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【 ORIGINAL ARTICLE 】

Distinct Relevance of Nightly Sleep Duration to Metabolic, Anthropometric, and Lifestyle Factors in Patients with Type 2 Diabetes

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Abstract:

Objective Although a number of studies have shown that both short and long sleep durations were associated with the risk of metabolic disorders related to obesity, the underlying mechanism is still not fully understood. In this study, we analyzed the association of sleep duration with metabolic, anthropometric, and lifestyle factors in patients with type 2 diabetes.

Methods The subjects were 279 patients with type 2 diabetes 63 (52-70) years old (median and interquartile range) with a body mass index of 25.0 (22.2-28.3) kg/m^2 and HbA1c levels of 8.7% (7.6-10.3%). Patients with advanced complications were excluded from the study. Diets were evaluated by registered dietitians using a software program. Body composition was assessed by the multifrequency bioelectrical impedance method.

Results The mean self-reported nightly sleep duration was 6.4 hours with no marked gender difference. Sleep duration was inversely correlated with the HbA1c levels, total energy intake, and intakes of carbohydrate, protein, and fat. The body fat ratio and skeletal muscle mass were correlated positively and negatively, respectively, with sleep duration. When the subjects were divided into three groups based on sleep duration, the intakes of total energy, carbohydrates, and fat tended to be high in those with <5.5 hours of sleep, and the percentage of patients who had habitual physical activities was lower in those with >7 hours of sleep.

Conclusion The observation that sleep duration is distinctly associated with excessive eating and a sedentary lifestyle may provide a basis for effective lifestyle management of patients with type 2 diabetes.

Key words: type 2 diabetes, obesity, sleep duration, dietary intake, habitual physical activity

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Introduction

Accumulating lines of evidence have shown that a short sleep duration is a risk factor for various health problems, including obesity/overweight (1-4), type 2 diabetes (1, 2), hypertension (3), and cardiovascular diseases (5, 6). In contrast, several epidemiological studies (7-10) and a meta-analysis (11) have shown that a long sleep duration is also associated with an increased risk of morbidity and mortality and that the correlation curve between sleep duration and obesity-related disorders, such as type 2 diabetes and cardiovascular diseases, is U-shaped (7, 9, 12-19). However, the mechanism by which both short and long sleep durations facilitate the onset of these obesity-related diseases is still not fully elucidated.

To assess the underlying mechanism of the U-shaped relationship, we analyzed the association of sleep duration with metabolic, anthropometric, and lifestyle factors in patients with type 2 diabetes.

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Table 1. Clinical Parameters of the Subjects.

Parameter	
Number (male/female)	279 (145/134)
Age (year)	63 (52-70)
Diabetes duration (year)	9.4 (3.0-16.8)
Body mass index (kg/m^2)	25.0 (22.2-28.3)
Body fat (%)	32.6 (25.9-37.4)
Skeletal muscle mass (kg)	24.2 (19.7-28.7)
HbA1c (%)	8.7 (7.6-10.3)
Fasting plasma glucose (mg/dL)	149 (123-194)
AST (U/L)	21 (17-28)
ALT (U/L)	23 (16-34)
ALP (U/L)	216 (183-263)
γ-GTP (U/L)	31 (20-54)
Albumin (g/dL)	4.04 (3.83-4.27)
HDL cholesterol (mg/dL)	45.8 (40.5-55.9)
LDL cholesterol (mg/dL)	116.2 (95.0-136.1)
Triglyceride (mg/dL)	140 (99-191)
eGFR (mL/min/1.73 m^2)	81.3 (66.5-100.5)
Diabetic retinopathy	96/268 (35.8%)
Diabetic neuropathy	107/279 (38.4%)
Diabetes medication	
Insulin alone or in combination	59 (21.1%)
Drugs except insulin	143 (51.3%)
None	77 (27.6%)
Hypnotic drugs	32 (11.5%)

Medians and interquartile ranges.

Materials and Methods

Subjects

This was a retrospective analysis of electrical medical records in Kurume University Hospital. Subjects were patients >20 years old with type 2 diabetes who were admitted to the hospital for the treatment of dysglycemia and/or diabetes self-management education; 279 individuals, including 145 men and 134 women, who were 63 (52-70) years old (median and interquartile range) with a body mass index (BMI) 25.0 (22.2-28.3) kg/m^2, and HbA1c 8.7% (7.6-10.3%) (Table 1) were included. The diagnosis of type 2 diabetes was established based on the American Diabetes Association and the Japan Diabetes Society criteria for diabetes and the absence of pancreatic autoimmune markers, including anti-glutamic acid decarboxylase (GAD) antibodies and anti-insulinoma-associated antigen-2 (IA-2) antibodies. The duration of diabetes was 9.4 (3.0-16.8) years. We excluded patients with renal failure, severe liver disease, heart failure, thyroid dysfunction, infectious diseases, obstructive sleep apnea syndrome, or malignant diseases. The diagnosis of depression was made based on medical information and an interview at admission or consultation with psychiatrists of Kurume University Hospital during hospitalization.

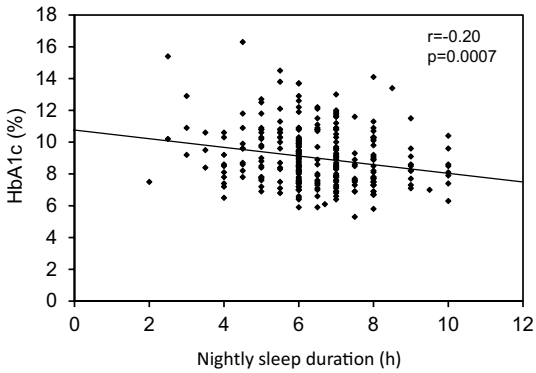

Figure 1. Correlation between nightly sleep duration and HbA1c levels.

The evaluation of nightly sleep duration, diet, body composition, and physical activities

Usual nighttime sleep duration was self-reported at the admission interview. Daytime naps were not included. Diets were evaluated by registered dietitians using a software program (Shokuwainari; Gleam, Kitakyushu, Japan). Alcohol ingestion twice a week or more was regarded as habitual drinking. Sweet snack intake on five days a week or more was regarded as habitual sweet snack consumption. Breakfast skipping was defined as eating breakfast <5 days per week. Body composition was assessed by the multifrequency (1, 5, 50, 250, 500, and 1,000 kHz) bioelectrical impedance method at each of 5 segments: arms, trunk, and legs (InBody720; InBody Japan, Tokyo, Japan). We defined habitual physical activity as ≥150 minutes of walking per week or equivalent, including occupational and household activities. The diagnosis of peripheral neuropathy was made based on the vibration time (128 Hz) at the lateral malleolus <10 seconds and negative Achilles tendon reflex in both legs.

The study was approved by the ethics committee of Kurume University.

Statistical analyses

Data are expressed as medians and interquartile ranges. The Kruskal-Wallis test, Mann-Whitney *U* test, and chi square test were used to compare the differences between groups. The statistical relationship between two continuous variables was evaluated by Pearson's correlation coefficient. The Cochran-Armitage trend test was used to detect trends in binomial proportions. Results with $p<0.05$ were considered statistically significant.

Results

The self-reported nightly sleep duration was 6 (6-7) hours with a mean value of 6.4 hours and standard deviation (SD) of 1.4 hours. There were no marked age- or gender-related differences. Sleep duration was inversely correlated with HbA1c levels at admission (Fig. 1). An anthropometric

Table 2. Correlation between Nightly Sleep Duration and Anthropometric Parameters. p values are Shown in Parentheses.

	BMI	%Body fat	Skeletal muscle mass
Pearson correlation coefficient	0.0045 (0.939)	0.1521 (0.008)	-0.1435 (0.013)
Age-adjusted	0.0297 (0.607)	0.1565 (0.009)	-0.1067 (0.048)
Age- and gender-adjusted	0.0300 (0.605)	0.1390 (0.009)	-0.0845 (0.037)

Table 3. Clinical Parameters of the Subjects in Group 1 (Sleep Duration<5.5 Hours), Group 2 (5.5-7 Hours), and Group 3 (>5 Hours).

Parameter	Group 1	Group 2	Group 3	p value
Number (male/female)	50 (29/21)	162 (83/79)	67 (33/34)	0.621
Age (year)	61 (48.5-70.5)	63 (51-69)	66 (58-73)	0.167
Body mass index (kg/m^2)	24.2 (21.8-27.8)	25.3 (22.7-28.2)	25.2 (21.6-28.6)	0.561
Body fat (%)	28.6 (22.7-35.5)	32.2 (26.5-36.7)	34.3 (25.9-40.8)	0.046
Skeletal muscle mass (kg)	24.5 (20.4-29.7)	24.3 (20.1-28.4)	23.1 (18.2-28.5)	0.294
HbA1c (%)	9.2 (8.0-10.7)	8.9 (7.6-10.3)	8.2 (7.3-9.3)	0.007
Fasting plasma glucose (mg/dL)	149 (121-192)	155 (129-199)	140 (113-180)	0.065
AST (U/L)	20 (16-25)	22 (17-30)	22 (18-29)	0.345
ALT (U/L)	22 (15-33)	24 (16-35)	25 (17-38)	0.296
ALP (U/L)	243 (195-261)	216 (184-270)	198 (170-253)	0.081
γ-GTP (U/L)	32 (22-49)	32 (20-55)	28 (16-55)	0.454
Albumin (g/dL)	3.98 (3.73-4.25)	4.04 (3.86-4.30)	4.04 (3.85-4.24)	0.346
HDL cholesterol (mg/dL)	44.5 (39.2-56.9)	46.4 (40.5-55.6)	46.0 (41.3-55.3)	0.854
LDL cholesterol (mg/dL)	119.1 (94.6-148.9)	114.6 (95.0-133.2)	116.5 (94.8-136.9)	0.606
Triglyceride (mg/dL)	143 (98-185)	134 (99-197)	144 (100-194)	0.674
Diabetes duration (year)	9.9 (3.3-17.2)	8.8 (3.3-15.6)	10.1 (2.6-18.0)	0.837
eGFR (mL/min/1.73 m^2)	85.4 (64.4-102.3)	82.8 (66.9-101.5)	76.5 (60.7-95.7)	0.373
Diabetic retinopathy	17/46 (37.0%)	53/159 (33.3%)	26/63 (41.2%)	0.531
Diabetic neuropathy	16/50 (32.0%)	64/162 (39.5%)	27/67 (40.3%)	0.591
Diabetes medication				0.236
Insulin alone or in combination	15	31	13	
Drugs except insulin	21	82	40	
None	14	49	14	
Hypnotic drugs	7/50 (14%)	16/162 (9.9%)	9/67 (13.4%)	0.614

Medians and interquartile ranges. p values were assessed using the Kruskal-Wallis test or the chi square test.

Table 4. Correlation between Nightly Sleep Duration and Intakes of Total Energy and Nutrients.

	Correlation coefficient	p value
Energy	-0.1544	0.0098
Carbohydrates	-0.1516	0.0108
Protein	-0.142	0.0174
Fat	-0.1801	0.0024
Dietary fiber	-0.1297	0.0277

analysis showed that the BMI was not associated with sleep duration, but the body fat ratio and skeletal muscle mass were correlated positively and negatively, respectively, with sleep duration (Table 2). These correlations were significant, even after adjusting for age or both age and gender.

When subjects were divided into three groups based on sleep duration (group 1, <5.5 hours; group 2, 5.5-7 hours; group 3, >7 hours), the age and gender were not markedly different among the groups (Table 3). The HbA1c was highest in group 1 and lowest in group 3, whereas the body fat ratio was highest in group 3 and lowest in group 1. There were no marked differences in the diabetes duration, estimated glomerular filtration rate, diabetic neuropathy, diabetic retinopathy, diabetic medication, or hypnotic drug use among the groups.

To find an explanation for the relationships of nightly sleep duration with HbA1c levels and anthropometric parameters, we analyzed the dietary intake of nutrients and habitual physical activities. There were inverse correlations between sleep duration and the intakes of total calories, carbohydrates, protein, fat, and dietary fiber (Table 4). The fat intake was significantly different among the groups, with the lowest value being noted in group 3 (Fig. 2). A trend was also observed in the intake of total energy and carbohydrate, although the differences did not reach statistical significance.

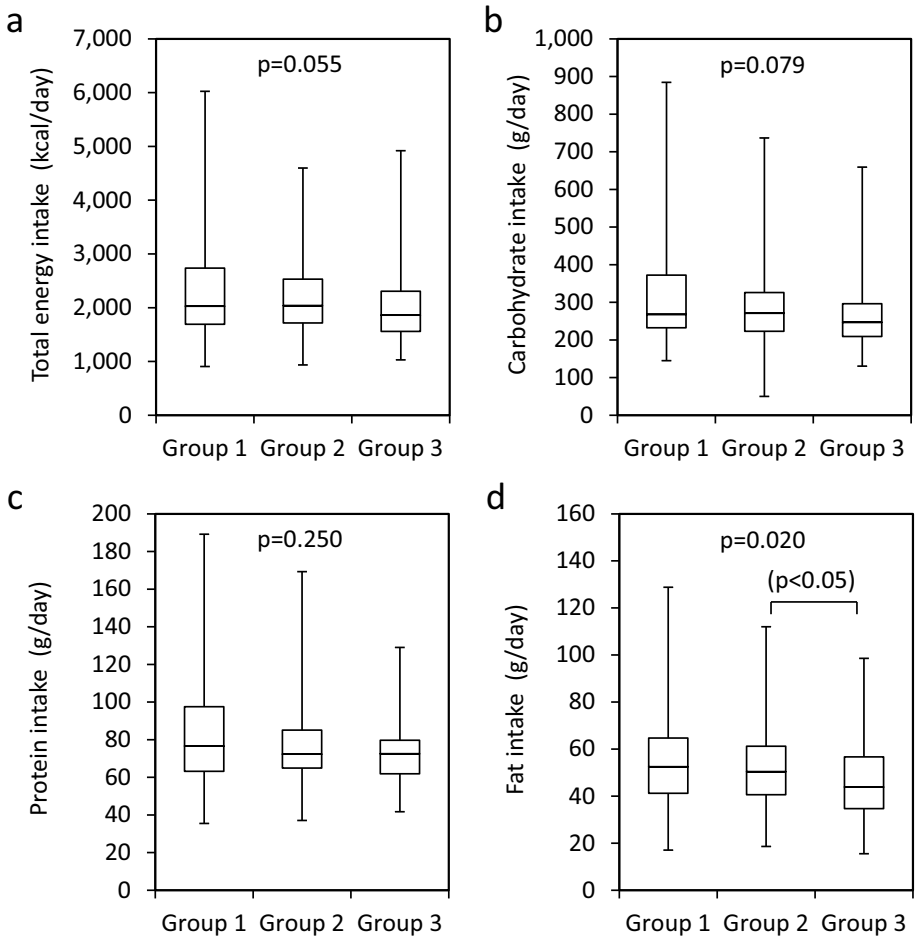

Figure 2. **Intakes of total energy (a), carbohydrate (b), protein (c), and fat (d) in group 1 (sleep duration<5.5 hours, n=50), group 2 (5.5-7 hours, n=162), and group 3 (>7 hours, n=67). Box boundaries show the medians and interquartile ranges, and whiskers show maximum and minimum values. p values among the three groups were assessed by the Kruskal-Wallis test. The p value in parenthesis is the result of a post-hoc analysis using Scheffe's method.**

In contrast, no significant difference was observed in habitual alcohol ingestion, habitual sweet snack consumption, or breakfast skipping based on the sleep duration (Fig. 3).

A significant negative trend was noted in the ratio of habitual physical activities of ≥150 minutes walking per week or equivalent among the 3 groups: 44.0%, 31.3%, and 25.4% in groups 1, 2, and 3, respectively (Fig. 4a). A post-hoc analysis showed that the percentage of patients who had habitual physical activities was significantly lower in group 3 than in group 1. Patients with habitual physical activities tended to be older with a lower BMI and lower %body fat than those without such habits (Table 5). The associations were also observed when men and women were analyzed separately, although the difference in the BMI did not reach statistical significance (p=0.093) in women. In subjects without habitual physical activities, the nighttime sleep duration was positively and negatively correlated with the body fat percentage and skeletal muscle mass, respectively (Table 6). However, in subjects who had habitual physical activities, these associations were not observed. There was no significant difference in the prevalence of diagnosed clinical depression among the three groups (Fig. 4b).

Discussion

In the present study, we showed a significant inverse correlation between nighttime sleep duration and HbA1c levels in patients with type 2 diabetes, in accordance with previous studies reporting that sleep deprivation was associated with metabolic disorders, such as obesity (1-3), insulin resistance (2), and type 2 diabetes (1, 2). The postulated mechanisms include alterations in appetite-regulating hormones (20-22), activation of the food reward system (23, 24), and an increase in inflammatory responses (25, 26).

However, several studies have demonstrated that a long sleep duration was also associated with the incidence of obesity (8, 10, 22), type 2 diabetes (8-10), and cardiovascular disease (7, 16). In the present study, a longer sleep duration was associated with a high body fat ratio and low skeletal muscle mass. Although the body fat ratio and skeletal muscle mass are related to age and gender, these associa-

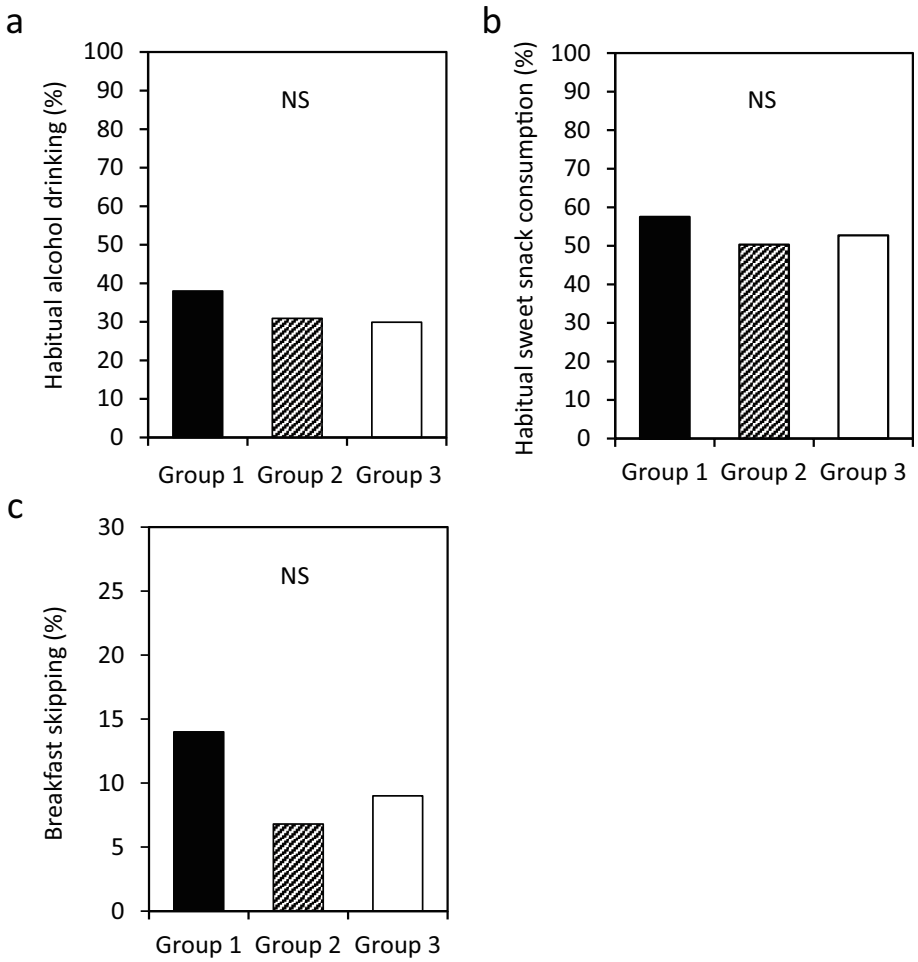

Figure 3. **The prevalence of self-reported habitual alcohol drinking (a), habitual sweet snack consumption (b), and breakfast skipping (c) in group 1 (sleep duration<5.5 hours, n=50), group 2 (5.5-7 hours, n=162), and group 3 (>7 hours, n=67). Alcohol ingestion twice a week or more was regarded as habitual drinking. Sweet snack intake on five days a week or more was regarded as habitual sweet snack consumption. Breakfast skipping was defined as eating breakfast<5 days per week. NS: not significant by the chi square test**

tions were statistically significant even after adjusting for age and gender.

To assess the reason for the correlation between sleep duration and body composition, we analyzed the subjects' dietary pattern and found that the daily intakes of carbohydrates, protein, fat, dietary fiber, and total energy were all negatively correlated the nighttime sleep duration. When the subjects were divided into three groups based on the nighttime sleep duration, the intakes of total energy, carbohydrate, and fat tended to be greater in group 1 (sleep duration <5.5 hours) than in group 3 (>7 hours). Thus, the excess intake of macronutrients was likely involved in the elevated HbA1c levels in group 1. Low intakes of carbohydrate and fat by patients in group 3 may be the reason why the U-shaped association in HbA1c was not observed in this study. However, these observations cannot explain the relationship between a nightly sleep duration >7 hours and unfavorable body composition.

It was reported that long sleepers ingested more alcohol and snacked more frequently than normal sleepers (27, 28). Furthermore, the nightly sleep duration may be associated with breakfast skipping, which is related to obesity (29) and a high body fat percentage (30). However, we found no marked difference in the prevalence of habitual alcohol drinking, habitual sweet snack consumption, or breakfast skipping among the three groups. Thus, the unhealthy body composition in long sleepers was unlikely to have resulted from the excess ingestion of alcohol or sweet snacks, or breakfast skipping.

We next assessed the ratio of individuals who had habitual physical activities in the three groups and found that the ratio was higher in group 1 than in group 3. This observation was unexpected, as it is well known that adequate physical exercise is associated with a good night's sleep (31). In this study, habitual physical activities were defined as activities requiring any movement by the large muscle groups, including walking, running, cycling, as well as more passive activities, such as domestic affairs and any employment-related pursuit that demanded similar muscular output. Hence, group 1 likely included patients who could

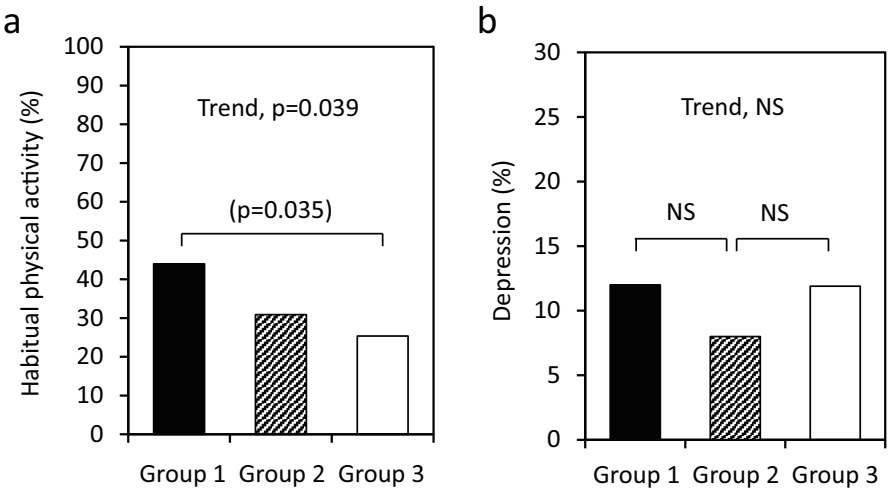

Figure 4. **The prevalence of habitual physical activity (a) and depression (b) in group 1 (sleep duration<5.5 hours, n=50), group 2 (5.5-7 hours, n=162), and group 3 (>7 hours, n=67). Habitual physical activity was defined as ≥150 minutes of walking per week or equivalent, including occupational and household activities. The dose-response association between sleep duration and the prevalence of habitual physical activities was assessed by the Cochran-Armitage trend test. The p value in parenthesis is the result of a post-hoc analysis using the chi square test. NS: not significant**

Table 5. **Clinical Parameters of the Subjects with and without Habitual Physical Activities.**

Parameter	Habitual physical activities		p value
	(-)	(+)	
Number (male/female)	190 (94/96)	89 (51/38)	0.222
Age (year)	61 (51-69)	66 (53.5-72)	0.037
Diabetes duration (year)	8.45 (2.6-16.6)	10.1 (3.8-17.1)	0.351
Body mass index (kg/m^2)	25.8 (22.5-28.8)	24.1 (21.7-26.2)	0.012
Male	26.0 (22.6-28.7)	24.4 (22.4-26.1)	0.047
Female	25.2 (22.4-28.9)	23.6 (21.5-26.5)	0.093
Body fat (%)	33.4 (26.6-39.4)	29.7 (23.2-34.1)	0.001
Male	28.4 (24.1-35.2)	26.1 (21.7-29.8)	0.039
Female	36.2 (32.8-42.2)	33.9 (31.7-37.4)	0.041
Skeletal muscle mass (kg)	23.9 (19.3-29.1)	24.4 (20.0-28.4)	0.987
HbA1c (%)	8.9 (7.5-10.3)	8.6 (7.7-10.2)	0.969
Fasting plasma glucose (mg/dL)	149 (123-195)	153 (125-194)	0.658
AST (U/L)	21 (16-28)	22 (18.5-31)	0.335
ALT (U/L)	22 (16-35)	24 (17-33)	0.269
ALP (U/L)	214 (185-268)	218 (174-258)	0.664
γ-GTP (U/L)	31 (19-54)	31 (21-60)	0.622
Albumin (g/dL)	4.01 (3.81-4.21)	4.07 (3.87-4.33)	0.048
HDL cholesterol (mg/dL)l	46.2 (40.1-55.9)	45.3 (41.3-55.3)	0.836
LDL cholesterol (mg/dL)	115.4 (94.0-135.0)	117 (95.7-140.1)	0.532
Triglyceride (mg/dL)	140 (103-188)	140 (91-198)	0.874
eGFR (mL/min/1.73 m^2)	84.5 (68.7-104.1)	76.3 (63.7-90.4)	0.047
Diabetic retinopathy	64/182 (35.2%)	32/86 (37.2%)	0.961
Diabetic neuropathy	77/190 (40.5%)	30/89 (33.7%)	0.275
Diabetes medication			0.116
Insulin alone or in combination	34 (18.0%)	25 (28.1%)	
Drugs except insulin	99 (52.0%)	44 (49.4%)	
No drug	57 (30.0%)	20 (22.5%)	
Hypnotic drugs	20 (10.5%)	12 (13.5%)	0.470

Medians and interquartile ranges. p values were assessed using the Mann-Whitney U test or the chi square test.

Table 6. Correlation between Nightly Sleep Duration and Anthropometric Parameters in Subjects with and without Habitual Physical Activities. p values are Shown in Parentheses.

	BMI	%Body fat	Skeletal muscle mass
Habitual physical activities (+)	-0.0298 (0.792)	0.0857 (0.424)	-0.0040 (0.971)
Habitual physical activities (-)	-0.0292 (0.689)	0.1557 (0.032)	-0.2068 (0.004)

not get enough sleep because of longer work hours. Low physical activity might have been associated with a low energy intake in group 3.

When the subjects were divided into two groups based on habitual physical activities, those without habitual physical activities had a greater BMI and higher body fat ratio than those with such activities. The association between sleep duration and body composition was observed in subjects without habitual physical activities but not in those who had habitual physical activities. These observations suggest that a long sleep duration is not deleterious when physical activities are sufficient and that the adipose body composition in group 3 was caused by both the low prevalence of habitual physical activities and low nonexercise thermogenesis due to a sedentary lifestyle.

Another possible explanation is that some patients in group 3 may have psychological problems that cause a physically inactive lifestyle, as hypersomnolence and physical inactivity are common features of major depressive disorders (32, 33). Depression increases the risk of cardiovascular morbidity and mortality, probably through an unfavorable lifestyle (34). However, while the prevalence of depression tended to be higher in groups 1 and 3 than in group 2 in our study, the difference was not statistically significant. Further studies will be required to elucidate the influence of depression on the association between sleep duration and metabolic disorders. Finally, the use of hypnotic drugs was not associated with clinical parameters in this study, indicating that the associations were unlikely attributable to the effects of hypnotics.

Several limitations associated with the present study warrant mention. This was a cross-sectional study of a single facility, and the number of subjects was not large. The nightly sleep duration was not evaluated by electroencephalography but by self-report. Habitual physical activities were also self-reported and not measured using accelerometers or pedometers. We did not use a standardized assessment tool to screen for depression; therefore, there may have been some overlooked cases. Finally, although some studies have defined long sleepers as subjects with a sleep duration of ≥10 hours, in the present study, only 8 subjects had a sleep duration of ≥10 hours. This may be because daytime naps were not included in the sleep duration. Further studies will be required to elucidate the influence of habitual physical activities on the association between nightly sleep duration and body composition in long sleepers.

In conclusion, although a U-shaped relationship was not observed between sleep duration and either HbA1c or body fat percentage, sleep duration was negatively and positively associated with HbA1c and body fat ratio, respectively, indicating that both sleep deprivation and oversleeping are deleterious to health. Thus, nightly sleep durations have distinct relevance to metabolic and anthropometric factors in patients with type 2 diabetes. These observations may provide a basis for effective lifestyle management of patients with type 2 diabetes.

The authors state that they have no Conflict of Interest (COI).

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