J Atheroscler Thromb, 2018; 25: 186-198.
http://doi.org/10.5551/jat.40527

Original Article

Self-reported Sleep Duration and Subclinical Atherosclerosis in a General Population of Japanese Men

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***Aim*: There are few data regarding associations between sleep duration and subclinical atherosclerosis in Japan. The aim of this study was to evaluate associations of self-reported sleep duration with calcification in the coronary arteries (CAC) and carotid intima media thickness (IMT) in Japanese men.**
***Methods*: This was a cross-sectional survey of 1093 randomly selected men from Kusatsu City, Japan. Average sleep duration on weekdays was estimated through questionnaire; CAC by computed tomography; and carotid IMT by ultrasonography.**
***Results*: The prevalence of CAC was 50.0% for participants with sleep duration <5.5 h, 43.9% with 5.5−6.4 h, 50.0% with 6.5−7.4 h, 49.3% with 7.5−8.4 h, and 62.5% with ≥8.5 h. In univariate analysis, participants with sleep duration ≥8.5 h had significantly higher prevalence of CAC than those with 6.5−7.4 h (p=0.043). After adjustment for age and other risk factors, however, the association was not significant (p=0.776). The average IMT was 0.85 mm for participants with sleep duration <5.5 h, 0.83 mm with 5.5−6.4 h, 0.85 mm with 6.5−7.4 h, 0.88 mm with 7.5−8.4 h, and 0.90 mm with ≥8.5 h. None of the differences in IMT observed in crude or multivariable-adjusted analyses was significant (all p>0.1).**
***Conclusion*: Self-reported sleep duration was not associated with increased CAC or carotid IMT in a general population of Japanese men.**

Key words: Sleep duration, Coronary artery calcification, Carotid intima media thickness, Epidemiology, Cardiovascular risk

Introduction

Cardiovascular disease is one of the leading causes of premature death in Japan and worldwide[1-3]. Although recent decades have seen reductions in the age-adjusted incidence rates of coronary heart disease and stroke in Japan, the actual number of events are expected to increase because of an aging population[4, 5]. Strategies based on better knowledge of cardiovascular risk factors are needed to effectively prevent cardiovascular events in Japan.

Several observational studies have investigated the link between sleep duration and incidence of or mortality due to cardiovascular disease. Some have suggested a U-shaped association, i.e., increased risk in individuals with short sleep duration as well as those with long sleep duration[6-12]. Possible mechanisms underlying the U-shaped association include elevated blood pressure[13], impaired glucose tolerance[14], and increased inflammation[15] in those with insufficient

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Received: March 14, 2017
Accepted for publication: June 7, 2017

sleep and raised inflammatory markers in those with long sleep duration[16]. Observational studies have also reported an association between sleep duration and subclinical atherosclerosis of coronary or carotid arteries[17-24], which has been shown to be an important intermediate marker of cardiovascular disease[25, 26]. Some studies reported comparable associations between men and women (SUMSUNG) while others reported the relationship in male participants only (CARDIA IMT). However, current evidence is derived mostly from studies of Western populations; the extent to which these data are applicable to Asian populations, including the Japanese, is uncertain.

Aim

The aim of this study was to investigate associations of self-reported sleep duration with coronary arteries calcification (CAC) and carotid intima media thickness (IMT) among Japanese men.

Methods

Study Design and Participants

SESSA (Shiga Epidemiological Study of Subclinical Atherosclerosis) is an epidemiological study of men randomly selected from the general population of a Japanese city, details of which have previously been described[27]. In brief, from May 2006 to March 2008, 1094 community-dwelling men aged 40−79 years were selected based on an age-stratified random sample from the Basic Residents' Register of Kusatsu City and received comprehensive physical examinations. After exclusion of a participant without information on sleep duration, a total of 1093 men were included in the present cross-sectional analysis of CAC. After further exclusion of 33 men without information on carotid ultrasound, a total of 1060 men were included in the analysis of carotid IMT. The study was approved by the Institutional Review Board of Shiga University of Medical Science (No. 17−19, 17−83); all participants provided written informed consent.

Sleep Duration

At the baseline examination, information on average sleep duration on weekdays in the 30 days prior to enrolment was obtained using a questionnaire and confirmed by trained staff. Five participant groups defined by the self-reported sleep duration (<5.5, 5.5−6.4, 6.5−7.4, 7.5−8.4, and ≥8.5 h per day) were used in the present analysis.

Other Risk Factors

A self-administered questionnaire was used to obtain information on demography, smoking habits (never, past, and current), alcohol drinking (types of alcohol, frequency, quantity), physical activity, and use of medication(s) for hypertension, dyslipidemia, diabetes mellitus, and sleep disorder. Regular exercise was defined as sports or other forms of exertion at least once a week. Participants with depressive symptoms were defined as those who had the Center for Epidemiologic Studies Depression Scale (CES-D) score ≥16[28]. Weight and height were measured to calculate body mass index (BMI). Blood pressure was measured using an automated sphygmomanometer (BP-8800; Omron Colin, Tokyo, Japan) with the patient in a seated position after a 5-min rest; the mean of two measurements was used as the final value. Venous blood was drawn after a 12-h fast and centrifuged soon after coagulation; plasma glucose levels were measured from sodium fluoride-treated plasma using a hexokinase glucose-6-phosphate-dehydrogenase enzymatic assay; and hemoglobin A1c (HbA1c) levels were measured using a latex agglutination inhibition assay as per Japan Diabetes Society (JDS) methods and converted into National Glycohemoglobin Standardization Program (NGSP) values using the following formula: HbA1c (NGSP) (%) = 1.02 × HbA1c (JDS) (%) + 0.25[29]. The concentration of standard lipids, including total cholesterol, was measured using enzymatic methods; high-density lipoprotein (HDL) cholesterol was measured after heparin-calcium precipitation. Lipid measurements were standardized per Center for Disease Control and Prevention/Cholesterol Reference Method Laboratory Network (CDC/CRMLN) guidelines[30]. Participants with regular exercise were defined as those who regularly exercised ≥1 h/week.

Coronary Artery Calcification

Detailed procedures for CAC measurement have previously been described[31]. CAC was assessed by either electron-beam computed tomography (EBCT) (n=762, 69.7%) using a C-150 scanner (Imatron, South San Francisco, CA, USA), or 16-channel multidetector-row CT (MDCT) (n=331) using an Aquilion scanner (Toshiba, Tokyo, Japan). Images were obtained from the level of the aortic root through the heart in 3-mm slices with a scan time of 100 ms (EBCT) or 320 ms (MDCT). Images were acquired at 70% of the cardiac cycle using electrocardiogram triggering during a single breath-hold. Quantification of CAC was performed using a DICOM workstation and AccuImage software (AccuImage Diagnostics, South San Francisco, CA, USA). CAC was considered present if there were a minimum of three contiguous pixels (each with area 1 mm^2) with a density of ≥130 Hounsfield units (HU). A region of interest was

placed around each high-density lesion in the epicardial coronary arteries. The peak density and area of the individual coronary calcifications were measured and the CAC score calculated per the Agatston method[32]. All CT images were read by one physician, trained in CT reading at the Cardiovascular Institute of the University of Pittsburgh, who was blinded to participants' demographics. The protocol described above was adopted from a separate cohort study performed by our research group[33], which showed high inter-rater reliability (intraclass correlation coefficient 0.98)[34]. In the present analysis, the presence of CAC was defined as a CAC score ≥10[35], but sensitivity analyses were conducted using a definition of a CAC score >0.

Intimal Media Thickness of the Carotid Artery

The IMT measurement protocol has previously been described[36]. Using a 7.5 MHz probe (Xario-660A; Toshiba Medical Systems, Tokyo, Japan), detailed B-mode images of the right and left common carotid artery (CCA), common carotid bifurcation, and internal carotid artery (ICA) were obtained with a standardized method established by the Ultrasound Research Laboratory of the University of Pittsburgh[37]. Images from the following segments were digitized: near and far walls of the distal CCA (1 cm proximal to the carotid bulb); far wall of the bulb; and a 1-cm area of the far wall of the ICA (a total of four locations per side). The carotid IMT was traced with an automatic image-reading program (AMS; Chalmers University of Technology, Gothenburg, Sweden). In this study, the mean carotid IMT comprised the mean of all average readings across the eight locations from the CCA, bulb, and ICA[36].

Statistical Analysis

Each participant characteristic was described as a mean (standard deviation [SD]) or median (interquartile range [IQR]) for continuous variables and a percentage for categorical variables. Differences were evaluated using the Kruskal-Wallis or chi-squared test, as appropriate. Crude and multivariable-adjusted logistic regression models were used to estimate odds ratios (OR) and 95% confidence intervals (CI) for the presence of CAC. Participants with a sleep duration of 6.5−7.4 h were used as reference, in accordance with findings from previous studies[6-12]. Analysis of covariance (ANCOVA) was used to test for associations between sleep duration and mean carotid IMT. The multivariable-adjusted models included confounding factors of age, BMI, smoking status, regular exercise, alcohol consumption, and type of CT (model 1). We also conducted multivariable analysis with further adjustment for possible mediators (i.e., established cardiovascular risk factors that have been shown to be associated with sleep duration) including systolic blood pressure, total cholesterol, HDL cholesterol, HbA1c, and medication status[38, 39] (model 2). Difference in associations between subgroups (age group, BMI group, smoking status, alcohol consumption, working status, use of sleeping pills, or presence of depressive symptoms) were assessed by adding interaction terms to the model. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). Two-tailed p values <0.05 were considered significant.

Results

Participant characteristics are shown in **Table 1**. Participants with longer sleep durations were older, had lower BMIs, and higher systolic blood pressures than those with shorter sleep durations.

The number of participants with CAC was 538 (49.2%). The prevalence was 50.0%, 43.9%, 50.0%, 49.3%, and 62.5% for individuals with sleep durations of <5.5, 5.5−6.4, 6.5−7.4, 7.5−8.4, and ≥8.5 h, respectively (**Table 2**). In a crude analysis, individuals with sleep duration ≥8.5 h had significantly higher CAC prevalence (OR 1.67; 95% CI, 1.02−2.73; $p=0.043$) than those with 6.5−7.4 h. However, the difference was not statistically significant after adjustment for age (OR 1.01; 95% CI, 0.60−1.72; $p=0.961$) or for age and other cardiovascular risk factors (OR 1.08; 95% CI, 0.63−1.86; $p=0.776$). Findings were similar when subjects with stroke and/or myocardial infarction were excluded from the analysis (**Supplementary Table 1**) or when a CAC score of >0 was used as threshold (**Supplementary Table 2**). There were no clear differences in association between sleep duration and CAC when participants were further stratified by age group, BMI group, smoking status, alcohol consumption, employment status, use of sleeping pills, or presence of depressive symptoms (all $p>0.2$ for heterogeneity; **Supplementary Table 3**). There were also comparable associations between sleep duration and CAC between the 762 participants who were assessed using EBCT and the 331 assessed using MDCT ($p=0.289$ for heterogeneity).

The overall mean carotid IMT was 0.86 mm; mean values were 0.85 mm, 0.83 mm, 0.85 mm, 0.88 mm, and 0.90 mm for individuals with sleep durations of <5.5, 5.5−6.4, 6.5−7.4, 7.5−8.4, and ≥8.5 h, respectively (**Table 3**). There were no significant differences among the five groups (all $p>0.1$). There were also no important associations between sleep duration and mean carotid IMT after adjustment for age or after adjustment for age and other cardiovascular risk factors (all $p>0.1$). There were no clear differ-

Table 1. Characteristics of male participants enrolled in SESSA (2006–2008) stratified by sleep duration ($n=1093$)

		Sleep duration (hours)					
	overall	<5.5	5.5–6.4	6.5–7.4	7.5–8.4	≥8.5	
Participant characteristic	($n=1093$)	($n=118$)	($n=278$)	($n=394$)	($n=223$)	($n=80$)	$p^{\ddagger}$
Age (years)	64.1 (9.9)	62.3 (11.6)	61.5 (10.8)	63.7 (9.4)	66.7 (7.9)	69.9 (7.5)	<0.0001
Body mass index (kg/m^2)	23.6 (3.0)	23.7 (2.9)	24.0 (2.9)	23.7 (2.9)	23.4 (3.0)	22.3 (3.3)	0.002
Systolic blood pressure (mmHg)	136.5 (19.1)	137.0 (21.9)	135.5 (19.3)	135.8 (18.2)	136.6 (18.8)	142.2 (18.1)	0.054
Diastolic blood pressure (mmHg)	79.7 (10.9)	81.1 (12.6)	79.7 (11.3)	79.8 (10.5)	79.0 (10.5)	78.7 (10.3)	0.518
Total cholesterol (mg/dL)	208.1 (33.7)	207.8 (32.0)	209.2 (34.7)	207.3 (31.6)	210.1 (35.5)	203.7 (37.6)	0.781
LDL cholesterol (mg/dL)*	124.7 (31.6)	123.7 (31.9)	125.0 (31.5)	124.4 (29.4)	127.2 (33.9)	120.1 (34.9)	0.638
HDL cholesterol (mg/dL)	58.6 (16.9)	58.6 (17.0)	59.5 (17.2)	58.2 (16.4)	57.9 (17.0)	59.8 (18.0)	0.767
Triglyceride (mg/dL)	106 (77–150)	111.5 (78–157)	106 (77–149)	106 (77–153)	108 (75–147)	96.5 (76.5–142.5)	0.853
Blood glucose (mg/dL)	102.7 (21.2)	101.7 (21.6)	102.2 (19.3)	102.8 (21.4)	104.8 (24.0)	100.3 (17.0)	0.657
HbA1c (%)	5.7 (0.8)	5.6 (0.7)	5.6 (0.8)	5.7 (0.8)	5.8 (0.9)	5.6 (0.8)	0.040
Current smokers	(32.0)	(33.9)	(30.9)	(30.5)	(33.6)	(36.3)	0.331
Regular exercise	(43.5)	(34.8)	(41.0)	(42.4)	(53.8)	(41.3)	0.006
Alcohol consumption (g/day)	23.1 (27.3)	26.5 (33.3)	23.5 (27.3)	21.6 (25.5)	23.1 (25.9)	24.5 (29.3)	0.943
Medication for hypertension	(28.8)	(30.5)	(27.0)	(27.7)	(28.7)	(38.8)	0.317
Medication for dyslipidemia	(11.3)	(13.7)	(12.2)	(10.9)	(9.5)	(12.7)	0.773
Medication for diabetes	(10.3)	(11.0)	(7.9)	(11.2)	(12.6)	(6.3)	0.312
Medication for sleep	(5.5)	(7.6)	(7.6)	(5.3)	(3.1)	(2.5)	0.131
Depressive symptoms†	(7.9)	(11.0)	(13.3)	(4.8)	(7.6)	(0.0)	<0.0001

Values are expressed as mean (standard deviation), median (interquartile range) or (%). *Calculated by the formula of Friedwald *et al.* †Center for Epidemiologic Studies Depression Scale score ≥16 ‡*P* values were estimated using Kruskal-Willis test for continuous and χ^2 test for categorical variables. IQR: interquartile range; LDL: low-density lipoprotein; HbA1c: hemoglobin A1c; HDL: high-density lipoprotein; SD: standard deviation; SESSA: Shiga Epidemiological Study of Subclinical Atherosclerosis

ence in associations between sleep duration and carotid IMT among subgroups ($p>0.05$ for heterogeneity; **Supplementary Table 4**).

Discussion

To our knowledge, this is the first study to investigate possible associations between sleep duration and subclinical atherosclerosis in a general Japanese population. Although participants with sleep duration ≥8.5 h were more likely to have CAC, the association disappeared after adjustment for age. There were also no clear associations between sleep duration and carotid IMT.

Previous studies investigating these associations have shown inconsistent results[40] and are summarized in **Supplementary Tables 5** and **6**. The Kangbuk Samsung Health Study ($n=29\ 203$, South Korea) reported a U-shaped association[23], whereas the Study of Women's Health Across the Nation (SWAN; $n=512$, female only, United States [USA]) demonstrated no clear association[17], as did the Heart Strategies Concentrating on Risk Evaluation (HeartSCORE) study ($n=195$, USA)[22]. The Coronary Artery Risk Development in Young Adults (CARDIA) study ($n=495$, USA) found increased CAC prevalence among participants with short sleep duration measured by actigraphy, but no association when sleep duration was self-reported[18]. Heterogeneity between studies may be attributable to differences in study design, participant characteristics, method of assessment of sleep duration (self-reported or objective), or definitions of CAC used.

Several observational studies in Western populations have reported higher carotid IMT among participants with short or long sleep duration, or both. The Study of Health in Pomerania (SHIPS; $n=2437$, Germany) found a higher carotid IMT among participants with sleep duration of <5 h and >9 h[19]. The Buffalo Cardio-Metabolic Occupational Police Stress study ($n=257$, USA) also demonstrated a U-shaped association between carotid IMT and sleep duration measured by actigraphy, though this was not present when sleep duration was self-reported[20]. The CARDIA study found increased carotid IMT in male participants with longer objective sleep duration, but not in female participants[21]. Although much more limited evidence is available for Asian populations, Abe *et al.*

Table 2. Prevalence and odds ratio of coronary artery calcification* among male participants enrolled in SESSA (2006–2008) stratified by sleep duration (n=1093)

	Sleep duration (hours)				
	<5.5	5.5–6.4	6.5–7.4	7.5–8.4	≥8.5
	(n=118)	(n=278)	(n=394)	(n=223)	(n=80)
CAC, n (%)	59 (50.0)	122 (43.9)	197 (50.0)	110 (49.3)	50 (62.5)
Crude OR (95%CI)	1.00 (0.66–1.51)	0.78 (0.58–1.07)	1.00	0.97 (0.70–1.35)	1.67 (1.02–2.73)
Age-adjusted OR (95%CI)	1.12 (0.71–1.77)	0.90 (0.64–1.26)	1.00	0.75 (0.53–1.06)	1.01 (0.60–1.72)
Multivariable-adjusted OR (95%CI) (model 1)†	1.12 (0.71–1.79)	0.87 (0.62–1.23)	1.00	0.72 (0.51–1.03)	1.08 (0.63–1.86)
Multivariable-adjusted OR (95%CI) (model 2)‡	1.07 (0.67–1.71)	0.85 (0.60–1.21)	1.00	0.71 (0.49–1.03)	1.03 (0.59–1.79)

*Defined as coronary artery calcification score ≥10.
†Adjusted for age, body mass index, smoking status, regular exercise, alcohol consumption, and types of computed tomography scan
‡Adjusted for age, body mass index, smoking status, regular exercise, alcohol consumption, types of computed tomography scan, systolic blood pressure, total cholesterol, high density lipoprotein cholesterol, hemoglobin A1c, and medication status.
CAC: coronary artery calcification; CI: confidence interval; OR: odds ratio; SESSA: Shiga Epidemiological Study of Subclinical Atherosclerosis

(n=2498, Japan) found increased incidence of carotid artery atherosclerosis among people with long sleep duration (≥7 h)[24]. Given the equivocal results of our own study, further observation of Asian populations is needed to confirm the association between sleep duration and carotid IMT.

In contrast to the studies described above, associations between sleep duration and cardiovascular disease incidence and mortality are well described[6-12]. The variability may be due to differences in study design, as most studies of subclinical atherosclerosis are cross-sectional, while a most cohort studies for clinical outcomes are prospective. In fact, there has been a prospective study that demonstrated a positive association between sleep duration and progression of CAC[18]. Further prospective investigation of sleep duration and subclinical atherosclerosis would provide a better understanding of possible associations with cardiovascular disease.

This study had several limitations. First, the cross-sectional design meant that longitudinal associations between sleep duration and atherosclerosis could not be ascertained from the data collected. Although sleep duration can be a cause as well as a consequence of atherosclerosis, a very limited number of prospective studies have investigated CAC progression. We believe the findings from this cross-sectional study, which reported the link between sleep duration and CAC in Japan for the first time, still add some epidemiological evidence to current knowledge in this area. Second, the number of subjects is somewhat small in some groups defined by sleep duration. However, this study had 80% power to detect clinically significant differences in the outcomes (≥36% relative increase in CAC and ≥0.07 mm increase in carotid IMT). In addition, estimates of sleep duration obtained through self-reported questionnaires may be limited in their accuracy, which may have biased the results to null hypothesis, and all participants were men, which may limit the generalizability of findings to women or other ethnicities.

Conclusion

Self-reported sleep duration was not associated with calcification of the coronary arteries or increased carotid intima media thickness in a general population of Japanese men.

Acknowledgments

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Table 3. Mean IMT among male participants enrolled in SESSA (2006−2008), stratified by sleep duration (n = 1060)

	Sleep duration (hours)				
	< 5.5	5.5−6.4	6.5−7.4	7.5−8.4	≥ 8.5
	(n = 114)	(n = 264)	(n = 390)	(n = 213)	(n = 79)
Crude mean, mm (95%CI)	0.85 (0.82−0.89)	0.83 (0.81−0.85)	0.85 (0.83−0.87)	0.88 (0.86−0.91)	0.90 (0.85−0.94)
Difference (95%CI)	0.00 (−0.02−0.02)	−0.02 (−0.03− −0.02)	Reference	0.03 (0.02-0.04)	0.05 (0.02-0.07)
Age-adjusted mean, mm (95%CI)	0.87 (0.84−0.90)	0.86 (0.83−0.88)	0.86 (0.84−0.87)	0.86 (0.83−0.88)	0.84 (0.80−0.88)
Difference (95%CI)	0.02 (0.00−0.03)	0.00 (0.00−0.00)	Reference	0.00 (−0.01−0.01)	−0.01 (−0.04−0.01)
Multivariable-adjusted mean, mm (95%CI) (model 1) *	0.87 (0.84−0.90)	0.85 (0.83−0.87)	0.85 (0.84−0.87)	0.86 (0.83−0.88)	0.85 (0.81−0.89)
Difference (95%CI)	0.02 (0.00−0.03)	0.00 (−0.01−0.00)	Reference	0.00 (0.00−0.01)	0.00 (−0.02−0.02)
Multivariable-adjusted mean, mm (95%CI) (model 2) †	0.87 (0.84−0.90)	0.85 (0.83−0.87)	0.85 (0.84−0.87)	0.86 (0.83−0.88)	0.85 (0.81−0.89)
Difference (95%CI)	0.01 (0.00−0.03)	0.00 (−0.01−0.00)	Reference	0.00 (−0.01−0.01)	0.00 (−0.03−0.02)

* Adjusted for age, body mass index, smoking status, regular exercise, alcohol consumption, and types of computed tomography scan
† Adjusted for age, body mass index, smoking status, regular exercise, alcohol consumption, types of computed tomography scan, systolic blood pressure, total cholesterol, high density lipoprotein cholesterol, hemoglobin A1c, and medication status.
CI: confidence interval; IMT: intima media thickness; SESSA: Shiga Epidemiological Study of Subclinical Atherosclerosis

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Notice of Grant Support

This work was supported by the Ministry of Edu-

cation, Culture, Sports, Science and Technology, Japan (Grants-in-Aid for Scientific Research: (A) 13307016; (A) 17209023; (A) 21249043; (A) 23249036; (A) 25253046; (A) 15H02528; and (B) 15H04773), and by GlaxoSmithKlein (grant R01HL068200).

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The authors declare no potential conflicts of interest with regard to this manuscript.

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Supplementary Table 1. Prevalence and odds ratios of coronary artery calcification* among male participants without prior stroke or myocardial infarction in SESSA (2006−2008) stratified by sleep duration (n=1027)

	Sleep duration (hours)				
	<5.5	5.5−6.4	6.5−7.4	7.5−8.4	≥8.5
	(n=106)	(n=262)	(n=375)	(n=211)	(n=73)
CAC, n (%)	50 (47.2)	109 (41.6)	184 (49.1)	99 (46.9)	43 (58.9)
Crude OR (95%CI)	0.93 (0.60−1.43)	0.74 (0.54−1.02)	1.00	0.92 (0.66−1.29)	1.49 (0.90−2.47)
Age-adjusted OR (95%CI)	1.08 (0.67−1.74)	0.84 (0.59−1.18)	1.00	0.71 (0.50−1.02)	0.94 (0.55−1.61)
Multivariable-adjusted OR (95%CI) (model 1)†	1.09 (0.67−1.77)	0.81 (0.57−1.15)	1.00	0.68 (0.47−0.99)	1.00 (0.58−1.75)
Multivariable-adjusted OR (95%CI) (model 2)‡	1.03 (0.63−1.70)	0.83 (0.58−1.18)	1.00	0.66 (0.45−0.96)	0.94 (0.53−1.67)

*Defined as coronary artery calcification score ≥10.
†Adjusted for age, body mass index, smoking status, regular exercise, alcohol consumption, and types of computed tomography scan
‡Adjusted for age, body mass index, smoking status, regular exercise, alcohol consumption, types of computed tomography scan, systolic blood pressure, total cholesterol, high density lipoprotein cholesterol, hemoglobin A1c, and medication status
CAC: coronary artery calcification; CI: confidence interval; OR: odds ratio; SESSA: Shiga Epidemiological Study of Subclinical Atherosclerosis

Supplementary Table 2. Prevalence and odds ratios of coronary artery calcification (defined as coronary artery calcification score >0) among male participants in SESSA (2006−2008) stratified by sleep duration (n=1093)

	Sleep duration (hours)				
	<5.5	5.5−6.4	6.5−7.4	7.5−8.4	≥8.5
	(n=118)	(n=278)	(n=394)	(n=223)	(n=80)
CAC, n (%)	82 (69.5)	170 (61.2)	257 (65.2)	150 (67.3)	58 (72.5)
Crude OR (95%CI)	1.21 (0.78−1.89)	0.84 (0.61−1.15)	1.00	1.10 (0.77−1.55)	1.41 (0.83−2.39)
Age-adjusted OR (95%CI)	1.52 (0.93−2.50)	1.02 (0.72−1.45)	1.00	0.81 (0.56−1.18)	0.79 (0.45−1.40)
Multivariable-adjusted OR (95%CI) (model 1)*	1.72 (1.00−2.95)	1.03 (0.71−1.51)	1.00	0.78 (0.52−1.15)	0.99 (0.54−1.81)
Multivariable-adjusted OR (95%CI) (model 2)†	1.63 (0.94−2.80)	1.03 (0.70−1.52)	1.00	0.75 (0.50−1.11)	0.95 (0.52−1.76)

*Adjusted for age, body mass index, smoking status, regular exercise, alcohol consumption, and types of computed tomography scan
†Adjusted for age, body mass index, smoking status, regular exercise, alcohol consumption, types of computed tomography scan, systolic blood pressure, total cholesterol, high density lipoprotein cholesterol, hemoglobin A1c, and medication status
CAC: coronary artery calcification; CI: confidence interval; OR: odds ratio; SESSA: Shiga Epidemiological Study of Subclinical Atherosclerosis

Supplementary Table 3. Odds ratios of coronary artery calcification* among selected subgroups of men enrolled in SESSA (2006–2008) stratified by sleep duration (n=1093)

Subgroup	Sleep duration (hours)					p‡
	<5.5	5.5–6.4	6.5–7.4	7.5–8.4	≥8.5	
Age <65 years (n=549)	1.10 (0.57–2.10)	0.91 (0.57–1.47)	1.00	0.67 (0.38–1.17)	1.86 (0.70–4.98)	0.711
Age ≥65 years (n=544)	1.23 (0.63–2.41)	0.77 (0.47–1.26)	1.00	0.79 (0.49–1.26)	1.05 (0.56–1.97)	
BMI <25 Kg/m^2 (n=771)	1.02 (0.58–1.77)	0.80 (0.52–1.21)	1.00	0.81 (0.54–1.22)	1.00 (0.55–1.82)	0.596
BMI ≥25 Kg/m^2 (n=322)	1.21 (0.51–2.91)	1.01 (0.54–1.90)	1.00	0.54 (0.26–1.11)	0.87 (0.27–2.86)	
Smoker (n=350)	1.11 (0.49–2.55)	1.05 (0.56–1.96)	1.00	0.76 (0.40–1.45)	0.57 (0.23–1.43)	0.369
Non-smoker (n=743)	1.09 (0.62–1.92)	0.78 (0.51–1.18)	1.00	0.67 (0.43–1.04)	1.60 (0.79–3.25)	
Alcohol consumption <46 g/day (n=886)	0.98 (0.58–1.64)	0.88 (0.60–1.30)	1.00	0.65 (0.44–0.97)	0.85 (0.46–1.57)	0.297
Alcohol consumption ≥46 g/day (n=207)	2.46 (0.82–7.35)	0.94 (0.42–2.13)	1.00	1.24 (0.54–2.85)	2.88 (0.85–9.77)	
Working (n=722)	1.15 (0.65–2.01)	0.89 (0.58–1.37)	1.00	0.81 (0.51–1.28)	0.79 (0.37–1.68)	0.450
Retired (n=371)	1.20 (0.51–2.84)	0.87 (0.48–1.59)	1.00	0.61 (0.34–1.09)	1.60 (0.69–3.70)	
Did not use sleeping pills (n=1033)	1.11 (0.69–1.78)	0.89 (0.62–1.27)	1.00	0.72 (0.50–1.04)	1.14 (0.66–1.98)	0.902
Used sleeping pills (n=60)	1.69 (0.14–20.74)	0.62 (0.13–3.07)	1.00	0.35 (0.03–3.94)	0.06 (0.00–1.70)	
No depressive symptoms† (n=1007)	1.30 (0.73–2.31)	0.92 (0.61–1.40)	1.00	0.77 (0.51–1.19)	1.22 (0.64–2.32)	0.726
Depressive symptoms (n=86)	0.61 (0.06–6.17)	0.51 (0.08–3.11)	1.00	0.17 (0.02–1.68)	Not calculable	

Model adjusted for age, body mass index, smoking status, regular exercise, alcohol consumption, and types of computed tomography scan except for each stratified variable.
* Defined as coronary artery calcification score ≥10.
† Center for Epidemiologic Studies Depression Scale score ≥16
‡ Test for heterogeneity
CI: confidence interval; OR: odds ratio; SESSA: Shiga Epidemiological Study of Subclinical Atherosclerosis

Supplementary Table 4. Mean IMT in selected subgroups of men enrolled SESSA (2006−2008) stratified by sleep duration (n=1060)

Subgroup	Sleep duration (hours)					p †
	<5.5	5.5−6.4	6.5−7.4	7.5−8.4	≥8.5	
Age <65 years (n=531)	0.79 (0.75−0.82)	0.76 (0.74−0.79)	0.78 (0.76−0.80)	0.78 (0.75−0.81)	0.81 (0.75−0.88)	0.612
Age ≥65 years (n=529)	0.96 (0.90−1.02)	0.93 (0.89−0.97)	0.92 (0.89−0.95)	0.94 (0.90−0.97)	0.94 (0.88−0.99)	
BMI <25 Kg/m^2 (n=752)	0.85 (0.81−0.89)	0.84 (0.82−0.87)	0.84 (0.82−0.86)	0.84 (0.82−0.87)	0.84 (0.80−0.89)	0.776
BMI ≥25 Kg/m^2 (n=308)	0.90 (0.85−0.96)	0.88 (0.85−0.91)	0.88 (0.85−0.91)	0.89 (0.85−0.94)	0.83 (0.75−0.91)	
Smoker (n=336)	0.86 (0.80−0.91)	0.83 (0.80−0.87)	0.82 (0.79−0.85)	0.82 (0.78−0.86)	0.83 (0.76−0.89)	0.941
Non-smoker (n=724)	0.88 (0.84−0.92)	0.86 (0.84−0.89)	0.87 (0.85−0.89)	0.87 (0.84−0.90)	0.86 (0.81−0.91)	
Alcohol consumption <46 g/day (n=862)	0.88 (0.85−0.92)	0.86 (0.84−0.89)	0.86 (0.84−0.88)	0.86 (0.83−0.89)	0.83 (0.79−0.87)	0.060
Alcohol consumption ≥46 g/day (n=198)	0.83 (0.75−0.91)	0.80 (0.75−0.86)	0.85 (0.80−0.90)	0.84 (0.78−0.89)	0.90 (0.81−0.99)	
Working (n=697)	0.84 (0.81−0.88)	0.81 (0.79−0.84)	0.83 (0.81−0.85)	0.82 (0.79−0.85)	0.85 (0.80−0.90)	0.341
Retired (n=363)	0.91 (0.84−0.98)	0.93 (0.89−0.97)	0.91 (0.87−0.94)	0.93 (0.89−0.97)	0.88 (0.82−0.94)	
Did not use sleeping pills (n=1001)	0.87 (0.84−0.91)	0.85 (0.83−0.87)	0.85 (0.83−0.87)	0.85 (0.83−0.88)	0.85 (0.81−0.89)	0.637
Used sleeping pills (n=59)	0.86 (0.73−0.99)	0.88 (0.80−0.97)	0.93 (0.84−1.02)	0.91 (0.75−1.07)	0.76 (0.49−1.04)	
No depressive symptoms* (n=977)	0.88 (0.85−0.92)	0.86 (0.83−0.88)	0.86 (0.84−0.88)	0.86 (0.83−0.88)	0.86 (0.82−0.89)	0.601
Depressive symptoms* (n=83)	0.78 (0.68−0.88)	0.80 (0.73−0.86)	0.81 (0.73−0.90)	0.83 (0.74−0.93)	Not calculable	

Model adjusted for age, body mass index, smoking status, regular exercise, alcohol consumption, and types of computed tomography scan except for each stratified variable.
*Center for Epidemiologic Studies Depression Scale score ≥16
†Test for heterogeneity
CI: confidence interval; IMT: intima media thickness; SESSA: Shiga Epidemiological Study of Subclinical Atherosclerosi

Supplementary Table 5. Summary of the previous studies examining the association between sleep duration and CAC

First Author, Publication Year	Country	Study Design	Participants	Age	Sleep Measurement	Results
Kim *et al.*[23], 2015 (Samsun)	Korea	Cross-sectional	29,203 men and women	Mean 42	Self-Report (PSQI)	U-shaped association
Matthews *et al.*[17], 2013 (SWAN)	USA	Cross-sectional	512 women	Mean 50	Self-Report (PSQI)	No clear association
Matthews *et al.*[22], 2011 (HeartSCORE)	USA	Cross-sectional	195 men and women	Mean 60	Self-Report (PSQI) Actigraphy, Polysomnography	No clear association
King *et al.*[18], 2008 (CARDIA)	USA	Longitudinal (5 years)	204 men 291 women	Mean 40	Self-Report (PSQI) Actigraphy	Increased CAC prevalence among participants with short sleep duration measured by actigraphy, but no clear association for self-reported sleep duration

CAC: coronary artery calcification; PSQI: Pittsburgh Sleep Quality Index

Supplementary Table 6. Summary of the previous studies examining the association between sleep duration and carotid IMT

First Author, Publication Year	Country	Study Design	Particitants	Age	Sleep Measurement	Results
Wolff *et al.*[19], 2008 (SHIP)	Germany	Cross-sectional	2,437 men and women	45-81	Self-Report	Increased carotid IMT among participants with sleep duration of <5 hours and >9 hours
Ma *et al.*[20], 2013	USA	Cross-sectional	190 men 67 women	Mean 42	Self-Report (PSQI) Actigraphy	U-shaped association for sleep duration measured by actigraphy, but not for self-reported sleep duration
Sands *et al.*[21], 2012 (CARDIA)	USA	Cross-sectional	260 men 357 women	37-52	Actigraphy	Increased carotid IMT in male participants with longer objective sleep duration, but not in female participants
Abe *et al.*[24], 2011	Japan	Cross-sectional	1064 men 1150 women	40-85	Self-Report	Long sleep duration (≥ 7 h) correlated with higher incidence of carotid artery atherosclerosis

IMT: intima media thickness; PSQI: Pittsburgh Sleep Quality Index