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Author(s)	Satoh, Hiroki; Nishihira, Jun; Wada, Tatsuhiko; Fujii, Satoshi; Tsutsui, Hiroyuki
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1 **The Relation between the Habitual Sleep Duration and Blood Pressure Values in**
2 **Japanese Male Subjects**

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4 Hiroki SATOH ^{1,2}, Jun NISHIHIRA ¹, Tatsuhiko WADA ¹, Satoshi FUJII ³

5 and Hiroyuki TSUTUI ²

6 ¹ Department of Clinical Management and informatics, Hokkaido Information University,

7 Ebetsu, Japan

8 ² Department of Cardiovascular Medicine, Hokkaido University Graduate School of Medicine,

9 Sapporo, Japan

10 ³ Department of Molecular and Cellular Pathobiology and Therapeutics,

11 Nagoya City University Graduate School of Pharmaceutical Sciences, Nagoya, Japan

12 Correspondence to: Hiroki SATOH

13 Department of Clinical Management and informatics, Hokkaido Information University

14 59-2, Nishi-Nopporo, Ebetsu, Hokkaido, 069-8585, Japan

15 Telephone: +81 11 385 4411 Fax: +81 11 384 0134

16 E-mail: h-satoh@do-johodai.ac.jp

17 Keywords: sleep duration; blood pressure; hypertension; Japanese male subjects;

18 epidemiology.

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1 Abstracts

2 Background: Previous studies have demonstrated that the sleep duration is closely associated
3 with metabolic risk factors, however, the relationship between the habitual sleep duration and
4 blood pressure values in Japanese population has not been fully established.

5 Methods: We performed a cross-sectional study of 1,670 Japanese male subjects to clarify the
6 relationship between the habitual sleep duration and blood pressure values. The study subjects
7 were divided into four groups such as <6, 6-, 7-, and ≥8 hours according to their nightly
8 habitual sleep duration.

9 Results: The rate of subjects with <6, 6-, 7-, and ≥8 hours sleep duration was 12.0, 37.6, 38.2,
10 and 12.2 (%), respectively. Compared to the group with 7-hours sleep duration (referent),
11 those with <6 and ≥8 hours groups have significantly greater systolic and diastolic blood
12 pressure values. The rate of hypertensive subjects, defined as systolic blood pressure more
13 than 140 mmHg and/or diastolic blood pressure more than 90 mmHg, with sleep duration
14 with <6, 6-, 7-, and ≥8 hours was 13.4, 5.7, 7.5, and 13.8 (%), respectively. Compared to the
15 group with 7-hours sleep duration (referent), the multivariate odds ratios (95% confidence
16 interval) of that with <6 and ≥8 hours for hypertension were 2.43 (1.40-4.20, P<0.01) and
17 2.28 (1.31-3.95, P<0.01), respectively, adjusted with conventional cardiovascular risk
18 factors.

19 Conclusions: The present study demonstrated both long and short habitual sleep duration was

1 significant high blood pressure values and the occurrence of hypertension in Japanese male

2 subjects.

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1 **Introduction**

2 Sleep loss, long-term sleep deprivation, and alternations in sleep duration are common
3 in modern society [1], with evidence showing that we are sleeping on average only 6.8 hours
4 per night, which is 1.5 hours less than we did one hundred years ago [2]. The change of sleep
5 condition exerts deleterious effects on detectable changes in metabolic [3, 4], endocrine [5],
6 and sympathetic tone [6]. These findings suggest that alternations of the habitual sleep
7 duration may predispose to overt the change of blood pressure values. Several previous
8 studies demonstrated that shorter sleep durations were found to be related to hypertension,
9 compared with subjects with 7 hours of sleep per night in Caucasian populations [7-10]. The
10 first United States National Health and Nutrition Examination Survey (NHANES-I)
11 elucidated that sleeping 5 hours or less per night was associated with a 60% increased risk of
12 incident hypertension in Caucasian middle-aged subjects during a mean follow-up of 8-10
13 years [10]. The Sleep Heart Health Study demonstrated that United States subjects sleeping
14 more than 9 hours per night had a 30% higher prevalence of hypertension as compared to
15 those sleeping between 7 and 8 hours per night [7]. The relationship between sleep duration
16 and the occurrence of hypertension in previous studies has been controversial, however, this
17 association among Japanese general population has not been fully investigated. Moreover, the
18 relationship between sleep duration and blood pressure values remain unanswered.

19 The purpose of the present study was to examine cross-sectional associations of sleep

1 duration with blood pressure values and hypertension occurrence in Japanese male subjects.

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1 **Materials and Methods**

2 *Study Subjects*

3 The study subjects consisted of 1,887 food and beverage company male employees,
4 aged from 38 from 58 years, who had their annual health examinations during the period from
5 April 2010 to March 2011. A total of 216 subjects were excluded for the following reasons:
6 medication of hypertension (n=201), medication of sleep disturbance (n=12), and medication
7 of depression (n=3). Thus, 1,671 male subjects were enrolled in the present study. The study
8 protocol was approved by the ethical committee of Hokkaido Information University and the
9 written informed consent was obtained from each subjects.

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11 *Baseline data measurement*

12 All study subjects were asked to complete a self-questionnaire that included smoking
13 habit, alcohol consumption, the frequency of exercise, family history of hypertension, and
14 medical history. The questionnaire was distributed to the subjects in advance of their annual
15 health check-up and was collected at the examination. The subjects who had never smoked
16 and ex-smokers were classified as “non-smokers”. Drinkers were defined as those who
17 consumed alcohol once per week or more. “Exercise” subjects were defined as those who
18 regularly exercised more than one per week. Hypertension, dyslipidemia, and diabetes
19 mellitus were defined as receiving medical agents at the health examination. Body mass index

1 (BMI) was calculated as body weight (kilograms) divided by squared height (meters). Blood
2 pressure was measured by a trained nurse using a standard mercury sphygmomanometer, with
3 the study subjects in the sitting position after at least a 5-min rest. A blood sample was
4 obtained from the antecubital vein in the morning after an overnight fast and serum was
5 separated. After precipitation by heparin-manganase, total cholesterol and high-density
6 lipoprotein (HDL)-cholesterol were measured by the phosphotungstate method. Triglyceride
7 was measured by enzymatically. Glucose was enzymatically determined by the hexokinase
8 method.

9

10 *Definition of hypertension*

11 Incident hypertension subjects were defined as systolic blood pressure ≥ 140 mmHg
12 and/or diastolic blood pressure ≥ 90 mmHg at their health examination.

13

14 *Statistical Analysis*

15 The study subjects were categorized into four groups according to sleep duration: <6 ,
16 $6-$, $7-$, and ≥ 8 hours. The characteristics of the study subjects were expressed as means \pm SD
17 for continuous variables, median (and interquartile range) for skewed distribution variables,
18 and percentages for categorical variables according to sleep duration. The differences of
19 variables among groups were examined by analysis of variance (ANOVA), Kruskal-Wallis

1 test, or chi-square test. Next, Bonferroni procedure was used between two groups as a post
2 hoc test. The association between sleep duration and hypertension was assessed by using the
3 multiple logistic regression analysis. The principle model included candidate variables for
4 age, BMI, smoking, alcohol, exercise, dyslipidemia, diabetes mellitus, family history of
5 hypertension, values such as systolic blood pressure, total cholesterol, triglyceride, high
6 density lipoprotein (HDL)-cholesterol, and glucose. A p value of less than 0.05 was
7 considered to indicate statistical significance. All statistical analyses were performed using
8 the SPSS statistical package for Windows version 11.0 (Chicago, IL, USA).

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1 **Results**

2 Table 1 shows the characteristics of study subjects according to sleep duration levels.

3 The mean age and BMI of the study patients was 50 ± 6 years and $23.8 \pm 2.8 \text{ kgm}^{-2}$, respectively.

4 The numbers (%) of the study subjects with sleep duration of <6 , 6-, 7-, and ≥ 8 hours were

5 201 (12.0), 628 (37.6), 638 (38.2), and 203 (12.2), respectively. Variables such as age, BMI,

6 alcohol, exercise, family history of hypertension, triglyceride, and high density lipoprotein

7 (HDL)-cholesterol were significantly different among the groups. Subjects with 7-hours sleep

8 duration were older and more likely to have non-drinkers.

9 Figure 1 shows systolic (A) and diastolic (B) blood pressure values according to

10 sleep duration levels. The mean systolic and diastolic blood pressure values of the study

11 subjects were 119 ± 15 and 74 ± 11 mmHg, respectively. The mean systolic blood pressure

12 values with sleep duration <6 , 6-, 7-, and ≥ 8 hours were 122 ± 14 , 119 ± 15 , 118 ± 15 , and

13 122 ± 17 mmHg, respectively (P for trend < 0.01). The mean diastolic blood pressure values

14 with sleep duration <6 , 6-, 7-, and ≥ 8 hours were 76 ± 11 , 75 ± 10 , 73 ± 11 , and 78 ± 12

15 mmHg, respectively (P for trend < 0.001). Compared with subjects with sleep duration of 7-

16 hours as a referent, those with sleep duration of both <6 and ≥ 8 hours had significantly

17 greater systolic and diastolic blood pressure values.

18 Table 2 shows that multivariate predictor of variables for hypertension by multiple

19 logistic regression analysis. The numbers (%) of the study subjects with hypertension were

1 139 (8.3%). Risk factors such as age, BMI, smoking, alcohol, family history of hypertension,
2 and glucose were significant and independent predictors for hypertension.

3 Table 3 shows odds ratio and 95% confidence interval (CI) of hypertension according
4 to sleep duration levels. The numbers (%) of hypertensive subjects with sleep duration <6, 6-
5 7-, and ≥ 8 hours were 27 (13.4), 36 (5.7), 48 (7.5), and 28 (13.8), respectively. On
6 multivariate analysis with sleep duration of 7- hours as the reference, the adjusted odds ratio
7 for subjects with sleep duration <6 hours for hypertension was 2.43 (95% CI: 1.40-4.20, P
8 <0.01). Similarly, that with sleep duration ≥ 8 hours for hypertension was 2.28 (95% CI:
9 1.31-3.95, P <0.01).

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1 **Discussion**

2 The present study demonstrates that sleep duration of both <6 and ≥ 8 hours are
3 significantly associated with high blood pressure values and hypertension occurrence in
4 Japanese male subjects.

5 Bonnet et al. reported that nearly one-third of adults had sleep duration less than 6
6 hours per night and sleep deficiency, long-term sleep deprivation, and alternations in sleep
7 duration have been common in modern society [1]. The quality and sleep duration have been
8 indicated as factors to affect the health condition in general population [11, 12]. In
9 epidemiologic studies, compared with subjects with 7-hours of habitual sleep duration, short
10 and long sleep durations were related to increase body mass index [13, 14], the development
11 of diabetes mellitus [15, 16], and the occurrence of cardiovascular disease [17-19]. Recent
12 epidemiological cohort studies indicated that short and long sleep duration were also closely
13 associated with mortality [20, 21]. Ikehara et al. demonstrated that both shorter and longer
14 sleep duration were associated with increased mortality due to all causes for both gender,
15 yielding a U-shaped relationship with total mortality with a nadir as 7-hours sleep duration
16 from a large-scale prospective study of 98,634 Japanese men and women in the Japan
17 Collaborative Cohort Study [22]. However, the relationship between sleep duration and blood
18 pressure values in Japanese general population has not been fully established.

19 Previous studies indicated that sleep disorders might play a crucial role in

1 determining blood pressure values both in the office and over the 24 hours and modulating the
2 day-night blood pressure profile [23, 24], which could affect the prognosis of hypertensive
3 patients [25, 26]. Recent studies demonstrated that both increased and reduced sleep duration
4 may be related to increase the risk of cardiovascular disease and hypertension [22, 27]. These
5 studies clarified that sleep duration defined as acutely induced sleep deprivation was closely
6 associated with blood pressure values, however, the relationship between the habitual sleep
7 duration and blood pressure values has still been controversial [28].

8 Previous studies reported that the habitual short sleep duration increased blood
9 pressure values in general population [29], however, this relationship might differ among ages
10 and ethnicity [7, 30]. The present study demonstrated that the habitual short sleep duration
11 was significantly associated with high blood pressure values and the occurrence of
12 hypertension in Japanese middle-aged male subjects, which confirmed the previous results.
13 The biological mechanisms mediating the association of the habitual short sleep duration with
14 the development and occurrence of hypertension are uncertain, however, the habitual short
15 sleep duration may disrupt circadian rhythm and autonomic balance [30, 31]. The alternations
16 in these functions might shift of the daily blood pressure profile to higher values, the
17 occurrence of the non-dipping pattern, the increase of blood pressure variability, and the
18 disturbances in the diurnal rhythm of cardiac output [32, 33].

19 The present study also demonstrated that the habitual long sleep duration was

1 significantly associated with high blood pressure values and the occurrence of hypertension.
2 The rate of drinkers was more likely to be higher in subjects with sleep duration ≥ 8 than < 6 ,
3 6-, and 7- hours (Table 1) and the covariate of alcohol was a significant and independent
4 predictor for hypertension (Figure 2). Sesso et al. indicated that light-to-moderate alcohol
5 consumption was a linear association with increasing the risk for the development of
6 hypertension [34]. Nakanishi et al. demonstrated that the risk for hypertension increased
7 according to the increment of alcohol consumption doses in Japanese middle-aged male
8 subjects [35]. Thus, these results may be a potential causal basis for the result in the present
9 study. Patel et al. reported that C-reactive peptide and interleukin-6 levels rose with increasing
10 the habitual sleep duration [36]. These inflammatory mediators might also increase the risk of
11 hypertension in subjects with the habitual long sleep [37].

12 The limitations of the present study are as follows. First, the sleep duration obtained
13 by a self questionnaire might differ from the measured precious sleep duration. However,
14 Lockely et al reported that good agreement was examined between self-reported sleep
15 duration and those obtained through actigraphic monitoring [38]. Second, the present study
16 examined blood pressure values once in the health examination. The accuracy of blood
17 pressure values would likely have a little effect on the results of this analysis. Third, the
18 present study was a cross-sectional observation study. The possibility of unmeasured
19 confounding variables, such as sedentary life style and obstructive sleep apnea, could not be

1 excluded.

2 In conclusion, we demonstrated that habitual both short and long sleep duration were
3 significantly associated with high blood pressure values and the occurrence of hypertension in
4 Japanese male subjects. Finally, it is important to note that adequate sleep duration should be
5 one of the important strategies for hypertension occurrence.

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1 **Figure legend**

2 Figure 1

3 Systolic (A) and diastolic (B) blood pressure values according to sleep duration levels.

4 *: P for trend.

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1 **Conflict of interest**

2 The authors declare that they have no conflict of interest.

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Table 1.
Characteristics of the study subjects according to sleep duration levels

	Total (n=1,670)	Sleep duration				P value
		< 6 (n=201)	6- (n=628)	7- (n=638)	≥ 8 (n=203)	
Age (years)	50 ± 6	48 ± 5	49 ± 6	51 ± 6	51 ± 5	<0.001
Body mass index (kg/m ²)	23.8 ± 2.8	24.4 ± 3.1	23.8 ± 2.8	23.6 ± 2.6	23.8 ± 2.8	<0.05
Smoking (%)	52.2	54.7	52.1	51.7	51.5	0.90
Alcohol (%)	74.3	74.1	73.6	71.2	85.2	<0.01
Exercise (%)	28.2	20.9	31.7	27.2	27.9	<0.05
Dyslipidemia (%)	4.0	4.0	3.5	3.8	6.4	0.32
Diabetes mellitus (%)	3.2	1.5	3.8	3.3	2.5	0.38
Family history of hypertension (%)	15.6	21.4	16.9	14.6	9.4	<0.01
Total cholesterol (mg/dL)	208 ± 33	206 ± 36	208 ± 31	208 ± 34	208 ± 33	0.90
Triglyceride (mg/dL)	106 (76-150)	104 (76-150)	127 (87-173)	105 (73-146)	104 (75-152)	<0.05
HDL-cholesterol (mg/dL)	57 ± 14	56 ± 13	57 ± 15	56 ± 14	59 ± 15	<0.05
Glucose (mg/dL)	96 ± 20	94 ± 12	96 ± 19	97 ± 20	97 ± 24	0.13

Values are means ± SD, median (and interquartile range), and percentage.

HDL, high-density lipoprotein.

Table 2.

Multivariate predictors of variables for hypertension by multiple logistic regression analysis

	Odds ratio	95%CI	P value
Age (per one year increase)	1.04	1.01-1.08	<0.05
Body mass index (per one kg/m ² increase)	1.17	1.09-1.25	<0.001
Smoking	1.87	1.26-2.78	<0.01
Alcohol	2.23	1.31-3.77	<0.01
Family history of hypertension	1.78	1.13-2.79	<0.05
Glucose (per 10mg/dL increase)	1.15	1.07-1.23	<0.001

CI, confidence interval.

Table 3.
Odds ratio and 95% CI for hypertension according to sleep duration levels

	Sleep duration (hours)			
	< 6 (n=201)	6- (n=628)	7- (n=638)	8 ≤ (n=203)
Hypertension n (%)	27 (13.4)	36 (5.7)	48 (7.5)	28 (13.8)
Unadjusted				
Odds ratio	2.73	1.33	1.00	2.45
95% CI	1.60-4.64	0.84-2.10	–	1.45-4.15
P value	<0.001	0.23	–	<0.01
Model 1 ^a				
Odds ratio	2.49	1.28	1.00	2.40
95% CI	1.43-4.33	0.80-2.05	–	1.40-4.12
P value	<0.01	0.30	–	<0.01
Model 2 ^b				
Odds ratio	2.43	1.27	1.00	2.28
95% CI	1.40-4.20	0.81-1.99	–	1.31-3.95
P value	<0.01	0.30	–	<0.01

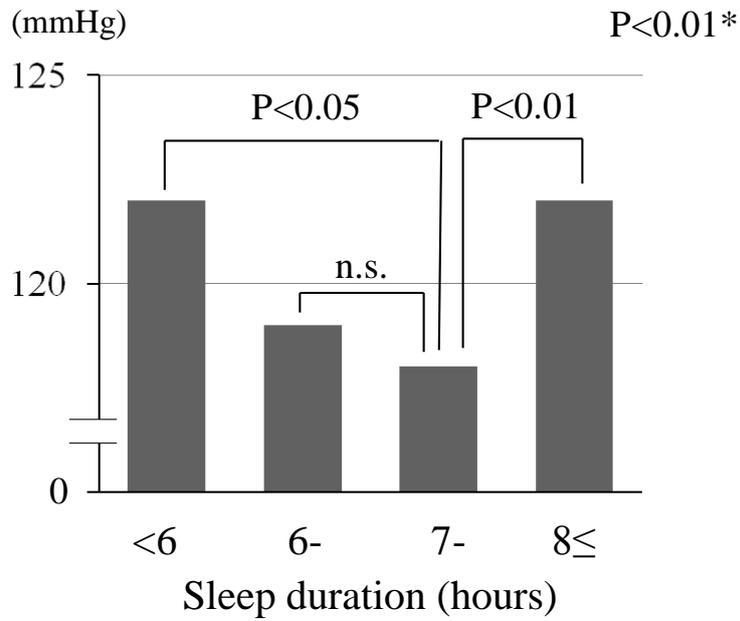
^a adjusted for age, body mass index, smoking, alcohol, exercise, and family history of hypertension.

^b Model 1 + adjusted for diabetes mellitus, dyslipidemia, total cholesterol, triglyceride, HDL-cholesterol, and glucose.

CI, confidence interval; HDL high-density lipoprotein.

Figure 1

(A) Systolic blood pressure



(B) Diastolic blood pressure

