# **ORIGINAL ARTICLE**

# Association of short sleep duration with impaired glucose tolerance or diabetes mellitus

Sayuri Katano<sup>1</sup>, Yasuyuki Nakamura<sup>1,2</sup>\*, Aki Nakamura<sup>1</sup>, Yoshitaka Murakami<sup>3</sup>, Taichiro Tanaka<sup>4</sup>, Toru Takebayashi<sup>5</sup>, Akira Okayama<sup>6</sup>, Katsuyuki Miura<sup>2</sup>, Tomonori Okamura<sup>7</sup>, Hirotsugu Ueshima<sup>2</sup> for HIPOP-OHP Research Group

# ABSTRACT

**Aims/Introduction:** To examine the cross-sectional relationship between sleep duration and impaired glucose tolerance (IGT), including diabetes mellitus (DM), we analyzed a large-scale healthy workers database in Japan.

**Materials and Methods:** We examined the baseline database of 4143 participants (3415 men and 728 women) aged 19–69 years. Sleep duration of participants was categorized into four groups: <6, 6 to <7, 7 to <8 and ≥8 h. The physical activity of each participant was classified according to the International Physical Activity Questionnaire (IPAQ). We defined IGT including DM (IGT/DM) in the present study according to previous studies as follows: fasting blood sugar level ≥110 mg/dL, or if <8 h after meals ≥140 mg/dL, or on medication for diabetes mellitus, or those diagnosed as having DM. Logistic regression was applied to estimate the odds ratio (OR) to examine the relationship between IGT/DM, sleep duration and other related factors.

**Results:** The number of participants with IGT/DM was 402 (9.7%). The factors that significantly associated with IGT/DM were age (OR 1.08, 95% confidence interval [CI] 1.07–1.10, P < 0.001), high blood pressure (OR 1.94, CI 1.52–2.47, P < 0.001), and <6 h of sleep duration in comparison with 6 to <7 h sleep (OR 2.32, CI 1.18–4.55, P = 0.015). The associations of difficulty in sleep initiation, IPAQ classification, current smoking and alcohol intake with IGT/DM were not statistically significant.

**Conclusions:** Our results showed that shorter sleep duration (<6 h of sleep duration per night) was associated with a risk of IGT/DM independent of other lifestyle habits and metabolic risk factors. (J Diabetes Invest, doi: 10.1111/j.2040-1124.2011.00114.x, 2011)

KEY WORDS: Impaired glucose tolerance, Diabetes mellitus, Short sleep duration

#### INTRODUCTION

Daily lifestyle habits, such as physical activity, smoking, alcohol drinking and dietary intake, are associated with the risk of developing impaired glucose tolerance (IGT) or diabetes mellitus  $(DM)^{1-4}$ . Recently, sleep duration, one of the daily lifestyle habits, has gained attention with regard to its association with lifestyle-related disease conditions. A U-shaped curvilinear relationship was observed (<6, 6, 7,  $\geq 8$  h) between sleep duration and impaired glucose tolerance<sup>5</sup>. Both a decrease and an increase in sleep duration were associated with an increase in cardiovascular and non-cardiovascular mortality<sup>6,7</sup>. Because IGT/DM carries a higher risk of cardiovascular-related mortality, the impact of short sleep duration on glucose regulation suggested a mechanism whereby short sleep duration was associated with an increase in mortality<sup>8,9</sup>. Furthermore, an

<sup>1</sup>Cardiovascular Epidemiology, Kyoto Women's University, Kyoto, Departments of <sup>2</sup>Health Science, and <sup>3</sup>Medical Statistics, Shiga University of Medical Science, Otsu, <sup>4</sup>Department of Health Sciences, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi, Chuo, <sup>5</sup>Department of Preventive Medicine and Eugline Health, School of Medicine, Keio University, <sup>6</sup>The First Institute of Health Service, Japan Anti-Tuberculosis Association, Tokyo, and <sup>7</sup>Department of Preventive Cardiology, National Cardiovascular Center, Suita, Japan \*Corresponding author. Yasuyuki Nakamura Tel: +81-75-531-9172 Fax: +81-75-531-9172 E-mail address: nakamurg@kyoto-wu.ac.jp

Received 26 July 2010; revised 15 February 2011; accepted 16 February 2011

association of sleep duration with mental health, cardiovascular disease and metabolic disorders has been reported in other studies<sup>10–12</sup>. Because previous studies were carried out in USA and European populations where the average body mass index (BMI) is higher, a study was needed in a population where obesity is relatively uncommon.

In the present study, we examined the cross-sectional relationship between sleep duration, quality and IGT, including DM, in a large-scale database of healthy workers in Japan.

# METHODS

#### Participants

We analyzed baseline data from the high-risk and population strategy for occupational health promotion (HIPOP-OHP) study<sup>13–16</sup>. In brief, HIPOP-OHP was an interventional survey to establish a methodology for reducing cardiovascular disease (CVD) risk factors in the workplace. This study population consisted of full-time workers at 12 large-scale companies throughout Japan. Each company had 500–1000 employees. Researchers followed the data of CVD risk factors, lifestyle habits and consciousness about health based on nutrition, physical activity and smoking for 4 years<sup>13–16</sup>. This study was carried out as part of the management of safety and health with the approval of the

Safety Hygiene Committee at each company. Accordingly, all employees were enrolled in this study. However, participation was voluntary, and we explained there was no need for participants to answer the required questionnaire if they did not want to. Approval for the study was obtained from the Institutional Review Board of Shiga University of Medical Science for ethical issues (No. 10–16). During 1999–2000, baseline data were collected from 7346 male and female workers aged 19–69 years.

The present study examined baseline data from 4143 participants (3415 men and 728 women) aged 19–69 years (mean  $\pm$  SD, 41.9  $\pm$  9.4 years) who underwent physical examination, a lifestyle survey and blood chemical examination.

#### Data Collection and Standardization

Physical and laboratory data were standardized according to the manual of the HIPOP-OHP research group<sup>16</sup>. Briefly, after 5 min of silent rest measured by a sandglass, blood pressure (BP) was measured twice for each participant using an automatic sphygmomanometer (BP-103iII; Omron Colin, Tokyo, Japan) at each company, and the mean value was recorded. To measure the lipid levels in each participant, the company established a contract with a clinical laboratory; the blood testing was standardized through the US Cholesterol Reference Method Laboratory Network (CRMLN)<sup>17</sup>. We calculated low-density lipoprotein cholesterol by Friedewald's formula<sup>18</sup> when triglyceride did not exceed 300 mg/dL. The BMI was calculated as weight (kg) divided by height squared (m<sup>2</sup>).

Sleep duration was investigated using the question, 'How many hours of sleep do you get on an average weekday per night?' in the lifestyle survey. Sleep duration of participants was categorized into four groups: <6, 6 to <7, 7 to <8 and  $\geq$ 8 h with reference to a precedent study<sup>5</sup>. Sleep quality was investigated using the question 'How often do you experience difficulty initiating sleep? 1. Often, 2. Sometimes, 3. Seldom', and 'How often, 2. Sometimes, 3. Seldom'.

Participants were asked about the type of, and time spent on, physical activities in their spare time for recreation, exercise or sport in the previous month. Physical activity of each participant was converted into MET-minutes per week (= MET level × minutes of activity/day × days per week) according to the International Physical Activity Questionnaire (IPAQ)<sup>19</sup>, and participants were classified into four classes of physical activity as high (≥3000 MET-minutes per week), moderate activity (<3000 but ≥1500 MET-minutes per week), some activity (<1500 but ≥600 MET-minutes per week) or sedentary (<600 MET-minutes per week).

Drinking habits for each subject were assessed by a questionnaire common to all companies<sup>14</sup>. The frequency of alcohol intake during a typical week and the total alcohol intake on each occasion were determined and used to calculate the alcohol intake per week. This value was then divided by seven to obtain the average alcohol intake per day. Subjects were asked to estimate their alcohol intake based on *gou*, a traditional Japanese drinking unit corresponding to 23 g of ethanol. One *gou* is equivalent to two USA and UK drink units, or 180 mL of sake, and its ethanol content is roughly equivalent to that of a bottle of beer (663 mL), two single shots of whiskey (70 mL), a half glass of *shochu* (110 mL) or 240 mL of wine. Drinkers were defined as those consuming more than 0.3 *gou* (0.6 drinks) per week (1 g of ethanol a day).

We defined IGT including DM in the present study according to previous studies as follows: fasting blood sugar level ≥110 mg/dL, or if <8 h after meals ≥140 mg/dL, or on medication for diabetes mellitus, or participants diagnosed as having DM<sup>3,20-23</sup>. We defined three other metabolic risk factors in the present study as follows: (i) high BP - systolic blood pressure (SBP) ≥130 mmHg, or diastolic blood pressure (DBP) ≥85 mmHg, or the use of an antihypertensive drug; (ii) dyslipidemia – either serum high-density lipoprotein-cholesterol (HDL) concentration <40 mg/dL, or serum triglycerides (TG) concentration ≥150 mg/dL, or on medication for dyslipidemia; and (iii) obesity – BMI  $\geq 25 \text{ kg/m}^{2}$  <sup>3,20,21,24,25</sup>. High BP, instead of usually defined hypertension (SBP  $\ge$  140 mmHg, or  $DBP \ge 90 \text{ mmHg}$ , or the use of an antihypertensive drug) was chosen as one of the metabolic risk factors based on the previous studies that showed high normal BP was associated with an increased risk of cardiovascular disease<sup>24,25</sup>.

#### **Statistical Analyses**

The Chi squared-test for nominal variables and one-way ANOVA for continuous variables were carried out to assess whether there were significant differences among the groups stratified by sleep duration. In the logistic regression, we included several potential confounders into the model. In model 1, we included sex, age, sleep duration (<6, 6 to <7, 7 to <8 and  $\geq$ 8 h; taking 6 to <7 h as a reference) and interaction term (bodyweight × sleep duration). In model 2, in addition to model 1 covariates, we included IPAQ classification, smoking (non-, past or current smoker; non-smoker served as a reference), alcohol intake (mL/day) and interaction terms (IPAQ  $\times$  male, current smoking  $\times$  male, alcohol intake  $\times$  male) as covariates. In model 3, in addition to model 2 covariates and interaction terms, we included high BP, dyslipidemia and obesity as covariates. In model 4, sleep duration of model 3 covariates was replaced by difficulty in sleep initiation (often, sometimes, seldom; taking seldom as a reference). In model 5, difficulty in sleep initiation of model 4 covariates was replaced by difficulty in sleep maintenance (often, sometimes, seldom; taking seldom as a reference). Model 6 included the covariates and interaction terms in model 4 plus sleep duration (<6, 6 to <7, 7 to <8 and  $\geq$ 8 h; taking 6 to <7 h as a reference) and interaction term (difficulty in sleep initiation  $\times$  sleep duration). We also made a sensitivity analysis in model 3 using a different classification of sleep duration as <6, 6-8, 8-9 and >9 h, taking 6-8 h as a reference. All statistical tests were two-sided and P < 0.05 was considered statistically significant. All analyses were carried out using SAS version 9.1 for Windows (SAS Institute, Cary, NC, USA).

# RESULTS

Among the 4143 participants (3415 men and 728 women), those with and without IGT/DM accounted for 402 and 3741, respectively. There were 642 people (11.5%) in the group of sleep duration <6 h, 1690 in the group of sleep duration 6 to <7 h (40.8%), 1415 in the group of sleep duration 7 to <8 h

(34.2%) and 396 in the group of sleep duration  $\geq 8$  h (9.6%). Characteristics of participants by group according to sleep duration are shown in Tables 1 and 2. There were fewer women among the groups with a longer sleep duration. Mean age, SBP, DBP, alcohol intake and percentage of current smokers were higher among the groups with a longer sleep duration. Mean

 Table 1 | Characteristics of participants by group according to sleep duration – HIPOP-OHP study

Variables/sleep duration	<6 h	6 to <7 h	7 to <8 h	≥8 h	Total	P
n	642	1690	1415	396	4143	
Age (years)	41.1 ± 9.3	42.0 ± 9.3	42.0 ± 9.5	42.9 ± 9.8	41.9 ± 9.4	0.023
Women (%)	22.0	21.0	13.6	10.4	17.7	< 0.001
IGT/DM (%)	11.1	8.8	9.9	10.6	9.7	0.349
SBP (mmHg)	117.6 ± 17.1	117.9 ± 16.7	118.7 ± 16.7	120.7 ± 16.4	118.4 ± 16.8	0.012
DBP (mmHg)	72.3 ± 11.9	72.7 ± 11.7	73.0 ± 11.7	74.9 ± 11.7	73.0 ± 11.7	0.003
High BP (%)	25.2	24.9	26.3	28.5	25.8	0.470
$BMI (kg/m^2)$	23.3 ± 3.6	23.1 ± 3.2	22.8 ± 3.0	22.9 ± 3.0	23.0 ± 3.2	0.007
Obesity (%)	27.4	23.7	19.9	22.2	22.8	< 0.001
Dyslipidemia (%)	28.5	25.2	26.4	29.4	26.5	0.238
IPAQ class	1.3 ± 0.6	$1.3 \pm 0.6$	$1.4 \pm 0.7$	$1.3 \pm 0.7$	1.3 ± 0.6	0.031
Current smoking (%)	43.6	45.4	48.6	57.3	47.4	< 0.001
Alcohol (mL/day)	18.2 ± 33.2	18.0 ± 28.2	21.4 ± 30.0	27.6 ± 39.6	20.1 ± 31.0	< 0.001

Chi squared-test for nominal variables and one-way ANOVA for continuous variables were used to examine the difference between the four groups according to sleep duration. We defined impaired glucose tolerance (IGT)/diabetes mellitus (DM) in this study as follows: fasting blood sugar concentration  $\geq$ 110 mg/dL, or if <8 h after meals  $\geq$ 140 mg/dL), or on medication for diabetes mellitus, or participants diagnosed as having DM. We defined three other metabolic factors as high blood pressure (BP): systolic blood pressure (SBP)  $\geq$ 130 mmHg, or diastolic blood pressure (DBP)  $\geq$ 85 mmHg, or the use of an antihypertensive drug; dyslipidemia: high-density lipoprotein <40 mg/dL, or triglycerides concentration  $\geq$ 150 mg/dL, or on medication for dyslipidemia; obesity: defined as body mass index (BMI)  $\geq$ 25 kg/m<sup>2</sup>. IPAQ, International Physical Activity Questionnaire classification; sleep duration, an average of sleeping hours per night on a weekday.

Table 2 | Sleep quality and other characteristics of participants by group according to sleep duration – HIPOP-OHP study

Variables/sleep duration	<6 h	6 to <7 h	7 to <8 h	≥8 h	Total	Р
Difficulty in sleep initiation	(%)					
Often	15.4	8.0	4.4	5.6	7.7	< 0.001
Sometimes	34.0	30.3	30.0	22.5	30.0	0.001
Seldom	49.4	59.6	63.6	69.7	60.4	< 0.001
Difficulty in sleep maintena	nce (%)					
Often	19.0 10.2		6.0	6.8	9.8	< 0.001
Sometimes	38.5	38.7	38.7	35.4	38.4	0.641
Seldom	41.4	49.4	53.6	55.3	50.2	< 0.001
Glucose (mg/dL)	96.2 ± 19.1	95.0 ± 18.7	96.3 ± 23.7	95.7 ± 18.6	95.7 ± 20.6	0.278
TCH (mg/dL)	197.3 ± 33.4	197.6 ± 34.0	196.5 ± 34.2	196.4 ± 34.1	197.1 ± 34.0	0.800
HDLc (mg/dL)	56.3 ± 14.7	57.6 ± 14.2	56.8 ± 14.2	57.8 ± 14.0	57.1 ± 14.3	0.147
TG (mg/dL)	121.3 ± 112.3	115.7 ± 84.7	120.4 ± 99.9	130.3 ± 106.5	119.5 ± 96.8	0.049
LDLc (mg/dL)	110.3 ± 31.5	111.1 ± 31.1	109.5 ± 32.9	105.6 ± 33.8	109.9 ± 32.1	0.023

Chi squared-test for nominal variables and one-way ANOVA for continuous variables were used to examine the difference between four groups according to sleep duration. We defined impaired glucose tolerance (IGT)/diabetes mellitus (DM) in this study as follows: fasting blood sugar concentration  $\geq$ 110 mg/dL, or if <8 h after meals  $\geq$ 140 mg/dL), or on medication for DM, or participants diagnosed as having DM. We defined three other metabolic factors as high blood pressure: systolic blood pressure  $\geq$ 130 mmHg, or diastolic blood pressure  $\geq$ 85 mmHg, or the use of an antihypertensive drug; dyslipidemia: high-density lipoprotein <40 mg/dL, or triglycerides (TG) concentration  $\geq$ 150 mg/dL, or on medication for dyslipidemia; obesity: defined as body mass index  $\geq$ 25 kg/m<sup>2</sup>. HDLc, serum high-density lipoprotein cholesterol concentration; LDLc, serum low-density lipoprotein cholesterol concentration TCH, serum total cholesterol concentration.

BMI and percentage of obesity were lower among the groups with a longer sleep duration. Mean IPAQ classification was different among the groups. There were no differences in mean blood glucose, prevalence of IGT/DM, high BP and dyslipidemia among the groups (Table 1).

There were fewer participants who had difficulty in sleep initiation or difficulty in sleep maintenance among the groups with a longer sleep duration. Mean glucose, total cholesterol and HDL cholesterol concentrations were not different among the groups. Although mean triglyceride and low-density lipoprotein cholesterol concentrations were different among the groups, there were no obvious trends (Table 2).

Results of logistic regression analysis on associations between IGT/DM and sleep duration and quality adjusted for other lifestyle habits are shown in Table 3. In model 1, independent factors that were associated significantly with IGT/DM were age (OR 1.09, 95% confidence interval [CI] 1.08–1.11, P < 0.001), being male (OR 2.60, CI 1.70-3.99, P < 0.001), <6 h sleep (OR 3.97, CI 2.60-6.07, P < 0.001), 7 to <8 h sleep (OR 0.37, CI 0.25-0.55, P < 0.001), and ≥8 h sleep (OR 0.12, CI 0.06-0.24, P < 0.001) in comparison with 6–7 h duration. In model 2, factors that were significantly associated with IGT/DM were age (OR 1.09, CI 1.07-1.11, P < 0.001) and <6 h (OR 4.07, CI 2.63-6.31, P < 0.001), 7 to <8 h sleep (OR 0.38, CI 0.26-0.57, P < 0.001) and  $\geq 8$  h sleep (OR 0.12, CI 0.06-0.25, P < 0.001) of sleep duration. In model 3, factors that were significantly associated with IGT/DM were age (OR 1.08, CI 1.06–1.09, P < 0.001), high BP (OR 1.99, CI 1.57-2.52, P < 0.001), obesity (OR 1.36, CI 1.00–1.83, P = 0.049), <6 h sleep (OR 2.46, CI 1.49–4.06, P < 0.001) and  $\geq 8$  h sleep (OR 0.33, CI 0.13-0.79, P = 0.013). Contribution of IPAQ (OR 1.57, CI 0.56-4.38, P = 0.389), alcohol intake (OR 1.05, CI 0.97-1.15, P = 0.221) and current smoking (OR 0.40, CI 0.12–1.36, P = 0.141) were not statistically significant. The interaction terms, current smoking × male

 Table 3 | Independent factors associated with impaired glucose tolerance/diabetes mellitus and sleep duration and lifestyle habits – results of logistic regression analysis

Covariates	Model 1		Model 2		Model 3		Model 4		Model 5		Model 6	
	OR	95% CI	OR	95% Cl	OR	95% Cl	OR	95% CI	OR	95% CI	OR	95% CI
Age (years)	1.09**	1.08-1.11	1.09**	1.07-1.11	1.08**	1.06-1.09	1.07**	1.06-1.09	1.07**	1.06-1.09	1.08**	1.07–1.10
Male	2.60**	1.70-3.99	1.41	0.41-4.88	1.48	0.43-5.13	1.64	0.48-5.64	1.73	0.51-5.91	1.19	0.30–4.76
Sleep												
<6 h	3.97**	2.60-6.07	4.07**	2.63-6.31	2.46**	1.49-4.06					2.32*	1.18–4.55
6 to <7 h	Ref	-	Ref	-	Ref	-					Ref	_
7 to <8 h	0.37**	0.25-0.55	0.38**	0.26-0.57	0.63	0.39-1.01					0.73	0.37–1.45
≥8 h	0.12**	0.06-0.24	0.12**	0.06-0.25	0.33*	0.13-0.79					0.39	0.10-1.52
Difficulty in sleep in	nitiation											
Often							1.82**	1.24-2.67			1.49	0.60-3.70
Sometimes							1.01	0.78–1.30			0.91	0.53–1.54
Seldom							Ref	_			Ref	-
Difficulty in sleep r	maintenar	nce										
Often									1.27	0.88–1.83		
Sometimes									0.88	0.69–1.12		
Seldom									Ref	_		
IPAQ class			1.53	0.54-4.31	1.57	0.56–4.38	1.69	0.61-4.72	1.60	0.58-4.42	1.99	0.61–6.57
Alcohol (mL/day)			1.06	0.97-1.15	1.05	0.97-1.15	1.05	0.97-1.15	1.05	0.97-1.15	1.06	0.97–1.16
Current smoking			0.34	0.10-1.15	0.40	0.12-1.36	0.40	0.12-1.36	0.41	0.12-1.41	0.35	0.10-1.21
High BP					1.99**	1.57-2.52	2.08**	1.64–2.64	2.11**	1.66–2.67	1.94**	1.52–2.47
Dyslipidemia					1.10	0.86-1.40	1.11	0.88-1.42	1.14	0.90-1.45	1.06	0.83–1.36
Obesity					1.36*	1.00-1.83	1.77**	1.38-2.27	1.77**	1.38–2.26	1.34	0.98–1.82

Results of analysis by logistic regression models on associations between impaired glucose tolerance/diabetes mellitus and lifestyle habits are shown. \*\*P < 0.01, \*P < 0.05. Model 1, adjusted for sex, age and sleep duration (<6, 6 to <7, 7 to <8 and ≥8 h; taking 6 to <7 h as a reference), and interaction term (bodyweight × sleep duration). Model 2, adjusted for covariates in model 1 plus International Physical Activity Questionnaire (IPAQ) classification, smoking (non-, past or current smoker; non-smoker serves as reference), alcohol intake (mL/day) and interaction terms (IPAQ × male, current smoking × male, alcohol intake × male, bodyweight × sleep duration). Model 3, adjusted for covariates and interaction terms in Model 2 plus high blood pressure (BP), dyslipidemia and obesity. Model 4, adjusted for sex, age, IPAQ classification, smoking (non-, past or current smoker; non-smoker serves as reference), alcohol intake (mL/day), high BP, dyslipidemia, obesity, difficulty in sleep initiation (often, sometimes, seldom; taking seldom as a reference) and interaction terms (IPAQ × male, current smoking × male, alcohol intake (mL/day), high BP, dyslipidemia, obesity, difficulty in sleep initiation (often, sometimes, seldom; taking seldom as a reference) and interaction terms in model 4 covariates, except for difficulty in sleep initiation, which was replaced by difficulty in sleep maintenance (often, sometimes, seldom; taking seldom as a reference). Model 6, adjusted for covariates and interaction terms in model 4 plus sleep duration (<6, 6 to <7, 7 to <8 and ≥8 h; taking 6 to <7 h as a reference) and interaction terms in model 4 plus sleep duration (<6, 6 to <7, 7 to <8 and ≥8 h; taking 6 to <7 h as a reference) and interaction term (difficulty in sleep initiation × sleep duration). (OR 3.09, CI 1.01–9.42, P = 0.048) and bodyweight × sleep duration (OR 1.01, CI 1.00–1.01, P = 0.006) contributed significantly. In model 4, factors that were significantly associated with IGT/DM were age (OR 1.07, CI 1.06–1.09, P < 0.001), high BP (OR 2.08, CI 1.64–2.64, P < 0.001), obesity (OR 1.77, CI 1.38– 2.27, P < 0.001) and difficulty in sleep initiation (OR 1.82, CI 1.24-2.67, P = 0.002, often vs seldom). In model 5, factors that were significantly associated with IGT/DM were age (OR 1.07, CI 1.06-1.09, P < 0.001), high BP (OR 2.11, CI 1.66-2.67, *P* < 0.001) and obesity (OR 1.77, CI 1.38–2.26, *P* < 0.001). Difficulty in sleep maintenance did not contribute significantly (OR 1.27, CI 0.88–1.83, P = 0.211, often vs seldom). In model 6, factors that were significantly associated with IGT/DM were age (OR 1.08, CI 1.07-1.10, P < 0.001), high BP (OR 1.94, CI 1.52–2.47, P < 0.001) and <6 h sleep (OR 2.32, CI 1.18–4.55, P = 0.015). Difficulty in sleep initiation did not contribute significantly (OR 1.49, CI 0.60-3.70, P = 0.386, often vs seldom). The interaction terms, current smoking  $\times$  male (OR = 3.49, 1.12–10.8, P = 0.031) and bodyweight × sleep duration (OR 1.01, CI 1.00–1.01, P = 0.004) contributed significantly.

The results of sensitivity analysis in model 3 using a different classification of sleep duration were similar as those using the original classification of sleep duration. There were 642 people in the group of sleep duration < 6 h, 3105 in the group of sleep duration 6 to <8 h, 376 in the group of sleep duration 8 to <9 h and 20 in the group of sleep duration  $\geq$ 9 h. Sleep duration <6 h was associated with a higher risk for IGT/DM (OR 1.93, CI 1.24–3.00, *P* = 0.004) in comparison with sleep duration 6 to <8 h.

### DISCUSSION

In the present study, we found significant positive associations between short sleep duration (<6 h compared with 6-7 h sleep duration) and IGT/DM. Although  $\geq 8$  h sleep inversely, and difficulty in sleep initiation positively associated with IGT/DM, concomitant inclusions of sleep duration and difficulty in sleep initiation covariates in a model resulted in the disappearance of statistical significance of these factors. Several previous studies showed that difficulties in maintaining sleep or short sleep duration were associated with an increased incidence of diabetes<sup>8,26–30</sup>. In a study by Spiegel et al.<sup>31</sup>, it was suggested that chronic sleep loss, behavioral or sleep disorder-related, might represent a novel risk factor for weight gain, insulin resistance and type 2 diabetes. One mechanism by which sleep deprivation might result in increased risk of insulin resistance and diabetes may be either by directly affecting parameters of glucose tolerance or indirectly through a disturbance in appetite regulation, leading to increased food intake and weight gain<sup>31</sup>. With regard to short sleep duration and metabolic disorders or weight gain, some have argued that in an environment where food is readily available, sleep deprivation might simply represent an increased opportunity to eat, especially if most wake time is spent in sedentary activities, such as watching television<sup>32</sup>. However, in the epidemiological literature, those studies that attempted to

quantify caloric intake found no relationship between sleep duration and dietary consumption<sup>33–36</sup>. Chronic partial sleep deprivation also clearly leads to feelings of fatigue, and this tiredness might lead to reductions in physical activity.

In some previous studies, long sleep duration was associated with increased type 2 diabetes risk<sup>27</sup>. Previous cross-sectional studies showed that short and long sleep duration were associated with an increased risk of developing IGT or DM, independent of confounding factors<sup>8,28,29</sup>. Chaput et al.<sup>30</sup> studied a longitudinal sample of 276 individuals aged 21-64 years with follow up for a mean of 6 years, and found that short and long sleeping times were associated with a higher risk of developing type 2 DM/IGT. However, in a study by Mallon et al.26, long sleep duration was not associated with risk of DM, whereas short sleep duration was significantly associated with it. Although the mechanisms of short sleep duration related to an increased risk of DM are relatively well understood as aforementioned, the mechanisms for long sleep duration for an increased risk of DM are not clear. It was speculated that in unrecognized conditions, such as sleep apnea syndrome, an increased need for sleep and risk of DM might coexist<sup>37,38</sup>. It is also speculated that long sleep duration might be an early symptom of DM<sup>29</sup>. However, none of the aforementioned postulated mechanisms for an association of long sleep duration with DM have been well proven.

The strengths of the present study include being populationbased, large-scale and multisite with highly standardized methods. Because the study included men and women of a broad range of ages, the findings are likely to be generalizable to middle-aged Japanese. However, the present study has some limitations. First, the present study was limited by its crosssectional design. Thus, the causal implications of short sleep duration for IGT/DM should be taken cautiously. Second, we did not measure waist circumference (WC). Although the measurement of WC is widely advocated as a simple anthropometric marker of health risk, we showed in a population based study that BMI and WC correlated very well in men and women, and that BMI could be used instead of WC in a study when the latter was not available<sup>39</sup>. Third, we did not have any data on food intake and sleep apnea. These might make important contributions to IGT/DM. Fourth, we used non-fasting blood samples and thus we might have misclassified participants with impaired glucose tolerance. However, previous studies by the present authors and others showed that IGT/DM identified by the same criteria as in the present study in non-fasting participants was an independent cardiovascular risk factor<sup>22,23</sup>.

In conclusion, the present results showed that a shorter sleep duration (<6 h of sleep per night) was associated with risk of IGT/DM independent of other lifestyle habits and metabolic risk factors.

## ACKNOWLEDGMENTS

The present study was funded by research grants from the Ministry of Health and Welfare of Japan (H10-12, No. 063,

Research on Health Services, Health Sciences Research Grants and H13, No. 010, Medical Frontier Strategy Research, Health Sciences Research Grants), the Ministry of Health, Labor, and Welfare of Japan (H14-15, No. 010, Clinical Research for Evidence-Based Medicine, Health, and Labor Sciences Research Grants), and the Japan Arteriosclerosis Prevention Fund 2004. The authors have no potential conflicts of interest to disclose. We thank Toshimi Yoshida of the Department of Health Science, Shiga University of Medical Science, for her excellent clerical support during this research. Investigators and members of the research group are listed in the appendix of reference 13.

# REFERENCES

- 1. Bhatt DL, Steg PG, Ohman EM, *et al.* International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. *JAMA* 2006; 295: 180–189.
- 2. Meigs JB, D'Agostino RBS, Wilson PW, *et al.* Risk variable clustering in the insulin resistance syndrome. The Framingham Offspring Study. *Diabetes* 1997; 46: 1594–1600.
- 3. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001; 285: 2486–2497.
- 4. Park YW, Zhu S, Palaniappan L, *et al.* The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988–1994. *Arch Intern Med* 2003; 163: 427–436.
- 5. Hall MH, Muldoon MF, Jeuning JR, *et al.* Self-reported sleep duration is associated with the metabolic syndrome in mid-life adults. *Sleep* 2008; 31: 635–643.
- 6. Ferrie JE, Shipley MJ, Cappuccio FP, *et al.* A prospective study of change in sleep duration; associations with mortality in the Whitehall II cohort. *Sleep* 2007; 30: 1659–1666.
- Eguchi K, Pickering TG, Schwartz JE, *et al.* Short sleep duration as an independent predictor of cardiovascular events in Japanese patients with hypertension. *Arch Intern Med* 2008; 168: 2225–2231.
- 8. Gottlieb DJ, Punjab NM, Newman AB, *et al.* Association of sleep time with diabetes mellitus and impaired glucose tolerance. *Arch Intern Med* 2005; 165: 863–868.
- Spiegel K, Knutson K, Leproult R, et al. Impact of sleep debt on metabolic and endocrine function. *Lancet* 1999; 354: 1435–1439.
- 10. Kaneita Y, Ohida T, Uchiyama M, *et al.* Excessive daytime sleepiness among the Japanese general population. *J Epidemiol* 2005; 15: 1–8.
- 11. Kaneita Y, Ohida T, Osaki Y, *et al.* Association between mental health status and sleep status among adolescents in Japan: a nationwide cross-sectional survey. *J Clin Psychiatry* 2007; 68: 1426–1435.

- 12. Xu Q, Song Y, Hollenbeck A, *et al.* Day napping and short night sleeping are associated with higher risk of diabetes in older adults. *Diabetes Care* 2010; 33: 78–83.
- 13. Okamura T, Tanaka T, Babazono A, *et al.* The high-risk and population strategy for occupational health promotion (HIPOP-OHP) study: study design and cardiovascular risk factors at the baseline survey. *J Hum Hypertens* 2004; 18: 475–485.
- 14. Okamura T, Tanaka T, Yoshita K, *et al.* Specific alcoholic beverage and blood pressure in a middle-aged Japanese population: the high-risk and population strategy for occupational health promotion (HIPOP-OHP) study. *J Hum Hypertens* 2004; 18: 9–16.
- 15. Naito M, Nakayama T, Okamura T, *et al.* Effect of a 4-year workplace-based physical activity intervention program on the blood lipid profiles of participating employees: the high-risk and population strategy for occupational health promotion (HIPOP-OHP) study. *Atherosclerosis* 2008; 197: 784–790.
- 16. Tamura U, Tanaka T, Okamura T, *et al.* Changes in weight, cardiovascular risk factors and estimated risk for coronary heart disease following smoking cessation in Japanese male workers: HIPOP-OHP Study. *J Atheroscler Thromb* 2010; 17: 12–20.
- 17. Nakamura M, Sato S, Shimamoto T. Improvement in Japanese clinical laboratory measurements of total cholesterol and HDL-cholesterol by the US Cholesterol Reference Method Laboratory Network. *J Atheroscler Thromb* 2003; 10: 145–153.
- 18. Friedewald WT, Levy RJ, Fredrickson DS. Estimation of the concentration of lowdensity lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clin Chem* 1972; 18: 499–502.
- 19. Craig CL, Marshall AL, Sjostrom M, *et al.* The International Physical Activity Questionnaire (IPAQ): a comprehensive reliability and validity study in twelve countries. *Med Sci Sports Exerc* 2003; 35: 1381–1395.
- 20. Alberti KG, Zimmet P, Shaw J, *et al.* The metabolic syndrome a new worldwide definition. *Lancet* 2005; 366: 1059–1062.
- 21. International Diabetes Federation. The IDF concensus worldwide definition of the metabolic syndrome. http://www.idf.org/webdata/docs/MetS\_def\_update2006.pdf.
- 22. Kadota A, Hozawa A, Okamura T, *et al.* Relationship between metabolic risk factor clustering and cardiovascular mortality stratified by high blood glucose and obesity: NIPPON DATA90, 1990–99. *Diabetes Care* 2007; 30: 1533–1538.
- 23. Vermeer SE, Sandee W, Algra A, *et al.* Impaired glucose tolerance increases stroke risk in nondiabetic patients with transient ischemic attack or minor ischemic stroke. *Stroke* 2006; 37: 1413–1417.
- 24. Vasan RS, Larson MG, Leip EP, *et al.* Impact of high-normal blood pressure on the risk of cardiovascular disease. *N Engl J Med* 2001; 345: 1291–1297.
- 25. Nakamura Y, Yamamoto T, Okamura T, *et al.* Combined cardiovascular risk factors and outcome: NIPPON DATA80, 1980–94. *Circ J* 2006; 70: 960–964.

- 26. Mallon L, Broman JE, Hetta J. High incidence of diabetes in men with sleep complaints or short sleep duration: a 12-year follow-up study of a middle-aged population. *Diabetes Care* 2005; 28: 2762–2767.
- 27. Tuomilehto H, Peltonen M, Partinen M, *et al.* Sleep duration, lifestyle intervention, and incidence of type 2 diabetes in impaired glucose tolerance: The Finnish Diabetes Prevention Study. *Diabetes Care* 2009; 32: 1965–1971.
- 28. Yaggi HK, Araujo AB, Mckinlay JB. Sleep duration as a risk factors for the development of type 2 diabetes. *Diabetes Care* 2006; 29: 657–661.
- 29. Ayas NT, White DP, Al-Delaimy WK, *et al.* A prospective study of self-reported sleep duration and incident diabetes in women. *Diabetes Care* 2003; 26: 380–384.
- 30. Chaput JP, Despres JP, Bouchard C, *et al.* Sleep duration as a risk factor for the development of type 2 diabetes or impaired glucose tolerance: analyses of the Quebec Family Study. *Sleep Med* 2009; 10: 919–924.
- 31. Spiegel K, Knutson K, Leproult R, *et al.* Sleep loss: a novel risk factor for insulin resistance and Type 2 diabetes. *J Appl Physiol* 2005; 99: 2008–2019.

- 32. Sivak M. Sleeping more as a way to lose weight. *Obes Rev* 2006; 7: 295–296.
- 33. Patel SR, Malhotra A, White DP, *et al.* Association between reduced sleep and weight gain in women. *Am J Epidemiol* 2006; 164: 947–954.
- 34. Patel SR, Hu FB. Short sleep duration and weight again: a systematic review. *Obesity* 2008; 16: 643–653.
- 35. Reilly JJ, Armstrong J, Dorosty AR, *et al.* Early life risk factors for obesity in childhood: cohort study. *BMJ* 2005; 330: 1357.
- Agras WS, Hammer LD, McNicholas F, et al. Risk factors for childhood overweight: a prospective study from birth to 9.5 years. J Pediatr 2004; 145: 20–25.
- Gottlieb DJ, Whitney CW, Bonekat WH, et al. Relation of sleepiness to respiratory disturbance index: the Sleep Heart Health Study. Am J Respir Crit Care Med 1999; 159: 502–507.
- 38. Punjabi NM, Sorkin JD, Katzel LI, *et al.* Sleep-disordered breathing and insulin resistance in middle-aged and overweight men. *Am J Respir Crit Care Med* 2002; 165: 677–682.
- 39. Nakamura Y, Turin TC, Kita Y, *et al.* The associations of obesity measures with the metabolic risk factors in a communitybased population in Japan. *Circ J* 2007; 71: 776–781.