Sleep duration and risk of obesity: A genome and epidemiological study

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Abstract. Obesity is one of the risk factors for metabolic and cardiovascular diseases. Although numerous epidemiological studies have reported a possible causal association between sleep duration and the risk of obesity, evidence for an association in adults remains unclear. Accordingly, the present study aimed to evaluate the association between sleep duration and the risk of obesity in an adult group. To this end, 5,719 adults (2,876 males and 2,843 females) who participated in a genome and epidemiology study, were analyzed. Data were obtained on sleep duration, body mass index (BMI) and other demographic data including age, sex, waist circumference, alcohol consumption and smoking status. The association between sleep duration and obesity was investigated using a Chi-squared test or logistic regression analysis. Multivariate logistic regression analysis revealed that a short sleep duration (≤6 h) was significantly associated with obesity after adjusting for various confounding factors (OR, 1.446; 95% CI, 1.254-1.667; P<0.0001). Strong associations between a short sleep duration (≤6 h) and obesity were identified in males (OR, 1.567; 95% CI, 1.258-1.953; P<0.0001) and the early midlife group (OR, 1.584; 95% CI, 1.320-1.902; P<0.0001). Furthermore, the risk of obesity significantly increased with a short sleep duration (≤6 h) in participants without hypertension (OR, 1.534; 95% CI, 1.263-1.863; P<0.0001) or diabetes (OR, 1.473; 95% CI, 1.272-1.705; P<0.0001). A short sleep duration was positively related to a high prevalence of obesity, and this association varied with sex, age, and the presence of metabolic disease. On the whole, the findings of the present study provide evidence that sleep duration can affect obesity.

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Abbreviations: BMI, body mass index; OR, odds ratio; CI, confidence interval; KoGES, Korean Genome and Epidemiology Study

Key words: sleep duration, obesity, cohort study, body mass index, metabolic disease

Introduction

Obesity is a major public health concern worldwide and is related to a number of health consequences, including hypertension, diabetes mellitus, dyslipidemia, cardiovascular disease and cancer (1,2). Obesity rates have markedly increased in recent years. The number of obese individuals worldwide was estimated at 500 million in 2005, and this number is expected to increase steadily to approximately 1.1 billion by 2030 (3). The prevalence of obesity among the Korean population has also been reported to have increased from 27% in 1998 to 32% in 2011 (4). Consequently, changing one's lifestyle factors is crucial to preventing or reducing the burden of obesity.

Disorders of sleep, an essential component of lifestyle, are associated with metabolic dysfunctions, which can lead to the progression of obesity (5). To date, studies have largely suggested that several hormones are involved in the regulation that occurs between sleep and body mass index (BMI) (6-8). Some researchers have also observed that sleep restriction increased food intake and that poor sleep could exert negative effects on maintaining nervous, endocrine and cardiovascular health (9). Moreover, recent epidemiological surveys have investigated the association between sleep time and the prevalence of obesity (10-12) as the hours of sleep represent the most essential measure of sleep. However, the overall findings remain unclear, as studies have shown associations that presented as an inverted bell-shaped (13), were negatively linear (14-16), or exhibited no correlation (17). Furthermore, these previous studies were mostly conducted in the United States (18), Europe (19), China (11,20) and Japan (21,22), with few studies conducted in Korea (23).

Therefore, using the Korean Genome and Epidemiology Study (KoGES) data, the present study examined the association between sleep duration and the probability of obesity in Korean adults and investigated age- and sex-specific differences. In addition, at the reference time point, the effects of sleep on the risk of obesity were investigated, depending upon whether the participants had hypertension or diabetes.

Patients and methods

Study participants and design. The study dataset was obtained from the KoGES. The KoGES is an ongoing prospective cohort study that was initiated in 2001 to assess the risk and

burden of chronic diseases in the general Korean population. Detailed information on the KoGES can be found in a previous study (24). The participants in the current study included 8,840 individuals from the Korea Association Resource (KARE), part of the KoGES dataset. The KARE participants were recruited from Ansan and Anseong, two regions in the south of Korea. The baseline KARE study was conducted from 2001 to 2002 and follow-up examinations were conducted every 2 years from 2003 through 2014. The KARE cohort study has previously been described in detail (25). Among the 8,840 KARE participants, subjects with missing or outlier values for crucial variables were excluded, and a total of 5,719 individuals participated in the present study. All participants provided written informed consent to participate in the study. The study was approved by the Ethics Committee of the Korean Center for Disease Control (KCDC), Republic of Korea (KBN-2018-050). The study procedure was approved by the Institutional Review Boards of Kyung Hee University [KHSIRB-18-040(EA)].

Classification of the participants. Demographic and medical information (i.e. age, height and weight) was obtained from the KoGES dataset (24). BMI was calculated by dividing the body weight (kg) of the participants by the height squared (m^2). Based on the BMI results, the participants were classified into 2 groups according to the criteria for obesity in Korea (non-obesity group, BMI <25 kg/m^2, n=3,349; and the obesity group, BMI ≥25 kg/m^2, n=2,370) (26). For subgroup analysis, the participants were divided into 2 groups according to age: An early midlife group (aged <55 years, n=5,104) and a late midlife group (aged ≥55 years, n=615). The participants whose history included a diagnosis of diabetes, who were taking an oral hyperglycemic or insulin, or whose fasting glucose plasma level was ≥126 mg/dl were categorized as patients with diabetes. The participants whose history included a diagnosis of hypertension, who were taking an antihypertensive drug, had an SBP not <140 mmHg or a DBP not <90 mmHg were categorized as patients with hypertension (27).

Sleep health and other measurements. Information on sleep duration was collected by the survey method using the following questions: i) How many hours do you sleep? ii) What time do you usually go to bed at night? and iii) What time do you usually get up in the morning? The participants completed a questionnaire on their sleep patterns, including sleep duration, bedtime and waking time. In accordance with the American National Sleep Foundation's sleep time recommendations, a long sleep duration was defined as sleeping for ≥9 h and a short sleep duration was defined as sleeping for ≤6 h (28). Based on these criteria, the patients were divided into 3 groups according to sleep duration, of ≤6 h (n=2,323), 7-8 h (n=2,935) and ≥9 h (n=461). In addition, certain demographic factors of the participants were investigated, such as total cholesterol, high-density lipoprotein, and triglyceride levels, alcohol consumption and smoking status.

Statistical analyses. All data are expressed as the means ± standard deviation or frequency and percentage (%). Continuous variables were evaluated by an independent t-test and categorical variables were assessed using the Chi-squared test. The odds ratios (ORs) and 95% confidence intervals (CIs) for obesity risk according to sleep duration were calculated using univariate and multivariate logistic regression analyses. The multivariable-adjusted models were as follows: The first model adjusted for age and sex (Model 1) and the second model adjusted for age, sex, waist circumference, alcohol consumption, smoking status, hypertension, diabetes and hyperlipidemia (Model 2). Subgroup analysis was performed for age (early midlife vs. late midlife) and sex (males vs. females). The analyses were performed using SPSS statistical software for Windows (version 23.0; IBM Corporation). All statistical analyses were two-sided, and P-values <0.05 were considered to indicate statistically significant differences.

Results

Clinical demographics and sleep patterns of obese and non-obese subjects. The clinical and demographic features of the participants in the present study are presented in Table I. At baseline, the mean age of the participants was 52.6 years, and 50.3% were males. There was no significant difference in the mean age of the participants between the obese and non-obese groups (52.59 years vs. 52.35 years, respectively, P=0.086). The proportion of males (46.2% vs. 53.2%, P<0.001) was significantly lower in the obese group than in the non-obese group. The mean BMI ± SD was 27.29±1.87 and 22.42±1.85 in the obese and non-obese groups, respectively. The percentage of current smokers (22.7 vs. 30.1%, P<0.001) was significantly higher in the non-obese group, whereas the percentage of current alcohol consumers (80.8 vs. 23.8%, P<0.001) was significantly higher in the obese group. In addition, the prevalence of hypertension (56.2 vs. 37.3%, P<0.001) was significantly higher in the obese group. However, the prevalence of diabetes did not vary significantly between the 2 groups (4.1 vs. 4.9%, P=0.167).

Univariate and multivariate logistic regression analysis for obesity according to sleep duration at baseline. The results of univariate and multivariate analysis are presented according to sleep duration in Table II. In the univariate analysis, the odds ratios for the prevalence of obesity were significantly higher in subjects with a short sleep duration (≤6 h) than in those with an optimal sleep duration (7-8 h) (OR, 1.6; 95% CI, 1.039-1.295; P=0.008). After adjusting for confounding factors, including age, sex, waist circumference, alcohol intake, smoking status, hypertension, diabetes and hyperlipidemia, the significant association between a short sleep duration and obesity persisted (≤6 h: Model 1: OR, 1.142; 95% CI, 1.022-1.275; P=0.019; Model 2: OR, 1.446; 95% CI, 1.254-1.667; P<0.0001).

Subgroup analyses according to age and sex. The participants were divided into subgroups based on age and sex. As shown in Table III, the multivariate odds ratios for obesity were significantly higher in the sleep-deprived participants (≤6 h) regardless of age and sex. However, stronger associations between a short sleep duration (≤6 h) and obesity were revealed in males and the early midlife group compared to females and the late midlife group (males: OR, 1.567; 95% CI, 1.258-1.953; P<0.0001; early midlife group: OR, 1.584; 95% CI, 1.320-1.902; P<0.0001).

Table I. Characteristics and sleep habits of the study participants.

Characteristic	All[a] (BMI, <25)	Non-obesity (BMI, ≥25)	Obesity	P-value[b]
No. of patients	5,719	3,349	2,370	
Age, years	52.59±8.95	52.75±9.20	52.35±8.57	0.086
Males, n (%)	2,876 (50.3)	1,781 (53.2)	1,095 (46.2)	<0.001
Body mass index, kg/m^2	24.44±3.04	22.42±1.85	27.29±1.87	<0.001
Waist circumference, cm	82.64±8.41	78.25±6.70	88.84±6.45	<0.001
Current smokers, n (%)	1,544 (27.0)	1,007 (30.1)	537 (22.7)	<0.001
Current alcohol consumers, n (%)	2,713 (47.4)	798 (23.8)	1,915 (80.8)	<0.001
Fasting glucose, mg/dl	88.15±21.53	86.5±21.35	90.48±21.57	<0.001
Systolic blood pressure, mmHg	122.32±18.45	119.88±18.18	125.77±18.29	<0.001
Diastolic blood pressure, mmHg	80.98±11.33	79.15±11.07	83.56±11.20	<0.001
Total cholesterol, mg/dl	193.35±36.47	188.74±36.08	199.86±36.04	<0.001
High-density lipoprotein, mg/dl	45.21±10.23	46.92±10.63	42.81±9.12	<0.001
Triglycerides, mg/dl	160.77±103.73	145.59±94.77	182.22±111.77	<0.001
Hypertension, n (%)	2,583	1,250 (37.3)	1,333 (56.2)	<0.001
Diabetes, n (%)	252	137 (4.1)	115 (4.9)	0.167
Hyperlipidemia, n (%)	121	66 (2.0)	55 (2.3)	0.365
Sleep duration				
≤6 h, n (%)	2,323	1,302 (56.0)	1,021 (44.0)	0.001
7-8 h, n (%)	2,935	1,751 (59.7)	1,184 (40.3)	
≥9 h, n (%)	461	296 (64.2)	165 (35.8)	

[a]Data are expressed as the mean ± standard deviation or number and percentage; [b]the P-value was generated using an independent t-test or Chi-squared test for continuous variables and categorical variables. BMI, body mass index.

Table II. Univariate and multivariate logistic regression analysis for obesity.

	Unadjusted			Model 1[b]			Model 2[c]		
Sleep duration	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
≥9 h	0.824	0.672-1.011	0.064	0.805	0.654-0.99	0.04	0.714	0.552-0.923	0.01
7-8 h (Ref.)[a]	1.00			1.00			1.00		
≤6 h	1.6	1.039-1.295	0.008	1.142	0.654-0.99	0.019	1.446	1.254-1.667	<0.0001

[a]Reference group was optimal sleep duration; [b]adjusted for age and sex; [c]adjusted for age, sex, waist circumference, alcohol consumption, smoking, hypertension, diabetes and hyperlipidemia. OR, odds ratio; CI, confidence interval.

Risk of obesity according to sleep duration in those with or without hypertension and diabetes at baseline. The participants were further divided into several groups based on the presence of hypertension or diabetes. In the presence or absence of hypertension and diabetes, the risk of obesity in the 3 groups (≤6, 7-8 and ≥9 h) divided by sleep duration is presented in Table IV. A significant elevation in the ORs for obesity was found in the participants with a short sleep duration (≤6 h) regardless of hypertension (≤6 h, participants with hypertension: Model 2: OR, 1.368; 95% CI, 1.107-1.690; P=0.004; participants without hypertension, Model 2: OR, 1.534; 95% CI, 1.263-1.863; P<0.0001). In addition, a significant association was found between obesity and a short sleep duration (≤6 h) only in participants without diabetes and not in the diabetic participants (≤6 h, subjects without diabetes, Model 2: OR, 1.473; 95% CI, 1.272-1.705; P<0.0001).

Discussion

The key findings of the present study were the following: i) A sort sleep duration among Korean adults significantly elevated the risk of obesity; ii) sleep and the risk of obesity were strongly associated with the male sex and participants in the early midlife group; iii) a short sleep duration significantly increased the risk of obesity in subjects without risk factors for hypertension or diabetes.

Obesity is a serious health concern worldwide and a strong risk factor for type 2 diabetes, hypertension, dyslipidemia and

Table III. Multivariate logistic regression in subgroup analysis for obesity.

				Sex						Age, years					
	Overall			Males			Females			<55			≥55		
Sleep duration	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value	Sleep duration	OR	95% CI	P-value	OR	95% CI	P-value
≥9 h	0.714	0.552-0.923	0.01	0.48	0.293-0.772	0.003	0.757	0.542-1.058	0.103	≥9 h	0.738	0.488-1.116	0.149	0.58	0.406-0.830	0.003
7-8 h (Ref.)[a]	1.00			1.00			1.00			7-8 h (Ref.)[a]	1.00			1.00		
≤6 h	1.446	1.254-1.667	<0.0001	1.567	1.258-1.953	<0.0001	1.288	1.064-1.558	0.009	≤6 h	1.584	1.320-1.902	<0.0001	1.299	1.034-1.631	0.025

[a]Referent group was optimal sleep duration. Adjusted for age, sex, waist circumference, alcohol consumption, smoking, hypertension, diabetes and hyperlipidemia. OR (95% CI) was generated by multivariable logistic regression analysis.

cardiovascular disease (29,30). Sleep deprivation can lead to adverse consequences, such as diabetes, high blood pressure and obesity (31-34). Epidemiological findings associating sleep duration with various diseases have been inconsistent thus far. For example, a Korean study reported that <5 h of sleep daily increased the risk of hypertension (34) and the same sleep duration was also reported to be a risk factor for cardiovascular disease (35,36). In Japanese subjects, cardiovascular-related deaths were found to be higher both in subjects who slept for ≤4 h and in subjects who slept ≥10 h (37). Furthermore, an inverted bell-shaped association was found between sleep duration and BMI, suggesting that both short and long durations of sleep were associated with an increased risk of obesity in adults (13,38). Previous studies have reported a significant association between sleep deprivation and the increased prevalence of adult obesity (39,40). Other studies have shown a linear association between sleep duration and obesity (41,42). A review of a cohort study indicated that sleep deprivation strongly predicted subsequent weight gain in children, with the association in adults remaining unclear (43). The results of the present study suggested an association between a short sleep duration and obesity in Korean adults, particularly in subjects without hypertension or diabetes. Epidemiological studies and experimental studies have reported that a reduction in sleep duration increases not only the prevalence of obesity, but also diabetes and hypertension (44,45). These studies demonstrated that a reduction in sleep duration decreased insulin sensitivity and glucose tolerance. They also confirmed that sleep restriction can increase sympathetic nervous activity, body weight, and blood pressure. The findings of the present study demonstrated that a short sleep duration led to an increased risk of obesity, regardless of the presence of hypertension or diabetes. In other words, these findings indicated that sleep duration was likely an important factor affecting the risk of obesity independently from the increased risk of obesity caused by the effects of hypertension and diabetes.

The association between sleep duration and obesity is not yet fully understood. However, several possible factors driving this association have been proposed. Sleep is associated with appetite-related hormones, such as ghrelin and leptin. Ghrelin, secreted from the stomach, stimulates appetite and food intake. Leptin, synthesized in adipocytes, mediates satiety signaling. Poor sleep is related to reduced leptin levels and elevated ghrelin levels, which suggests that increases in caloric intake caused by hormonal changes can lead to obesity (6,43,46-48). Insufficient sleep is also associated with altered body temperature rhythms and increased tiredness, both of which influence the maintenance of energy balance and contribute to obesity (43). Habitual sleep deficits can also lead to weight gain as a result of unhealthy behavior and lifestyle choices, such as insufficient exercise and irregular dietary habits (45,49,50). Sleep deprivation is also related to reduced melatonin levels. Melatonin, secreted from the pineal gland, maintains the circadian rhythm and is involved in the regulation of body weight gain and energy metabolism. Decreased levels of melatonin lead to reductions in metabolic activity as well as further weight gain (51).

Table IV. Odds ratios for the risk of obesity according to sleep duration in participants with or without hypertension.

Hypertension or diabetes	Sleep duration	Model 1[b]			Model 2[c]		
		OR	95% CI	P-value	OR	95% CI	P-value
With hypertension	≥9 h	0.877	0.66-1.164	0.363	0.667	0.458-0.971	0.034
(n=2,583)	7-8 h (Ref.)[a]	1.00			1.00		
	≤6 h	1.164	0.986-1.375	0.072	1.368	1.107-1.690	0.004
Without hypertension	≥9 h	0.683	0.492-0.948	0.023	0.602	0.402-0.903	0.014
(n=3,136)	7-8 h (Ref.)[a]	1.00			1.00		
	≤6 h	1.148	0.983-1.342	0.081	1.534	1.263-1.863	<0.0001
With diabetes	≥9 h	3.017	0.934-9.741	0.065	2.046	0.456-9.168	0.35
(n=252)	7-8 h (Ref.)[a]	1.00			1.00		
	≤6 h	0.996	0.593-1.673	0.988	0.971	0.509-1.853	0.929
Without diabetes	≥9 h	0.772	0.624-0.954	0.017	0.626	0.474-0.828	0.001
(n=5,467)	7-8 h (Ref.)[a]	1.00			1.00		
	≤6 h	1.15	1.027-1.288	0.016	1.473	1.272-1.705	<0.0001

[a]Reference group was optimal sleep duration; [b]adjusted for age and sex; [c]adjusted for age, sex, waist circumference, alcohol consumption, smoking, hypertension, diabetes and hyperlipidemia. OR (95% CI) was generated by multivariable logistic regression analysis.

The present study also elucidated the impact of sex and age on the association between sleep and obesity, which appeared to be more pronounced in early midlife subjects (<55 years of age) than in the late midlife population (≥55 years of age), and was more pronounced in males than in females. These results were similar to those of the Korean National Health and Nutrition Examination Survey (KNHANES) (23). The difference in the age-related risk of obesity can be explained by the fact that early midlife adults eat unhealthy meals more frequently than late midlife adults (52). The sex-specific differences in the risk of obesity are attributed to hormonal changes. Considering that females have higher levels of leptin than males, females with sleep deprivation have a reduced appetite and a diminished risk of obesity (53). Ghrelin levels are significantly higher in males than in females. Differences in the association between ghrelin and leptin levels with obesity according to sex suggest the existence of sex-dependent variations in appetite and energy homeostasis (54,55). However, additional studies are required to investigate the sex- and age-specific differences underlying sleep patterns and obesity.

The present study described a sleep-obesity association based on age and sex. An analysis of the sleep-obesity association was also conducted, and the present study was able to exclude significant contributions from hypertension or diabetes. However, the present study had a few limitations. First, it did not investigate the effects of healthy behavior and lifestyle habits, such as diet and exercise on weight gain. Second, questionnaires were used to investigate sleep patterns, including habitual bedtime and waking time, which may have resulted in unreliable and biased estimates. However, the majority of previous studies also used surveys to determine sleep patterns. In addition, some studies have suggested that the responses to the questionnaires were similar to those obtained by instrumental measurements (12,39). Third, it was impossible to adjust the outcomes for all possible confounding factors (e.g., sleep quality and insomnia status) associated with sleep-obesity analysis. Fourth, for the group with diabetes, there were limits in examining the correlation of each metabolic syndrome group (hypertension, diabetes, or obesity) with sleep duration due to the small sample size. Additional research is required using larger sample sizes. Finally, all of the participants were from two residential areas in the south of Korea (Ansan and Anseong). Therefore, they cannot be considered representative of the entire Korean population. Thus, additional studies are warranted to extrapolate the current findings to other jurisdictions and populations.

In conclusion, the present study identified that a short sleep duration was significantly associated with an increase in obesity in Korean adults. The association between a short sleep duration and an increase in the risk of obesity was stronger in the early midlife group and stronger for males, and the association was independent of the presence of hypertension and diabetes. There is a growing prevalence of obesity in modern society. Given this trend, it is important to determine whether sufficient sleep can serve as a strategy for the prevention of obesity. The findings of the present study provide evidence that sleep restriction is related to the high prevalence of obesity. However, additional studies are warranted to elucidate the biological mechanisms and gene interactions to fully elucidate the association between sleep and obesity.

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Availability of data and materials

The present study was based on data from the Korean Genome and Epidemiology Study (KoGES) performed by the Korean Centers for Disease Control and Prevention (KCDC). The present study did not produce the data and the authors do not own it. The KoGES data are publicly available at: http://korea-biobank.re.kr, 82-1661-9070. The datasets used in the current study are not publicly accessible, but are available from the corresponding author upon reasonable request.

Authors' contributions

The study concept was designed by HOK, IK, WC and KSY. HOK performed the statistical analysis, prepared tables and drafted the manuscript. IK and WC commented on the manuscript and tables, and KSY assisted with data management and in finalizing the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of the Korean Centers for Disease Control (KBN-2018-050) and the Institutional Review Board of Kyung Hee University (KHSIRB-18-040(EA). Informed consent was obtained from all participants at the time of data collection.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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