for a minimum of 20 min three times a week. Marital status was classified as with or without a spouse. Occupation was divided into working and not working. Residential area was defined as urban or rural; urban included both large and small cities. Educational level was classified as high if the respondent had completed university education. Household incomes were divided into four quartiles.

Anthropometric and laboratory measurements

Weight and height were measured by well-trained medical professionals. Standing height was measured with each subject facing directly ahead, with shoes off, the feet together, the arms at the sides, and the heels, buttocks, and upper back in contact with the wall. Height was measured in cm to the nearest mm using a SECA 225 (Germany). Waist circumference (WC) was

measured to the nearest mm at the level of the midpoint between the iliac crest and the costal margin, at the end of a normal expiration. Weight was measured in kg, to the nearest 10 g, using a GL-6000-20 scale (Cass Korea, Seoul, Korea). Body mass index (BMI) was calculated as weight (kg)/height (m²). Blood pressure (BP) was measured with each subject in a sitting position after a 5-min rest period. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured on the right arm using a mercury sphygmomanometer (Baumanometer, W.A. Baum Co., Copiague, NY, USA). Systemic hypertension was defined as a systolic blood pressure >140 mmHg and/or a diastolic blood pressure >90 mmHg, or current use of systemic anti-hypertensive drugs. Blood samples were obtained from the antecubital vein following a 10–12 h (overnight) fast. The serum levels of glycemia, total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol, were measured using enzymatic methods (Hitachi Automatic Analyzer 7600, Hitachi, Tokyo, Japan). Diabetes was defined as a fasting blood glucose level >126 mg/dL or current use of antidiabetic medication. Metabolic syndrome (MetS) was considered present if at least three of the following criteria were met: WC ≥90 cm in males or ≥80 cm in females (the modified Asian criteria); TG ≥150 mg/dL or prescription of TG-lowering medication; a reduced level of HDL cholesterol (<40 mg/dL in males or <50 mg/dL in females); an SBP ≥130 mmHg, a DBP ≥85 mmHg, or use of antihypertensive medication; and an FBS level ≥100 mg/dL or use of anti-diabetes medication or previously diagnosed diabetes mellitus [16]. We also measured serum creatinine levels and calculated estimated glomerular filtration rates (eGFRs; mL/min/1.73m²) using the following equation from the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI): $eGFR = 141 \times \min(\text{serum creatinine}/\kappa, 1)^\alpha \times \max(\text{serum creatinine}/\kappa, 1)^{-1.209} \times 0.993^{\text{age}} \times 1.018$ [if female] $\times 1.159$ [if African-American], where κ was 0.7 for females and 0.9 for males; α was -0.411 for males and -0.329 for females; min indicates minimum serum creatinine/ κ , or 1; and max indicates maximum serum creatinine/ κ or 1 [17]. Chronic kidney disease was considered present when the eGFR was <60 mL/min/1.73m².

Statistical analysis

All statistical analyses were performed using the survey module of Statistical Analysis Software (SAS) (v. 9.3; SAS Institute, Cary, NC, USA); this was appropriate, considering the complex sample design and sampling weights of KNHANES. Again, KNHANES seeks to derive nationally representative data. All continuous variables are given as means with standard errors (SEs), and all categorical variables as numbers with percentages. The Rao-Scott chi-squared test or Student's *t*-test (run using the PROC SURVEYFREQ module of SAS) and logistic regression analysis (using the PROC SURVEYLOGISTIC module of SAS) were employed to explore associations between dyspnea and various risk factors using a complex sampling design. Upon multiple logistic regression analysis, we first adjusted for age and sex (model 1); next for these variables plus BMI (model 2); and finally for the variables of model 1 plus smoking status, alcohol intake, regular exercise, income, and educational level (model 3). The prevalences of dyspnea (with 95% confidence intervals [CIs]) were calculated. All *p*-values were two-tailed and a *p* value <0.05 was considered to reflect statistical significance.

Results

General characteristics of the study population

Subject demographics are summarized in Table 1. Of the 17,806 participants aged ≥19 years, 1,218 (6.8%) complained of dyspnea. The mean age of participants with subjective voice problems was significantly lower than that of participants without such problems (*p*<0.0001). The mean sleep duration of all participants was 6.84±0.02 h/day. The mean sleep duration was

Table 1. Analysis of factors potentially associated with dyspnea.

Parameter	Subjective Voice Problem (n = 17,806)		
	Yes (n = 1,218)	No (n = 16,588)	P-value
Age (years)	45.22±0.24	49.34±0.62	< .0001*
Gender_ men(%)	50.1(0.4)	39.2(1.8)	< .0001*
Body mass index (kg/m ²)	23.69±0.04	23.8±0.14	.4365
Waist circumference (cm)	81.07±0.13	81.32±0.37	.4978
Sleep duration(hours/day)	6.85±0.02	6.69±0.06	< .0001*
Alcohol consumption(%)			
Non-drinker	24.6(0.5)	31.7(1.6)	
Mild to moderate drinker	65.4(0.5)	59.8(1.6)	
Heavy drinker	10.0(0.3)	8.4(1.1)	
Smoking(%)			.0894
Never smoker	56.7(0.5)	60.6(1.7)	
Ex-smoker	17.2 (0.4)	16.3(1.2)	
Current smoker	26.1(0.5)	23.1(1.6)	
Diabetes(%)	8.3(0.3)	9.1(0.9)	.4126
Hypertension(%)	27.0(0.5)	32.7(1.7)	.0005*
Metabolic syndrome(%)	25.7(0.5)	30.9(1.8)	.0026*
CKD(eGFR <60) (%)	6.1(0.2)	10.4(1.0)	< .0001*
Regular exercise (%)	19.6(0.5)	19.7(1.5)	.9256
Job_ working (%)	64.1(0.5)	61.1(1.7)	.0474*
Marital status_ with spouse (%)	80.0(0.7)	79.5(1.4)	.7038
Residential area_ urban (%)	80.0(1.7)	78.9(2.6)	.5479
Education; ≥ high (%)	71.4(0.7)	63.6(1.9)	< .0001*
Income; lowest quartile (%)	15.7(0.5)	23.3(1.6)	.5996

Values are presented as mean ± SE or %(SE).

* Significant at $p < 0.05$

Abbreviation: CKD; chronic kidney disease, eGFR; estimated glomerular filtration rate

<https://doi.org/10.1371/journal.pone.0182286.t001>

significantly longer in those with than without dyspnea ($p = 0.0056$). The prevalence of dyspnea was higher in females (7.7%) than males (5.7%). All of age, gender, sleep duration, alcohol consumption, hypertension, metabolic syndrome, chronic kidney disease, occupation, and educational level were significantly associated with subjective voice problems.

Prevalence of subjective voice problems by sleep duration

Fig 1 shows the prevalence of subjective voice problems by sleep duration exhibited a U-shape, with the lowest point being at a sleep duration of 7-8h. The prevalence of dyspnea was significantly lower when the sleep duration was 7 h/day ($p < 0.0001$, 0.0003, and 0.0055 for all subjects, males, and females, respectively). Male dyspnea was most prevalent in those who slept ≥ 9 h/day, and lowest at a sleep duration of 7 h/day. For females, the figures were ≤ 5 h/day and 8 h/day.

Multivariable analysis of associations between subjective voice problems and sleep duration

Odds ratios and 95% CIs were obtained by multivariable logistic regression. The risks of dyspnea in the five subgroups categorized by sleep duration were calculated. Table 2 shows that dyspnea was significantly associated with sleep duration. After adjustment for covariates

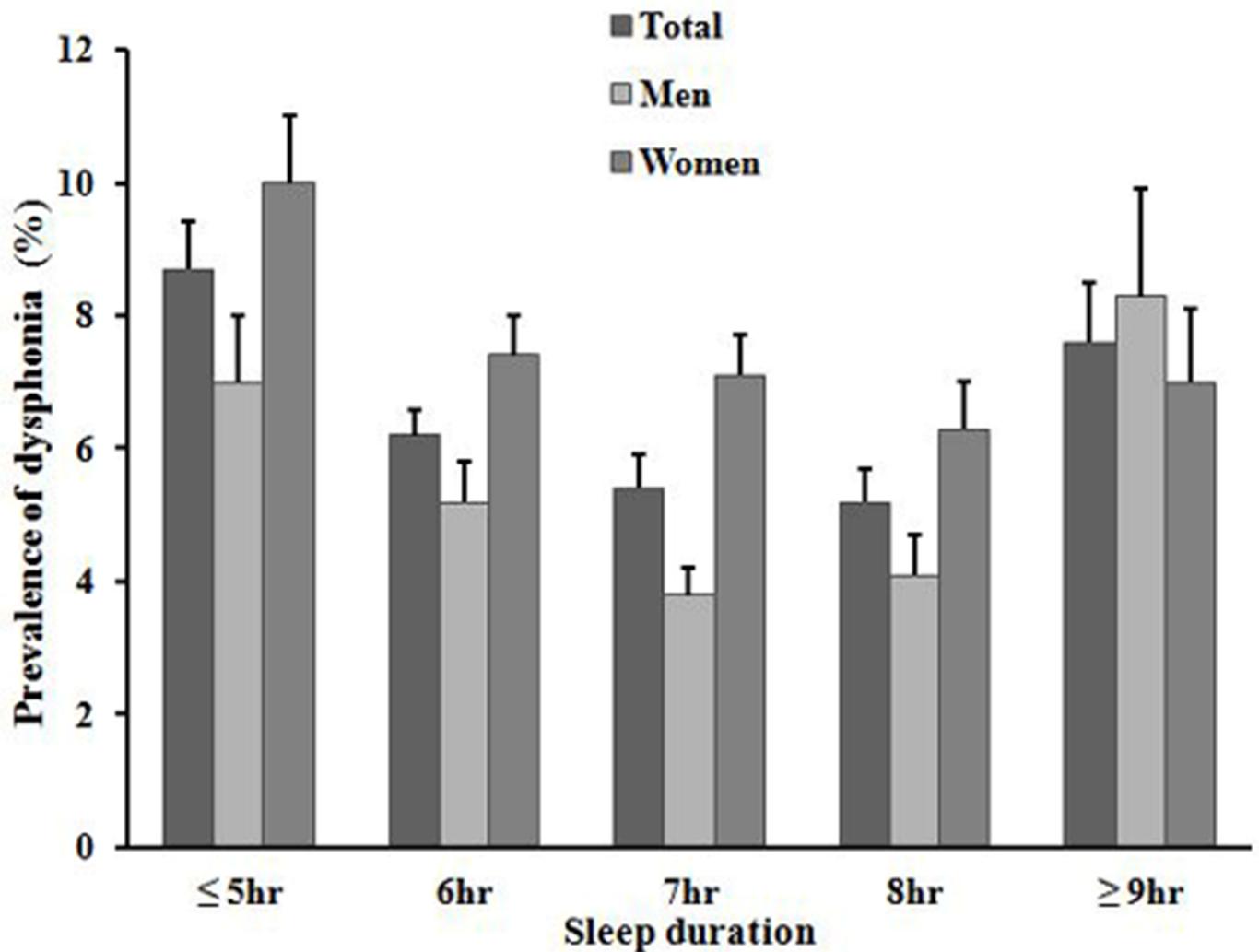


Fig 1. The prevalence of dyspnea by sleep duration.

<https://doi.org/10.1371/journal.pone.0182286.g001>

(age, sex, smoking status, alcohol consumption, regular exercise, low income, and high-level education), both a sleep duration of ≤ 5 h/day (OR = 1.454, 95% CI, 1.153–1.832) and a sleep duration of ≥ 9 h/day (OR = 1.365, 95% CI, 1.017–1.832) were significantly associated with the development of dyspnea, compared to the reference sleep duration (7 h). However, dyspnea was significantly more likely to be associated with sleep duration in males. In particular, males who slept for ≤ 5 h/day, ≥ 9 h/day were at a 1.69 fold (OR = 1.649, 95% CI, 1.12–2.53), 2-fold (OR = 2.028, 95% CI, 1.22–3.35) higher odds of dyspnea, respectively. Only females who slept for ≤ 5 h/day were at a 1.34-fold (OR = 1.340, 95% CI, 1.020–1.760) higher odds. These figures did not change when a sleep duration of 8 h was used as the reference duration.

Association between long-term dyspnea (≥ 3 weeks) and sleep duration

The distribution of persistent dyspnea (≥ 3 weeks) by sleep duration is shown in Fig 2. The prevalence of short-term and long-term dyspnea differed significantly by sleep duration

Table 2. Adjusted odds ratios of dysphonia according to sleep duration.

Sleep duration	Odds ratio(95% confidence intervals)		
	Model 1	Model 2	Model 3
Total (n = 17,806)			
≤5 hrs	1.437(1.145–1.803)*	1.421(1.131–1.785)*	1.454(1.153–1.832)*
6 hrs	1.158(0.954–1.406)	1.156(0.952–1.405)	1.426(1.017–2.000)*
7 hrs	1	1	1
8 hrs	0.965(0.772–1.205)	0.962(0.770–1.202)	0.954(0.764–1.191)
≥9 hrs	1.398(1.042–1.876)*	1.406(1.047–1.888)*	1.365(1.017–1.832)*
Men (n = 7,578)			
≤5 hrs	1.651(1.113–2.448)*	1.649(1.113–2.445)*	1.686(1.124–2.529)*
6 hrs	1.426(1.017–2.000)*	1.425(1.016–2.001)*	1.444(1.032–2.021)*
7 hrs	1	1	1
8 hrs	1.053(0.735–1.510)	1.051(0.734–1.504)	1.027(0.717–1.471)
≥9 hrs	2.124(1.308–3.451)*	2.116(1.297–3.450)*	2.028(1.227–3.352)*
Women (n = 10,228)			
≤5 hrs	1.355(1.043–1.76)*	1.330(1.023–1.730)*	1.340(1.020–1.760)*
6 hrs	1.025(0.815–1.289)	1.021(0.812–1.284)	1.013(0.802–1.280)
7 hrs	1	1	1
8 hrs	0.889(0.672–1.176)	0.889(0.671–1.178)	0.889(0.668–1.183)
≥9 hrs	1.002(0.699–1.437)	1.011(0.705–1.451)	0.967(0.674–1.389)

Model 1 was adjusted for age, sex

Model 2 was adjusted for age, sex, and BMI

Model 3 was adjusted for age, sex, smoke, alcohol, exercise, income, and education.

* Significant at $P < 0.05$

<https://doi.org/10.1371/journal.pone.0182286.t002>

($p < 0.0001$). The overall prevalence of long-term dysphonia was 3.2%. The graph of [dysphonia ≥ 3 weeks in duration] against [sleep hours] was U-shaped, with a nadir at a sleep duration of 7–8 h. After analysing by gender, the U-shaped distribution of persistent dysphonia by sleep duration was shown in men but not women. When adjusted for covariates (age, sex, smoking status, alcohol consumption, regular exercise, low income, and high-level education), the odds ratio changed (Fig 3). The odds ratio for dysphonia ≥ 3 weeks in duration, graphed against sleep duration, was U-shaped, with the nadir at a sleep duration of 7–8 h. The odds ratio was 1.574 (95% CI, 1.203–2.247) for a sleep duration ≤ 5 h but 1.358 (95% CI, 0.912–2.642) for a sleep duration of ≥ 9 h. The odds of long-term dysphonia was thus higher when the sleep duration was short rather than long. The analysis by gender showed the U-shaped distribution of odds ratio for long-term dysphonia in men but not women.

Discussion

This is the first population-based study to explore the associations between sleep duration and dysphonia in adults, by gender. Subjective voice problems were associated with abnormal sleep duration, especially in males. As self-perception of a vocal problem is always explored during a voice examination, most previous epidemiological studies on voice disorders have focused on subjective symptoms [18–22]. Dysphonia is any alteration in voice production, and is self-perceived. Dysphonia has many etiologies. Rosen et al. classified voice disorders into four major categories; organic, functional, movement, and systemic [23].

The possibility that sleep duration might influence the development of dysphonia or voice disorders has not previously been investigated. This is thus the first study to use multivariate

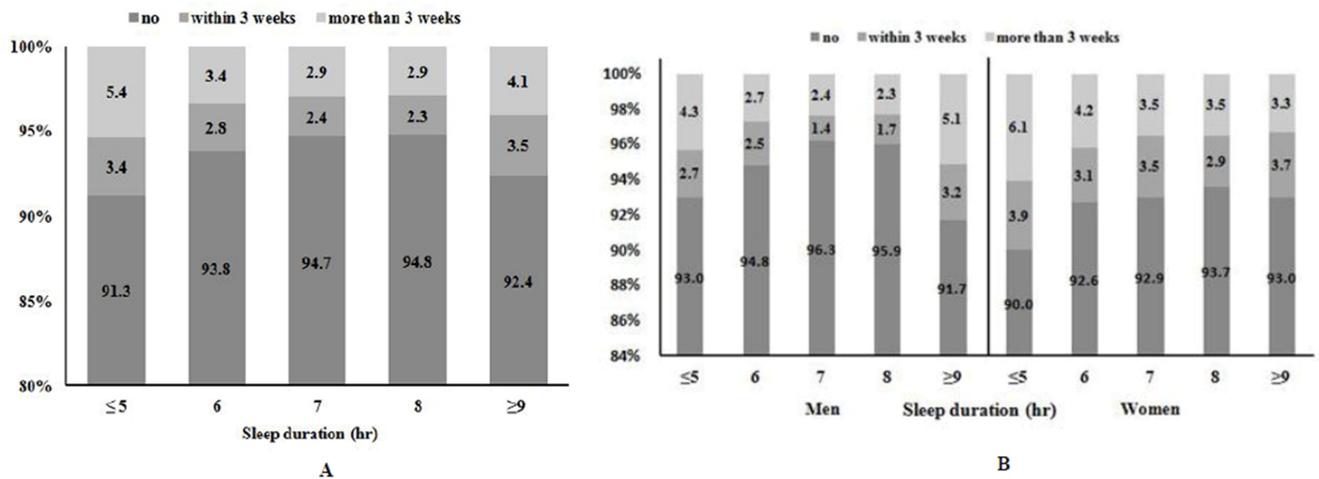


Fig 2. Distribution of dyspnea by sleep duration, stratified by duration of symptom. (A) Data for all participants and (B) data for men and women.

<https://doi.org/10.1371/journal.pone.0182286.g002>

analysis to show that sleep duration is significantly associated with dyspnea. Sleep duration may be abnormally short or long. Although the definitions of abnormal sleep duration might vary among papers, by different nations, cultures, and so on, short sleep has been usually defined as <7 h on average and long sleep as ≥ 9 h [2]. Both short and long sleepers are more likely to be in poorer overall health and to have been diagnosed with more medical conditions than normal sleepers [1–4]. Appropriate sleep is important in terms of both general health and quality of life. In our present population-based cross-sectional study, we found that the mean sleep duration was significantly longer in participants with than without dyspnea. Surprisingly, it also appears that long sleep duration is associated with dyspnea. After adjusting for confounders, longer sleep duration (≥ 9 h/day) showed the increased association with dyspnea. Although the reason for this association is unclear, males who slept longer were at a 2.0-fold higher odds of dyspnea than were those who slept for 7 h. Long sleep duration (≥ 9

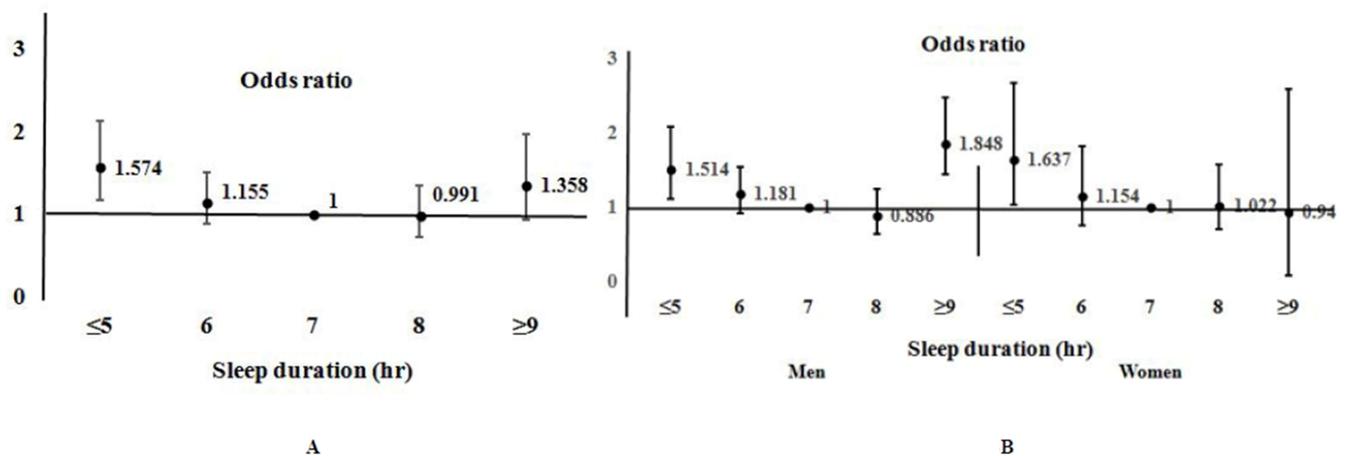


Fig 3. The odds ratio of dyspnea that lasts more than three weeks by sleep duration. (A) Data for all participants and (B) data for men and women.

<https://doi.org/10.1371/journal.pone.0182286.g003>

h/day) has been associated with many sleep, medical, neurological, and psychiatric disorders [24]. According to previous reports, long sleep duration may mediate inflammatory, metabolic, or immune responses related to the risk of respiratory diseases [25, 26]. Therefore, we assumed that inflammatory or immune response of larynx can affect voice production and might induce dysphonia in long sleep duration.

Laryngeal disease is more common in males and subjective voice problems more common in females [27, 28]. Similarly, we found that dysphonia was more common in females than males. It was hypothesized that between-gender structural differences in laryngeal anatomy render females more vulnerable to voice disorders; the female vocal folds are shorter than those of males and have less hyaluronic acid (essential for wound repair) in the superficial layer of the lamina propria [28, 29].

Murry et al. showed that voice quality measured using the GRBAS scale (a perceptual rating of dysphonia severity) was strongly correlated with quality-of-life as measured using the V-RQOL (voice-related quality of life) instrument, especially in subjects aged <66 years [30]. Dysphonia severity was negatively associated with voice-related quality of life assessed using a voice symptom scale [31]. In particular, long-term dysphonia had a profound negative impact on the quality-of-life [13]. Although many voice problems are acute self-limiting infectious processes, voice problems persisting for >3 weeks are usually considered to be chronic and associated with various predisposing factors, including vocal fold mucosal disease, other medical conditions, and/or a neurogenic voice disorder [14]. The most common cause of community-acquired dysphonia is viral laryngitis, which persists for 1–3 weeks. Dysphonia persisting for longer requires further evaluation to ensure that no malignancy or other morbid condition has been missed, and to allow treatment of the specific vocal pathology, if indicated [14]. In the present study, we calculated adjusted odds ratios for long-term dysphonia by sleep duration. Compared to 7 h of sleep, a sleep duration of ≤ 5 h/day was associated with a 1.6-fold increased odds of development of long-term dysphonia. Thus, sleep deprivation may be associated with long-term dysphonia caused by significant vocal pathology.

One previous study found that fatigue is highly associated with functional dysphonia [32]. Fatigue may all affect behavior, leading to reduced activity, low mood, and reduced voice use [32]. Bagnall et al. found that fatigue caused by sleep deprivation triggered vocal changes, compromising the quality of vocal performance and contributing to the development of voice disorders [33]. In contrast to the (male-specific) association between excessive sleep and dysphonia, it was found that sleep deprivation was associated with dysphonia in both males and females. It is thus likely that sleep deprivation affects dysphonia development more than does excessive sleep; short sleep may be caused by insomnia, a psychiatric disorder, or obstructive sleep apnea (OSA). In particular, OSA may cause poor sleep and voice problems; bidirectional relationships have been found between OSA, on the one hand, and laryngeal sensory disturbances, laryngopharyngeal reflux, and a chronic cough, on the other [34–37]. OSA is a common sleep-related breathing disorder characterized principally by repetitive episodes of obstructive apnea and hypopnea during sleep [38]. Extraesophageal reflux (such as a laryngopharyngeal reflux) shares several risk factors with OSA; these are obesity, male sex, and alcohol use [38]. The symptoms of extraesophageal reflux vary and include regurgitation, heartburn, hoarseness, vocal fatigue, throat clearing, postnasal drip, cough, dysphagia, and globus. In addition, extraesophageal reflux is significantly more common in OSA patients than the general population. Eskiizmir et al. hypothesized that OSA and extraesophageal reflux may be related via a vicious cycle; an increased respiratory effort contributes to gastric acid reflux that, in turn, contributes to OSA progression by triggering inflammation that changes the upper airway mechanics via mucosal damage and sensory dysfunction [36]. Based on both previous

data and our present results, it is clear that sleep disturbance, especially sleep deprivation, is associated with voice disorders.

A recent review article commented that functional dysphonia is associated with multiple psychosocial factors including anxiety, depression, and reduced quality of life [39]. Willinger et al. found that depression and anxiety symptoms were markedly more prevalent in patients with functional dysphonia [40]. According to recent meta-analysis, both short and long sleep duration is significantly associated with increased risk of depression in adults [41]. Therefore, we presume that psychological factors, physical problems like fatigue and organic changes related to sleep problems or abnormal sleep duration may trigger vocal changes, compromise the quality of vocal performance, develop voice disorders and be finally associated with functional dysphonia.

In summary, considering above, it might be suggested that many diseases such as extraesophageal reflux, OSA and psychologic disorders, and inflammatory or immune response of larynx in relation with abnormal sleep time might affect voice production and yielded a U-shaped relationship between sleep duration and dysphonia.

Our study has certain limitations. First, we did not categorize the severity of self-reported voice problems as mild, moderate, or severe; we did not perform objective tests for analysing the quality of voice. Second, we did not use detailed or validated questionnaire on voice problems. Third, we did not seek to diagnose any laryngeal pathology; we did not identify subjects with infectious or reflux laryngitis (common causes of voice problems). Thus, we did not differentiate voice problems by severity or type and perform subgroup analysis according to underlying diseases. Fourth, our study subdivided subjects in 5 subgroups based on sleep duration, independent of the underlying cause of the sleep limitation, such decision means that we did not take into consideration specific co-morbidities such as gastro-esophageal reflux, OSA, parasomnia, presence of any organic disease, and so on, which might bridge the possible gap between sleep duration and voice disorder. Fifth, some related risk factors with dysphonia, such as voice overuse, occupation, medication, and environmental status, were not evaluated in this study because KNHANES did not include such information. Lastly, cross-sectional study cannot identify causal relationships. Thus, future longitudinal studies are required. However, the major strength of our work is that after adjusting for many confounders, we are the first to demonstrate an association between abnormal sleep duration and dysphonia.

Conclusions

A U-shaped association is evident between sleep duration and mortality; we found a similar relationship between dysphonia and abnormal sleep duration in our population-based epidemiological study. Abnormally short and long sleep played a more significant role in dysphonia development in Korean adult males, but not females. In addition, sleep deprivation had a greater impact than did excessive sleep on the development of long-term dysphonia. Accurate epidemiological information contributes to healthcare planning, the development of preventative screening projects, and the provision of rehabilitative services. Our findings indicate that sleep disturbances should be controlled to prevent development of voice disorders. The mechanisms underlying the associations that we found should be studied further.

Acknowledgments

We thank the 150 residents of the otolaryngology departments of the 47 training hospitals in South Korea and members of the Division of Chronic Disease Surveillance in the Korea Centers for Disease Control & Prevention for participating in this survey and the dedicated work they provided.

Author Contributions

Conceptualization: Jung-Hae Cho, Young-Hoon Joo, Chan-Soon Park.

Data curation: Jung-Hae Cho.

Formal analysis: Jung-Hae Cho, Christian Guilminault.

Investigation: Young-Hoon Joo, Sang-Kyun Jin, Kyung-Do Han, Chan-Soon Park.

Methodology: Kyung-Do Han.

Resources: Young-Hoon Joo, Sang-Kyun Jin, Kyung-Do Han.

Software: Young-Hoon Joo.

Supervision: Christian Guilminault, Chan-Soon Park.

Validation: Christian Guilminault.

Writing – original draft: Jung-Hae Cho, Chan-Soon Park.

Writing – review & editing: Jung-Hae Cho, Chan-Soon Park.

References

1. Ikehara S, Iso H, Date C, Kikuchi S, Watanabe Y, Wada Y, et al. Association of sleep duration with mortality from cardiovascular disease and other causes for Japanese men and women: the JACC study. *Sleep*. 2009; 32(3):295–301. Epub 2009/03/20. PMID: [19294949](#); PubMed Central PMCID: PMCPmc2647783.
2. Gallicchio L, Kalesan B. Sleep duration and mortality: a systematic review and meta-analysis. *J Sleep Res*. 2009; 18(2):148–58. Epub 2009/08/04. <https://doi.org/10.1111/j.1365-2869.2008.00732.x> PMID: [19645960](#).
3. Ferrie JE, Shipley MJ, Cappuccio FP, Brunner E, Miller MA, Kumari M, et al. A prospective study of change in sleep duration: associations with mortality in the Whitehall II cohort. *Sleep*. 2007; 30(12):1659–66. Epub 2008/02/06. PMID: [18246975](#); PubMed Central PMCID: PMCPmc2276139.
4. Patel SR, Malhotra A, Gottlieb DJ, White DP, Hu FB. Correlates of long sleep duration. *Sleep*. 2006; 29(7):881–9. Epub 2006/08/10. PMID: [16895254](#); PubMed Central PMCID: PMCPmc3500381.
5. Gottlieb DJ, Redline S, Nieto FJ, Baldwin CM, Newman AB, Resnick HE, et al. Association of usual sleep duration with hypertension: the Sleep Heart Health Study. *Sleep*. 2006; 29(8):1009–14. Epub 2006/09/02. PMID: [16944668](#).
6. Taheri S, Lin L, Austin D, Young T, Mignot E. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. *PLoS Med*. 2004; 1(3):e62. Epub 2004/12/17. <https://doi.org/10.1371/journal.pmed.0010062> PMID: [15602591](#); PubMed Central PMCID: PMCPmc535701.
7. Yeo Y, Ma SH, Park SK, Chang SH, Shin HR, Kang D, et al. A prospective cohort study on the relationship of sleep duration with all-cause and disease-specific mortality in the Korean Multi-center Cancer Cohort study. *J Prev Med Public Health*. 2013; 46(5):271–81. Epub 2013/10/19. <https://doi.org/10.3961/jpmph.2013.46.5.271> PMID: [24137529](#); PubMed Central PMCID: PMCPmc3796652.
8. Faubel R, Lopez-Garcia E, Guallar-Castillon P, Balboa-Castillo T, Gutierrez-Fisac JL, Banegas JR, et al. Sleep duration and health-related quality of life among older adults: a population-based cohort in Spain. *Sleep*. 2009; 32(8):1059–68. Epub 2009/09/04. PMID: [19725257](#); PubMed Central PMCID: PMCPmc2717196.
9. Chiu HF, Xiang YT, Dai J, Chan SS, Yu X, Ungvari GS, et al. Sleep duration and quality of life in young rural Chinese residents. *Behav Sleep Med*. 2013; 11(5):360–8. Epub 2013/03/07. <https://doi.org/10.1080/15402002.2013.764524> PMID: [23461412](#).
10. Lo CM, Lee PH. Prevalence and impacts of poor sleep on quality of life and associated factors of good sleepers in a sample of older Chinese adults. *Health Qual Life Outcomes*. 2012; 10:72. Epub 2012/06/20. <https://doi.org/10.1186/1477-7525-10-72> PMID: [22709334](#); PubMed Central PMCID: PMCPmc3445836.
11. Bhattacharyya N. The prevalence of voice problems among adults in the United States. *Laryngoscope*. 2014; 124(10):2359–62. <https://doi.org/10.1002/lary.24740> PMID: [24782443](#).

12. Roy N, Merrill RM, Gray SD, Smith EM. Voice disorders in the general population: prevalence, risk factors, and occupational impact. *Laryngoscope*. 2005; 115(11):1988–95. <https://doi.org/10.1097/01.mlg.0000179174.32345.41> PMID: 16319611.
13. Cohen SM. Self-reported impact of dysphonia in a primary care population: an epidemiological study. *Laryngoscope*. 2010; 120(10):2022–32. Epub 2010/09/11. <https://doi.org/10.1002/lary.21058> PMID: 20830762.
14. Schwartz SR, Cohen SM, Dailey SH, Rosenfeld RM, Deutsch ES, Gillespie MB, et al. Clinical practice guideline: hoarseness (dysphonia). *Otolaryngol Head Neck Surg*. 2009; 141(3 Suppl 2):S1–S31. <https://doi.org/10.1016/j.otohns.2009.06.744> PMID: 19729111.
15. McGlinchey EL, Talbot LS, Chang KH, Kaplan KA, Dahl RE, Harvey AG. The effect of sleep deprivation on vocal expression of emotion in adolescents and adults. *Sleep*. 2011; 34(9):1233–41. Epub 2011/09/03. <https://doi.org/10.5665/SLEEP.1246> PMID: 21886361; PubMed Central PMCID: PMC3157665.
16. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. 2009; 120(16):1640–5. Epub 2009/10/07. <https://doi.org/10.1161/CIRCULATIONAHA.109.192644> PMID: 19805654.
17. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J, et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int*. 2005; 67(6):2089–100. Epub 2005/05/11. <https://doi.org/10.1111/j.1523-1755.2005.00365.x> PMID: 15882252.
18. Merrill RM, Anderson AE, Sloan A. Quality of life indicators according to voice disorders and voice-related conditions. *Laryngoscope*. 2011; 121(9):2004–10. Epub 2011/10/26. <https://doi.org/10.1002/lary.21895> PMID: 22024857.
19. Kim KH, Kim RB, Hwang DU, Won SJ, Woo SH. Prevalence of and Sociodemographic Factors Related to Voice Disorders in South Korea. *J Voice*. 2015. Epub 2015/05/20. <https://doi.org/10.1016/j.jvoice.2015.04.010> PMID: 25985718.
20. Byeon H. The association between lifetime cigarette smoking and dysphonia in the Korean general population: findings from a national survey. *PeerJ*. 2015; 3:e912. Epub 2015/05/07. <https://doi.org/10.7717/peerj.912> PMID: 25945309; PubMed Central PMCID: PMC4419546.
21. Byeon H. Prevalence of Perceived Dysphonia and Its Correlation With the Prevalence of Clinically Diagnosed Laryngeal Disorders: The Korea National Health and Nutrition Examination Surveys 2010–2012. *Ann Otol Rhinol Laryngol*. 2015; 124(10):770–6. Epub 2015/04/25. <https://doi.org/10.1177/0003489415583684> PMID: 25907671.
22. Byeon H. Gender differences in risk factors of benign vocal fold disease in Korea: the fifth Korea National Health and Nutritional Examination Survey. *Logoped Phoniatr Vocol*. 2015; 1–7. Epub 2015/02/24. <https://doi.org/10.3109/14015439.2015.1004365> PMID: 25698081.
23. Rosen CA, Murry T. Nomenclature of voice disorders and vocal pathology. *Otolaryngol Clin North Am*. 2000; 33(5):1035–46. Epub 2000/09/14. PMID: 10986070.
24. Ohayon MM, Reynolds CF 3rd, Dauvilliers Y. Excessive sleep duration and quality of life. *Ann Neurol*. 2013; 73(6):785–94. <https://doi.org/10.1002/ana.23818> PMID: 23846792; PubMed Central PMCID: PMC4142503.
25. Parish JM. Sleep-related problems in common medical conditions. *Chest*. 2009; 135(2):563–72. Epub 2009/02/10. <https://doi.org/10.1378/chest.08-0934> PMID: 19201722.
26. Nieto FJ, Peppard PE, Young T, Finn L, Hla KM, Farre R. Sleep-disordered breathing and cancer mortality: results from the Wisconsin Sleep Cohort Study. *Am J Respir Crit Care Med*. 2012; 186(2):190–4. Epub 2012/05/23. <https://doi.org/10.1164/rccm.201201-0130OC> PMID: 22610391; PubMed Central PMCID: PMC3406081.
27. Hah JH, Sim S, An SY, Sung MW, Choi HG. Evaluation of the prevalence of and factors associated with laryngeal diseases among the general population. *Laryngoscope*. 2015; 125(11):2536–42. Epub 2015/07/15. <https://doi.org/10.1002/lary.25424> PMID: 26154733.
28. Van Houtte E, Van Lierde K, D'Haeseleer E, Claeys S. The prevalence of laryngeal pathology in a treatment-seeking population with dysphonia. *Laryngoscope*. 2010; 120(2):306–12. Epub 2009/12/04. <https://doi.org/10.1002/lary.20696> PMID: 19957345.
29. Ward PD, Thibeault SL, Gray SD. Hyaluronic acid: its role in voice. *J Voice*. 2002; 16(3):303–9. Epub 2002/10/25. PMID: 12395982.

30. Murry T, Medrado R, Hogikyan ND, Aviv JE. The relationship between ratings of voice quality and quality of life measures. *J Voice*. 2004; 18(2):183–92. Epub 2004/06/15. <https://doi.org/10.1016/j.jvoice.2003.11.003> PMID: 15193651.
31. Jones SM, Carding PN, Drinnan MJ. Exploring the relationship between severity of dysponia and voice-related quality of life. *Clin Otolaryngol*. 2006; 31(5):411–7. Epub 2006/10/04. <https://doi.org/10.1111/j.1749-4486.2006.01291.x> PMID: 17014451.
32. O'Hara J, Miller T, Carding P, Wilson J, Deary V. Relationship between fatigue, perfectionism, and functional dysponia. *Otolaryngol Head Neck Surg*. 2011; 144(6):921–6. Epub 2011/04/16. <https://doi.org/10.1177/0194599811401236> PMID: 21493299.
33. Bagnall AD, Dorrian J, Fletcher A. Some vocal consequences of sleep deprivation and the possibility of "fatigue proofing" the voice with Voicecraft(R) voice training. *J Voice*. 2011; 25(4):447–61. Epub 2011/03/16. <https://doi.org/10.1016/j.jvoice.2010.10.020> PMID: 21402470.
34. Novakovic D, MacKay S. Adult obstructive sleep apnoea and the larynx. *Curr Opin Otolaryngol Head Neck Surg*. 2015; 23(6):464–9. <https://doi.org/10.1097/MCO.0000000000000209> PMID: 26488535.
35. Gilani S, Quan SF, Pynnonen MA, Shin JJ. Obstructive Sleep Apnea and Gastroesophageal Reflux: A Multivariate Population-Level Analysis. *Otolaryngol Head Neck Surg*. 2015. Epub 2015/12/10. <https://doi.org/10.1177/0194599815621557> PMID: 26645532.
36. Eskiizmir G, Kezirian E. Is there a vicious cycle between obstructive sleep apnea and laryngopharyngeal reflux disease? *Med Hypotheses*. 2009; 73(5):706–8. Epub 2009/06/06. <https://doi.org/10.1016/j.mehy.2009.04.042> PMID: 19493631.
37. Baker SR, Ross J. Sleep apnea syndrome and supraglottic edema. *Arch Otolaryngol*. 1980; 106(8):486–91. Epub 1980/08/01. PMID: 7396796.
38. Zanation AM, Senior BA. The relationship between extraesophageal reflux (EER) and obstructive sleep apnea (OSA). *Sleep Med Rev*. 2005; 9(6):453–8. <https://doi.org/10.1016/j.smr.2005.05.003> PMID: 16182575.
39. Deary V, Miller T. Reconsidering the role of psychosocial factors in functional dysponia. *Curr Opin Otolaryngol Head Neck Surg*. 2011; 19(3):150–4. Epub 2011/04/19. <https://doi.org/10.1097/MCO.0b013e328346494d> PMID: 21499101.
40. Willinger U, Völkl-Kernstock S, Aschauer HN. Marked depression and anxiety in patients with functional dysponia. *Psychiatry Res*. 2005; 134(1):85–91. <https://doi.org/10.1016/j.psychres.2003.07.007> PMID: 15808293
41. Zhai L, Zhang H, Zhang D. Sleep duration and depression among adults: a meta-analysis of prospective studies. *Depress Anxiety*. 2015; 32(9):664–70. Epub 2015/06/06. <https://doi.org/10.1002/da.22386> PMID: 26047492.