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Original Article

The impact of the sleep duration on NAFLD score in Korean middle-aged adults: a community-based cohort study

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ABSTRACT

Background: Accumulated evidences indicates that sleep duration and sleep quality may potentially trigger the development of non-alcoholic fatty liver disease (NAFLD), but no studies have explored this causality. In this study, we aimed to investigate the effect of sleep duration on the incidence of NAFLD in Korean middle-aged adults.

Methods: All participants were selected from the cohort of the Korean Genome and Epidemiology Study (KoGES) for a 10-year period. NAFLD was defined by Fatty Liver Index (FLI), NAFLD liver fat score (NLFS), Hepatic Steatosis Index (HSI) and Lipid Accumulation Product (LAP). Multiple logistic regression analysis was used to assess the relationship between sleep duration and NAFLD defined by NAFLD scores. ANCOVA and Spline curve was also used to verify the differences in means of NAFLD scores according to the four sleep duration groups.

Results: In comparison with those of individuals in the reference group, the OR (95% CI) for NAFLD was 2.230 (1.304–3.813) for group of people who slept more than 8 h, 1.869 (1.298–2.691) for 7–8 h after adjusting for several confounding factors. The odds ratio for the incidence of NAFLD was 1.462 (1.029–2.077) for the group of people who sleep more than 8 h, 1.271 (1.001–1.615) for 7–8 h after adjusting for age, sex, BMI, SBP, DBP, TG, HDL, FDG, smoking, physical activity, daytime napping and night-time shifting ($p < 0.01$).

Conclusion: These findings indicate a relationship between long sleep duration and the elevation of NAFLD scores and support the causality of sleep duration and incidence of NAFLD in Korean middle-aged adults.

1. Introduction

The population of South Korea has the shortest average sleeping time among people in Organization for Economic Co-operation and Development (OECD) countries. Programs that aim to improve the quality of life as well as improve sleep quality are being pursued at the national level, and studies are being conducted to find out its clinical significance. The results of a Korean cohort study showing that short sleep times increase the risk of hypertension and metabolic syndrome have been reported and are explained by the fact that complex and various metabolic abnormalities related to insulin resistance are associated with clinical features [1]. While the effect of insulin resistance on sleep duration has not yet been clarified, in light of these prior findings, a positive link between insulin resistance and sleep duration may be expected. From the same perspective, recent studies have pointed to hyperinsulinemia and insulin resistance as pathogenic factors in non-alcoholic fatty liver disease (NAFLD) [2]. Furthermore, the prevalence of NAFLD in Korean adults is increasing steadily with changes of lifestyle. The deposition of fat without alcohol may have various effects on the liver, and the correlation between NAFLD and risk factors for chronic diseases such as abdominal obesity, blood sugar control disorder, hypertension, and lipid abnormality have been revealed [3–5].

In the light of these findings, we inferred that NAFLD is closely associated with sleep duration. Although the mechanisms between

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NAFLD and sleep duration are currently unknown, recent researches have disclosed some possible links between NAFLD and sleep duration. Several studies noted that inadequate sleep is known to be associated with several poor health outcomes. Notably, inadequate sleep could also be another risk factor for NAFLD, as observed in several epidemiologic studies, even though the results were inconsistent [6–8]. Studies have also been carried out on specific gender and age groups in China, Japan, and South Korea that have revealed that NAFLD is also associated with lifestyle and occupational characteristics, including sleeping time and quality [9–12]. However, most of the studies that have reported the relationship between sleep duration and nonalcoholic fatty liver disease have not explained the causal relationship, and there is controversy about the correlation between each factor, especially in South Korea [12,13]. This study was undertaken using accessible indicators to assess possible causal relationships between sleep duration and NAFLD, taking into account various risk factors and useful diagnostic tools.

2. Material and methods

2.1. Survey overview and study population

The Korean Genome Epidemiology Study (KoGES), conducted by the Centers for Disease Control and Prevention (CDC), was a principal cohort study providing valuable evidence for the prevention of major chronic diseases such as hypertension, obesity, and diabetes in South Korea. In order to identify major genetic and environmental risk factors associated with contracting diseases, they established a prospective cohort project that laid the foundation for the general population and long-term track record of disease outbreaks and changes in the living environment. A large-scale cohort was conducted for the general population aged 40–69 years [14]. During the cohort, biomarkers such as epidemiological data, blood, urine, and genomes were collected through surveys and examinations related to health and lifestyle; later, a periodic follow-up was produced in Korea over 10 years [14]. This study has been evaluated as a good cohort to identify the incidence and risk factors of chronic diseases. Among the 8841 middle-aged Korean men and women who participated in the cohort study for more than three years, those who were diagnosed with sleep disturbances, taking sleep-related drugs or who had a history of hepatitis or positive serologic markers for hepatitis B and C were excluded. High-risk drinking groups of 40 g or more alcohol intake per day for women and 60 g or more alcohol intake per day for men were excluded. Finally, excluding missing values, 5427 subjects were studied. The study was approved by the institutional review boards of Yonsei university Yongin severance hospital (IRB No. 9-2018-0007).

2.2. Definition of sleep duration

The American Society for Sleep Research has identified the period 7–8 h as the recommended sleeping time for middle-aged people and 6–7 h as adequate sleeping time. Based on these criteria, we divided the participants into four groups: those sleeping less than 6 h, those sleeping 6 h to less than 7 h, those sleeping 7 h–8 h, and those who slept more than 8 h.

2.3. Definition of NAFLD

We used four indexes that can predict NAFLD using highly accessible biomarkers and disease history. FLI is a validated previously, as a standard for diagnosing NAFLD. Therefore, we selected the most sensitive and specific variable among the various NAFLD scores based on the FLI.

2.3.1. Fatty liver index (FLI)

We used FLI, a validated surrogate maker, as a standard for diagnosing NAFLD in the first period data. The formula used to calculate the FLI is as follows:

$$FLT = \frac{e^{(0.953\times \log e\, TG + 0.139\times \mathrm{BMI} + 0.718\times \log e\, GGT + 0.053\times WC - 15.745)}}{1 + e^{(0.953\times \log e\, TG + 0.139\times BMI + 0.718\times \log e\, GGT + 0.053\times WC - 15.745)}} \times 100$$

According to the report by Bedogni et al. [15], we categorized the study participants into three groups based on the value of FLI which varies from 0 to 100: FLI < 30, described as not having NAFLD; FLI 30 to 59, defined as intermediate FLI; and FLI ≥60, defined as having NAFLD. NAFLD can be excluded if it is less than 30, and NAFLD can be diagnosed as sensitivity of 82% and specificity of 76% if it is 60 or more. This index has been validated by comparison with US sensitivity of 90% and specificity of 83% [15,16].

2.3.2. Lipid accumulation product (LAP)

Recent studies suggest that the lipid accumulation product is significantly associated with metabolic abnormalities. The aim of this study was to assess the accuracy of the lipid accumulation product (LAP) as an effective screening tool for diagnosing NAFLD in the general population. LAP was calculated as follows:

$$LAP = [WC - (65 \text{ in men}, 58 \text{ in women})] \times TG$$

To obtain a deeper understanding of the relationship between LAP levels and the prevalence of NAFLD, we divided the study population into four groups according to LAP quartiles referring to the previous study [17–19]. The highest quartile was defined as having NAFLD [17–19].

2.3.3. NAFLD liver fat score (NLFS)

NAFLD Liver Fat Score was derived from a Finnish population. The gold standard was magnetic resonance spectroscopy (MRS). The score incorporates simple variables but may be a test to take into account when assessing steatosis easily on the bench without referring to radiology [20,21]. NAFLD can be excluded if it is less than −0.640.

$$NLFS = -2.89 + 1.18 \times \text{Metabolic Syndrome (yes} = 1, \text{no} = 0) + 0.45 \times DM \text{ (yes} = 2, \text{no} = 0) + 0.15 \times \text{Fasting insulin} + 0.04 \times AST + 0.94 \times AST/ALT$$

2.3.4. Hepatic steatosis index (HSI)

HSI is a simple, efficient screening tool for NAFLD that may be utilized for selecting individuals for liver ultrasonography, ruling out NAFLD with a sensitivity of 93.1%, or detecting NAFLD with a specificity of 92.4%, respectively. NAFLD can be excluded if it is less than 36 [20].

$$HSI = 8 \times ALT/AST + BMI + \text{Sex (2 in women, 0 in men)} + DM \text{ (yes} = 2, \text{no} = 0)$$

2.4. Statistical analysis

The four sleep duration groups were compared using the χ^2 test and one-way analysis of variance (ANOVA). All data were reported as mean ± standard deviations (SD). Multiple logistic regression analysis was used to assess the relationship between sleep duration and NAFLD defined by FLI score after adjusting for age, sex, BMI,

SBP, DBP, TG, HDL, FDG, smoking, physical activity, daytime napping and night-time shifting. The LAP value was found to be the most sensitive and specific for the NAFLD compared to NLFS and HSI by the AUC area and ROC curve based on the FLI. The difference in NAFLD score, defined by NLFS, HSI, and LAP scores, according to sleeping time was also assessed using analysis of covariance (ANCOVA). Multiple logistic regression was used to assess the relationship between sleep duration and incidence of NAFLD, defined by LAP, after adjusting for age, sex, BMI, SBP, DBP, TG, HDL, FDG, smoking, physical activity, daytime napping and night-time shifting. Cox regression analysis was used to calculate the possible risk of developing NAFLD over sleep duration. NAFLD scores were also analyzed by ANCOVA to verify whether the differences in means of NAFLD scores accorded with sleep duration after adjustment for age as covariates. Results are presented as odds ratios (ORs) with 95% confidence intervals. All statistical significance was determined at a p-value < 0.05. In order to see the continuous relation between the mean value of NAFLD score and sleep duration, we draw the spline curve obtained by smoothing the Y axis after receiving the prediction probability through logistic regression.

3. Results

The characteristics of the study population are summarized in Table 1. The total of 5427 participants was included in this study. The mean value of age was 50.76 years. Statistically significant differences according to sleep duration were found with respect to the following variables: WC, SBP, DBP, GTP, Fasting Insulin, HOMA-IR, smoking status, physical activity, daytime nap and night time shifting. However, the weight, BMI, Lipid profile, fasting glucose, Hs-CRP and HbA1c did not show any significant differences. The proportion of NAFLD defined by FLI was not significantly different between the four groups (Table 1). Table 2 shows the association between NAFLD defined by FLI and sleep duration. Compared with the group with the shortest sleep duration, the ORs and 95% CIs were 2.230 (1.304–3.813) for the group of people who sleep more than 8 h, 1.869 (1.298–2.691) for 7–8 h and 1.662 (1.122–2.463) for 6 h to less than 7 h after adjusting for age, sex, BMI, SBP, DBP, TG, HDL, FDG, physical activity, smoking, day-time napping and night-time shifting (Table 2). The NAFLD is defined based on the FLI, and the effective area of LAP, NLFS, and HSI is obtained based on this. When the ROC curve is drawn, the effective area of the LAP is 0.924 (0.916–0.932), which is the most sensitive and specific definition (Fig. 1). In the ANCOVA study, the mean value of FLI and LAP according to the sleep duration was calculated by the Bonferroni post hoc test. The two scores of the group sleeping more than 7 h were higher than those of the group with the shortest sleep duration (Fig. 2).

In the cohort study, the odds ratio for the incidence of NAFLD defined by LAP was 1.462 (1.029–2.077) for the group of people who sleep more than 8 h, 1.271 (1.001–1.615) for 7–8 h after adjusting for age, sex, BMI, SBP, DBP, TG, HDL, FDG, smoking, physical activity, daytime napping and night-time shifting ($p < 0.05$). The odds ratio for the group of people who sleep between 6 to less and 7 h did not have a statistically significant value, which showed a similar tendency to Model 1 and Model 2 (Table 3). In the ANCOVA study, the average of LAP, HSI and NLFS scores

Table 1
Baseline characteristics of study population (n = 5427).

	Sleep Duration (hours)				*P value*
	<6 h	6 h to <7 h	7 h–8 h	>8 h	
Number (n)	810	1494	2731	392	
Age (years)	50.61 ± 8.6	49.49 ± 8.1	50.95 ± 8.6	54.63 ± 9.3	0.000*
Gender (Female, %)	58.7	53.1	48.7	53.9	0.000†
Weight (kg)	63.18 ± 10.7	64.13 ± 9.9	63.90 ± 10.0	62.30 ± 9.7	0.004*
BMI (kg/m^2)	24.72 ± 3.2	24.74 ± 3.0	24.56 ± 3.0	24.48 ± 3.2	0.148*
WC (cm)	80.97 ± 9.2	81.75 ± 8.7	82.22 ± 8.4	83.35 ± 8.7	0.000*
SBP (mm Hg)	118.03 ± 18.2	118.43 ± 17.3	119.90 ± 17.8	124.28 ± 18.8	0.000*
DBP (mmHg)	78.04 ± 11.5	78.51 ± 11.3	79.66 ± 11.4	81.05 ± 10.8	0.000*
TG (mg/dl)	158.75 ± 100.9	152.66 ± 92.3	161.88 ± 104.9	158.48 ± 86.5	0.041*
HDL-C (mg/dl)	45.00 ± 10.6	44.71 ± 9.8	44.22 ± 9.9	44.51 ± 9.3	0.180*
GTP (IU/L)	29.75 ± 48.7	29.79 ± 37.8	34.13 ± 61.9	36.34 ± 58.0	0.016*
FBG (mg/dl)	87.46 ± 22.5	87.46 ± 20.7	88.00 ± 23.0	89.0 ± 23.5	0.632*
Insulin (mcIU/mL)	7.10 ± 3.5	7.29 ± 3.9	7.59 ± 4.9	7.99 ± 6.4	0.002*
CRP (mg/L)	0.21 ± 0.5	0.23 ± 0.4	0.21 ± 0.4	0.31 ± 0.8	0.000*
HOMA_IR	1.54 ± 0.9	1.60 ± 1.0	1.67 ± 1.2	1.76 ± 1.4	0.001*
HbA1c (%)	5.75 ± 0.9	5.73 ± 0.8	5.74 ± 0.8	5.84 ± 0.9	0.126*
NAFLD score					
FLI	29.62 ± 23.6	30.34 ± 23.64	31.92 ± 24.2	32.95 ± 23.2	0.018*
NLFS	−1.33 ± 1.3	−1.29 ± 1.3	−1.18 ± 1.5	−1.06 ± 1.5	0.002*
HSI	33.34 ± 4.5	33.48 ± 4.6	33.21 ± 4.6	32.94 ± 4.6	0.125*
LAP	88.90 ± 80.9	85.63 ± 73.0	91.48 ± 79.7	94.58 ± 69.8	0.065*
NAFLD (%)					
FLI	13.7	15.4	17.1	16.6	0.100†
NLFS	26.0	27.7	29.4	33.1	0.014†
HSI	20.6	22.5	19.7	18.8	0.076†
LAP	23.9	21.5	16.6	27.7	0.000†
Smoking (%)	20.6	22.9	26.5	28.3	0.000
Physical activity (%)	24.3	27.9	37.3	44.5	0.000
Daytime nap (%)	39.6	35.7	37.5	42.3	0.020
Night time shifting (%)	4.2	2.4	1.7	2.2	0.001

Abbreviations: BMI, body mass index; CRP, c-reactive protein; DBP, diastolic blood pressure; FBG, fasting blood glucose; FLI, fatty liver index; GTP, gamma-glutamyl transpeptidase; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; HSI, hepatic steatosis index; LAP, lipid accumulation product; NAFLD, nonalcoholic fatty liver disease; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference.

* P values calculated by ANOVA. Data are mean ± SD.

† P values calculated by χ^2 test or linear-by-linear association.

Table 2
OR and CI for NAFLD defined by FLI score according to sleep duration.

Model	Sleep Duration (hours)			
	<6 h	6 h to <7 h	7 h–8 h	>8 h
Model I	1	1.143 (0.896–1.458)	1.299 (1.040–1.623)*	1.255 (0.906–1.740)
Model II	1	1.085 (0.846–1.391)	1.166 (0.930–1.464)	1.154 (0.826–1.613)
Model III	1	1.662 (1.122–2.463)*	1.869 (1.298–2.692)†	2.230 (1.304–3.813)†

Model I: unadjusted.
Model II: adjusted for age and sex.
Model III: adjusted for age, sex, BMI, SBP, DBP, TG, HDL, FDG, physical activity, smoking, daytime napping and night-time shifting.
*P values < 0.05, †P values < 0.01.

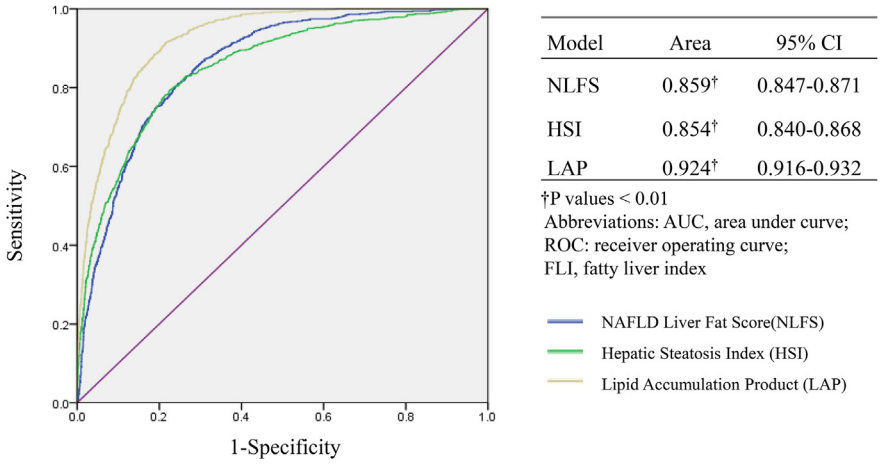

Fig. 1. AUC and ROC curve of FLI for the prediction of fatty liver.

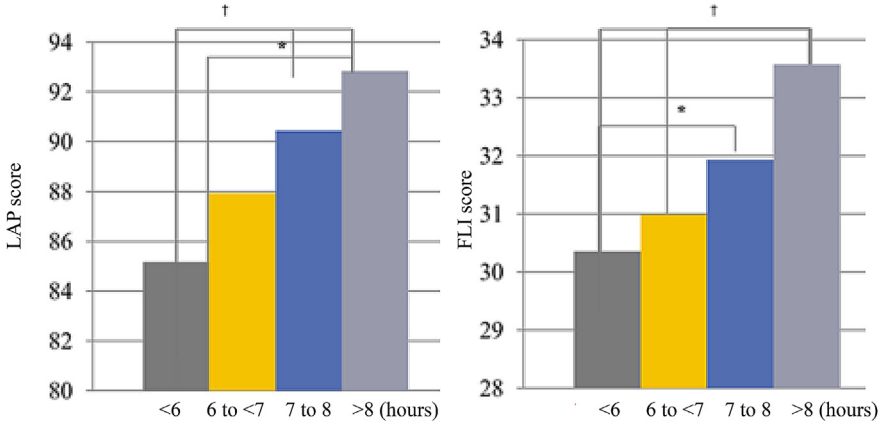

Fig. 2. NAFLD score according to sleep duration by ANCOVA.

Table 3
OR and CI for NAFLD defined by LAP according to sleep duration.

Model	Sleep Duration (hours)			
	<6 h	6 h to <7 h	7 h–8 h	>8 h
Model I	1	1.055 (0.850–1.310)	1.168 (0.960–1.420)	1.270 (0.963–1.674)
Model II	1	1.067 (0.859–1.326)	1.165 (0.958–1.418)	1.227 (0.929–1.622)
Model III	1	1.054 (0.812–1.369)	1.271 (1.001–1.615)*	1.462 (1.029–2.077)*

Model I: unadjusted.
Model II: adjusted for age and sex.
Model III: adjusted for age, sex, BMI, SBP, DBP, TG, HDL, FDG, physical activity, smoking, daytime napping and night-time shifting.
*P values < 0.0.

according to the sleep duration over a 10-year period was calculated by the Bonferroni post hoc test. The LAP and HSI scores of the group sleeping more than 7 h were higher than those of the group with the shortest sleep duration, and the NLFS score was not statistically significant (Fig. 3). We analyzed the Cox 2 regression by considering the number of NAFLDs defined as LAP over a 10-year period and the time it took to develop it. Compared to the group with the shortest sleep time, the group with a sleep duration of over 8 h had a Hazard ratio of 1.382 (1.085–1.760) in the unadjusted model and 1.295 (1.014–1.652) in the age- and sex-corrected group ($p < 0.01$). In Model 3, the HR of the group who sleep more than 8 h is 1.495 (1.059–2.109) after adjusting for age, sex, BMI, SBP, DBP, TG, HDL, FDG, smoking, physical activity, daytime napping and night-time shifting ($p < 0.05$) (Table 4). As seen in Penalized B-spline, the mean value of NAFLD score defined by LAP was the lowest in the sleep duration of 6 h. In addition, the mean value of NAFLD tended to increase when the sleep duration was shorter or longer than 6 h in the cross-sectional study. In the cohort study, the probability of new onset NAFLD defined by LAP also the lowest in the sleep duration of 6 h. When the sleep duration was shorter or longer than the 6 h, the probability tended to increase (see Figs. 4 and 5).

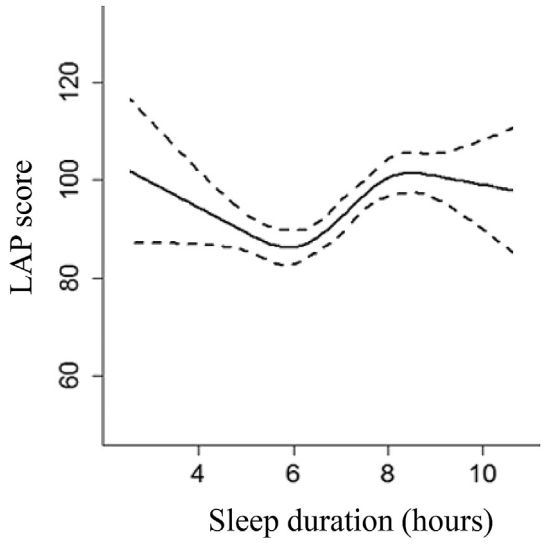

Fig. 4. Mean value of NAFLD score defined by LAP over sleep duration using spline curve.

4. Discussion

In this nationally representative cohort study, the long sleep duration was positively and independently associated with NAFLD scores after adjusting for potential confounding variables. These positive associations remained after additionally adjusting for representative metabolic indicators associated with NAFLD, smoking, physical activity, daytime napping and night-time shifting. These findings support that the longer sleeping time are associated with a higher incidence of NAFLD, irrespective of sleep quality and other risk factors for NAFLD. To date, a systematic review and meta-analysis suggested a small but significantly increased risk of NAFLD among participants who had short sleep duration. However, most of the included studies were cross-sectional studies. In addition, the results of these cross-sectional studies show inconsistent results [9–12].

A Korean cross-sectional study reported that short sleep duration was associated with a higher risk of NAFLD, which is consistent with most studies to date. Nevertheless, the Korean study was restricted to a selected population, so the conclusions cannot be generalized to community-based populations [12,13]. We also observed that short sleep duration and longer daytime napping were significantly associated with an increased risk of NAFLD, but this study is limited to middle-aged and elderly Chinese [22]. Based on these studies, we could infer several potential mechanisms that could explain the observed association between NAFLD and short sleep. First, some of the inflammatory cytokines essential for the pathogenesis of NAFLD, such as interleukin-6 and tumor necrosis factor alpha, have been shown to be caused by improper sleep [23,24]. Second, sleep deprivation can increase appetite as a result of hormone changes, such as increased ghrelin

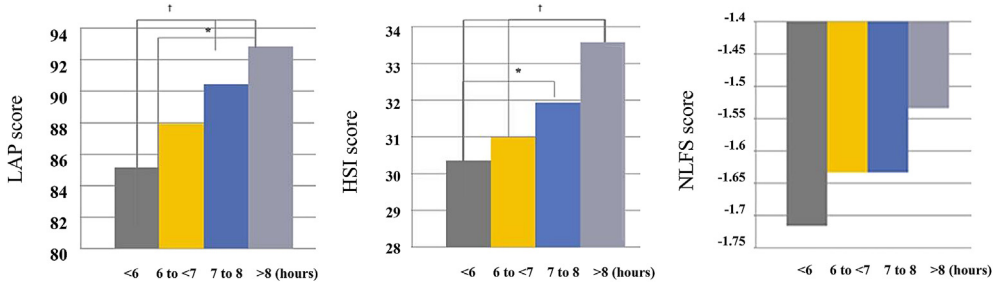

Fig. 3. Mean NAFLD scores according to sleep duration by ANCOVA.

Table 4
Cox regression analysis - HR and CI for new onset NAFLD defined by LAP according to sleep duration.

	Sleep Duration (hours)			
	<6 h	6 h to <7 h	7 h–8 h	>8 h
Model I	1	1.022 (0.8843–1.239)	1.190 (1.001–1.415)*	1.382 (1.085–1.760)†
Model II	1	1.048 (0.865–1.271)	1.196 (1.005–1.423)*	1.295 (1.014–1.652)†
Model III	1	1.148 (0.880–1.497)	1.270 (1.994–1.622)	1.495 (1.059–2.109)*

Model I: unadjusted.
Model II: adjusted for age and sex.
Model III: adjusted for age, sex, BMI, SBP, DBP, TG, HDL, FDG, physical activity, smoking, daytime napping and night-time shifting.
*P values < 0.05, †P values < 0.01.

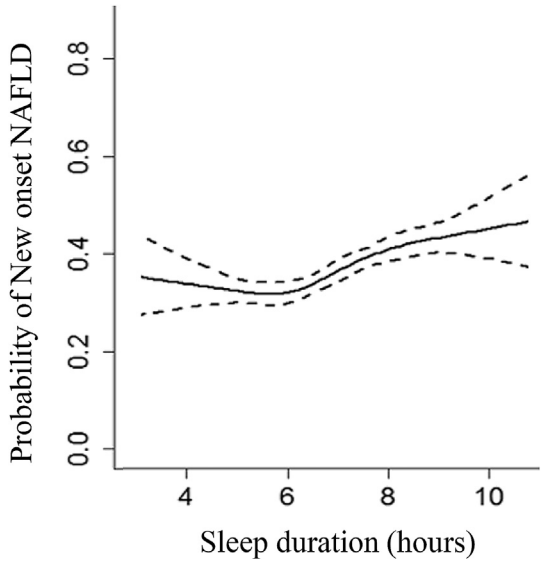

Fig. 5. Probability of new onset NAFLD defined by LAP over sleep duration using spline curve.

levels and decreased leptin levels. People who get improper sleep also tend to take less regular exercise because of a busy lifestyle or physical fatigue [25,26]. Third, studies have shown that the hypothalamic–pituitary-adrenal axis increases plasma levels of corticosteroids and cortisol, which are known to be associated with insulin resistance, affected by abnormal sleep patterns. In addition, cortisol and other glucocorticoids are known to promote lipid mobilization from peripheral adipose tissue, and promote fatty formation in the liver [27,28].

Contrary to this hypothesis, a Japanese study suggested that those who slept for 7–8 h were more likely to have NAFLD than those who slept for less than 6 h [11]. Our study also showed a higher NAFLD score for groups with longer sleep duration than for groups with shorter sleep duration after adjusting several confounding factors including daytime napping and night-time shifting, suggesting that the longer sleeping time, the greater risk of NAFLD. Moreover, there are some hypotheses that support this result. Existing concepts of total energy expenditure include resting metabolic rate, physical activity, and diet-induced thermogenesis. Short sleep duration could have positive or negative effects on all these components as a result of increased waking hours, metabolic disturbances or behavior changes. Thus, sleeping is less energy consuming than staying awake, even if an individual remains very sedentary during the extra time spent awake, because the metabolic rate when resting is higher than the metabolic rate when sleeping. Therefore, energy expenditure would be expected to decrease as sleep duration increases [29]. From an integrative point of view, this study supports both of these hypotheses and trends and reveals the benefit of recommended sleep duration.

Several limitations of our study also should be noted. First, sleep duration was recorded only in the baseline data, and the change was not observed. Second, various forms of sleep quality, such as sleep segments, were not considered. Third, marital status or occupation that could fundamentally affect sleep duration were not mentioned. Fourth, all chronic diseases with liver compromising were not excluded. Fifth and finally, defining NAFLD by means of an index, having biomarkers and disease history without an image study may be both an advantage in terms of accessibility and a disadvantage in terms of accuracy in this paper. Future studies should use a prospective validation design to adjust for these limitations when investigating diverse populations and dealing with various nations. Despite these limitations, our study had several strengths, which were primarily its sampling size, the use of a community-based study population, and the fact that it was the first cohort study to analyze the relationship between sleep duration and NAFLD in South Korea.

In summary, these findings provide evidence of the relationship between sleep duration and the elevation of NAFLD scores and support the causality between sleep duration and the incidence of NAFLD in Korean middle-aged adults. Further studies to elucidate the underlying biological mechanism are needed. Additionally, a more comprehensive approach should be undertaken to investigate the association of hepatic steatosis and sleep duration. Despite these weaknesses, our study could provide a rationale for further studies to confirm the possibility of reducing the incidence of NAFLD by maintaining proper sleep duration.

Author contributions

Ji-Hye Kim and Jae-Yong Shim designed the study and wrote and edited the manuscript. Ji-Hye Kim and Jae-Yong Shim performed the statistical analyses and interpreted the data. Ji-Hye Kim, Dong-Hyuk Jung, Jung-Il Lee, Yu-Jin Kwon and Jae-Yong Shim contributed to the discussion and revised the manuscript. Jae-Yong Shim, as the corresponding author, coordinated the study, interpreted the data, contributed to the discussion, and wrote the manuscript. All authors have read and approved the final version of the manuscript.

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Conflict of interest

The authors declare no conflicts of interest with respect to the present manuscript.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2019.02.012.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2019.02.012.

References

[1] Song MY, Sung E, Jung SP, et al. The association between sleep duration and hypertension in non-obese premenopausal women in Korea. Korean J Fam Med 2016;37(2):130–4.
[2] Lonardo A, Ballestri S, Marchesini G, et al. Nonalcoholic fatty liver disease: a precursor of the metabolic syndrome. Dig Liver Dis 2015;47(3):181–90.
[3] Tuyama AC, Chang CY. Non-alcoholic fatty liver disease. J Diabetes 2012;4(3):266–80.
[4] Rivera CA. Risk factors and mechanisms of non-alcoholic steatohepatitis. Pathophys 2008;15:109–14.
[5] Caballeria L, Pera G, Auladell MA. Prevalence and factors associated with the presence of nonalcoholic fatty liver disease in an adult population in Spain. Eur J Gastroenterol Hepatol 2010;22:24–32.
[6] Xi B, He D, Zhang M, et al. Short sleep duration predicts risk of metabolic syndrome: a systematic review and meta-analysis. Sleep Med Rev 2014;18:293–7.
[7] Shan Z, Ma H, Xie M, et al. Sleep duration and risk of type 2 diabetes: a meta-analysis of prospective studies. Diabetes Care 2015;38:529–37.
[8] Dietrich P, Hellerbrand C. Non-alcoholic fatty liver disease, obesity and the metabolic syndrome. Best Pract Res Clin Gastroenterol 2014;28:637–53.
[9] Hsieh SD, Muto T, Murase T, et al. Association of short sleep duration with obesity, diabetes, fatty liver and behavioral factors in Japanese men. Intern Med 2011;50:2499–502.

[10] Imaizumi H, Takahashi A, Tanji N, et al. The association between sleep duration and non-alcoholic fatty liver disease among Japanese men and women. Obes Facts 2015;8:234–42.
[11] Miyake T, Kumagi T, Furukawa S, et al. Short sleep duration reduces the risk of nonalcoholic fatty liver disease onset in men: a community-based longitudinal cohort study. J Gastroenterol 2015;50:583–9.
[12] Kim CW, Yun KE, Jung HS. Sleep duration and quality in relation to non-alcoholic fatty liver disease in middle-aged workers and their spouses. J Hepatol 2013;59:351–7.
[13] Yu JH, Ahn JH, Yoo HJ. Obstructive sleep apnea with excessive daytime sleepiness is associated with non-alcoholic fatty liver disease regardless of visceral fat. Korean J Intern Med 2015;30:846–55.
[14] Park SY, Kim YJ, Lee EG. KoGES (Korean Genome and Epidemiology Study) epidemiologic data online access process. Public Health Wkly Rep KCDC 2014;8:481–4.
[15] Bedogni G, Bellentani S, Miglioli L, et al. The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population. BMC Gastroenterol 2006;6:33.
[16] Yadav D, Choi E, Ahn SV, et al. Fatty liver index as a simple predictor of incident diabetes from the KoGES-ARIRANG study. Medicine 2016;95(31):e4447.
[17] Bozorgmanesh M, Hadaegh F, Azizi F. Predictive performances of lipid accumulation product vs adiposity measures for cardiovascular diseases and all-cause mortality, 8.6-year follow-up: tehran lipid and glucose study. Lipids Health Dis 2010;9:100.
[18] Hosseinpanah F, Barzin M, Mirbolouk M, et al. Lipid accumulation product and incident cardiovascular events in a normal weight population: tehran lipid and glucose study. Eur J Prev Cardiol 2016;23:187–93.
[19] Haijiang D, Weijun W, Ruifang C, et al. Lipid accumulation product is a powerful tool to predict non-alcoholic fatty liver disease in Chinese adults. Nutr Metab 2017;14:49.
[20] Kotronen A, Peltonen M, Hakkarainen A, et al. Prediction of non-alcoholic fatty liver disease and liver fat using metabolic and genetic factors. Gastro 2009;137:865–72.
[21] Wlazlo N, Greevenbroek MM, Ferreira I, et al. The diagnosis of non-alcoholic fatty liver disease. Aliment Pharmacol Ther 2012;35:204–5.
[22] Kui P, Lin L, Zhengyi W, et al. Short sleep duration and longer daytime napping are associated with non-alcoholic fatty liver disease in Chinese adults. J Diabetes 2017;9:827–36.
[23] Jarrar MH, Baranova A, Collantes R. Adipokines and cytokines in non-alcoholic fatty liver disease. Aliment Pharmacol Ther 2008;27:412–21.
[24] Prather AA, Marsland AL, Hall M, et al. Normative variation in self-reported sleep quality and sleep debt is associated with stimulated pro-inflammatory cytokine production. Biol Psychol 2009;82:12.
[25] Spiegel K, Leproult R, Balériaux M, et al. Leptin levels are dependent on sleep duration: relationships with sympathovagal balance, carbohydrate regulation, cortisol, and thyrotropin. J Clin Endocrinol Metab 2004;89:5762–71.
[26] Spiegel K, Tasali E, Leproult R, et al. Twenty four-hour profiles of acylated and total ghrelin: relationship with glucose levels and impact of time of day and sleep. J Clin Endocrinol Metab 2011;96:486–93.
[27] Targher G, Bertolini L, Rodella S. Associations between plasma adiponectin concentrations and liver histology in patients with nonalcoholic fatty liver disease. Clin Endocrinol (Oxf) 2006;64:679–83.
[28] Vgontzas AN, Bixler EO, Lin HM. Chronic insomnia is associated with nyctohemeral activation of the hypothalamic-pituitary- adrenal axis: clinical implications. J Clin Endocrinol Metab 2001;86:3787–94.
[29] Bonnet MH, Berry RB, Arand DL. Metabolism during normal, fragmented, and recovery sleep. J Appl Physiol 1991;71:1112–8.