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Prospective observation on the association of snoring with subclinical changes in carotid atherosclerosis over four years

Jinyoung Kim^{a,*}, Allan Pack^{b,c}, Greg Maislin^{b,c}, Seung Ku Lee^d, Seong Hwan Kim^e, and Chol Shin^{d,f}

Jinyoung Kim: jinki@nursing.upenn.edu

^aUniversity of Pennsylvania School of Nursing, Philadelphia, PA, USA

^bCenter for Sleep and Circadian Neurobiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

^cDivision of Sleep Medicine/Department of Medicine, University of Pennsylvania, PA, USA

^dInstitute of Human Genomic Study, Korea University Ansan Hospital, Ansan, South Korea

^eDivision of Cardiology, Department of Internal Medicine, Korea University Ansan Hospital, Ansan, South Korea

^fDivision of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Korea University Ansan Hospital, Ansan, South Korea

Abstract

Objective—Although there is a growing interest in the independent effect of snoring on carotid atherosclerosis, few studies have observed the relationship between snoring and change in carotid atherosclerosis prospectively. Therefore, the present study aimed to examine prospectively the association of snoring with subclinical changes in carotid atherosclerosis during a four-year period.

Methods—Participants in an ongoing prospective cohort study ($n = 3129$) were enrolled. Subclinical changes in carotid atherosclerosis were assessed using: (i) mean and maximum intima-media thickness (IMT) on both common carotid arteries; (ii) prevalence of elevated IMT (maximum IMT > 1.0 mm); and (iii) presence of plaque. Measurement was performed using B-mode ultrasonogram at baseline and after two and four years. Subjects were classified into three groups, based on self-reported snoring frequency at baseline: habitual, occasional, and non-snorer.

Results—After adjustment for conventional cardiovascular risk factors and self-reported witnessed sleep apnea, the present study found significant cross-sectional differences in mean and

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*Corresponding author. Address: University of Pennsylvania School of Nursing, 418 Curie Blvd, Claire M. Fagin Hall #310B, Philadelphia, PA 19104, USA. Tel.: +1 215-746-4448; fax: +1 215-898-3056.

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maximum IMT between female snorers and non-snorers at baseline only. The changes in IMTs and presence of plaque over four years, however, did not differ by three groups, with different snoring frequency in both genders.

Conclusions—Snoring did not accelerate subclinical change in carotid atherosclerosis during a four-year follow-up, although baseline difference in IMT between snorers and non-snorers was significant in women, independent of witnessed sleep apnea. Additional longer-term studies with objective assessment of snoring are needed.

Keywords

Atherosclerosis; Cardiovascular disease; Carotid atherosclerosis; Prospective study; Sleep-related breathing disorders; Snoring

1. Introduction

There is a growing interest in the independent effect of snoring on the development of cardiovascular disease and stroke [1–5]. Epidemiologic studies indicate that self-reported snoring is associated with cardiovascular diseases, such as myocardial infarction [2], stroke [3,4], and coronary artery disease [5], independent of known confounding factors including age, obesity, high blood pressure, and drinking or smoking habits. However, in these earlier studies there was no assessment of the presence or severity of obstructive sleep apnea (OSA). OSA is characterized by repeated apnea/hypopnea events during sleep, known to lead to oxidative stress [6] and sympathetic activation [7]. Snoring is a major feature of this disorder. Thus, the association between snoring and cardiovascular outcomes could be due to the presence of OSA in a proportion of snoring subjects. However, recent studies have begun to address whether the association is independent of OSA [8,9].

Recent in-vivo and in-vitro studies have raised the hypothesis that vibration induced by snoring might have an impact on the atherosclerotic process in adjacent arteries such as the carotid arteries [10–12]. Animal studies provide evidence of a likely mechanism [12,13]. Induced vibration in rat tails led to intimal thickening in blood vessels.¹³ A study using a rabbit model identified that snoring-induced vibration energy was transmitted to carotid arteries [12], which might, therefore, produce changes in these blood vessels. In humans, Lee and colleagues found a result supporting this hypothesis [14]. They used a cross-sectional design and showed that heavy snoring (>50% night snoring) without severe OSA significantly increased the risk for carotid atherosclerosis, but not femoral atherosclerosis [14]. However, two epidemiological studies reported conflicting results, showing an association between self-reported snoring and carotid atherosclerosis [15,16]. Thus, there is still insufficient evidence to conclude that snoring itself does lead to atherosclerosis of the carotid vessels. An important next step in evaluating the role of snoring is to perform a prospective study assessing whether snoring is a risk factor for future development of carotid atherosclerosis, independent of OSA.

The purpose of the present study was to examine prospectively the association of snoring with subclinical changes in carotid atherosclerosis, measured by change in intima-media thickness (IMT) on carotid arteries and the presence of plaques, after adjustment for

conventional cardiovascular risk factors and witnessed sleep apnea. This was done using a four-year follow-up study with participants in an ongoing large cohort.

2. Methods

2.1. Subjects

Subjects in the present study are participants in the Korean Genome and Epidemiology Study (KoGES), which is an ongoing cohort study of Korean middle-aged and older adults [17,18]. The KoGES was begun in 2001 to investigate the prevalence and incidence of chronic diseases in Korean adults and their genetic, environmental, and lifestyle determinants. Randomly selected 5020 residents in Ansan city, which is located in the southern part of the Seoul National Capital Area of Korea, underwent a comprehensive health examination including interviews between 2001 and 2002, and have since been followed up biennially. The study reported here was approved by an institutional review committee in Korea University Ansan Hospital, and written consent was obtained from all participants.

For this study, we included 1834 men and 1653 women who underwent an ultrasonogram on the third examination of the KoGES between 2005 and 2006, when measurement of IMT on carotid arteries began. Subjects who reported physician-diagnosed cardio/cerebrovascular disease, such as stroke, myocardial infarction, heart failure, etc., were excluded ($n = 60$). Individuals who were being treated with medication on diabetes mellitus, known to be closely associated with elevated IMT [19], and taking drugs to treat dyslipidemia, known to decrease IMT [20], were also excluded from the analysis ($n = 247$). There were subjects who did not supply questionnaire data about snoring ($n = 51$). Although the sample size was small, subjects with missing values were slightly but significantly more obese than subjects who did respond to the snoring question (revised Supplementary Table 1). They were also excluded. After making these exclusions, 1624 men and 1505 women entered the analysis. Of the participants at baseline, 85% (1361 men and 1305 women) and 81% (1290 men and 1260 women) were followed up after two (year 2) and four years (year 4), respectively.

2.2. Subclinical carotid atherosclerosis

Carotid atherosclerosis in the present study was assessed as follows: (i) mean and maximum IMT on both common carotid arteries; (ii) prevalence of elevated IMT (maximum IMT ≥ 1.0 mm); and (iii) presence of plaque. Measurement of carotid atherosclerosis was performed using B-mode ultrasonogram (Titan™, Sonosite, Tokyo, Japan) with a 7.5 MHz linear array transducer. For IMT measurements, images of distal common carotid arteries were obtained at far and near walls ~ 1 cm proximal to the bifurcation on both sides. The mean values of IMT were calculated by averaging the mean IMTs obtained from the four segments on the common carotid arteries. The maximum value of IMT was similarly obtained from the four individual maximum IMTs. An elevated IMT was said to be present when maximum IMT was ≥ 1.0 mm, based on previous investigations [21,22]. To assess the presence of plaque, carotid arteries including common, internal, and external arteries and at the bifurcation area were scanned on both sides. Plaque was defined as a distinct area identified with either a focal area of hyperechogenicity or a focal protrusion into the lumen of the vessel ($>25\%$ of

the vessel diameter). For this study, IMTs and plaques measured at baseline, year 2, and year 4 were used to examine the subclinical change in carotid atherosclerosis over time. Two sonographers were trained with an authorized protocol [23] and certified. To evaluate agreement in IMT measurements, sonographers examined scans from 20 volunteers. The intra-class correlation coefficients of mean and maximum IMTs were >0.90 for both far and near walls (range, 0.910–0.941).

2.3. Assessment of snoring, witnessed sleep apnea, and other covariates

Study participants completed interviewer-administered questionnaires including questions on age, current smoking, alcohol intake (at least once a month), regular exercise (at least three days/week), current medication, and snoring. Snoring frequency was assessed using a five-point scale: never, infrequently, sometimes (one to three nights/week), often (four or five nights/week), and almost every night. Individuals were grouped into habitual snorers (snoring at least four nights/week), occasional snorers (snoring less than four nights/week or infrequently), and non-snorers. To examine the test-retest reliability of the snoring questionnaire, a subset of 200 participants in the KoGES were queried about their snoring habits two weeks after the first test. Agreement between the responses was good with a κ -statistic value of 0.73. Snorers were also asked if they had ever heard that they had a witnessed sleep apnea (yes/no). The self-reported answers on snoring and witnessed sleep apnea were confirmed by a bed partner or a family member in a subset of participants. Body mass index (BMI) was calculated as weight (kg)/height (m^2). Measurements of blood pressure (BP) were repeated twice using mercury sphygmomanometers after at least a 5 min period of rest. The average of measurements was calculated for systolic and diastolic BP. To assay levels of lipids and glucose, blood was drawn from a vein in the morning after an 8 h fasting period. Lipid profiles were measured enzymatically by the Advia 1650 system (Bayer, Leverkusen, Germany) at the certified commercial laboratory (Seoul Clinical Laboratories, Inc., Seoul, Korea).

2.3. Statistical methods

Across the snoring groups, baseline characteristics and the prevalence of elevated IMT and plaque were compared by analysis of variance and χ^2 -tests. After adjusting for covariates including age, BMI, BP, fasting glucose, cholesterol levels (total cholesterol, high-density lipoprotein (HDL)-cholesterol), triglycerides, lifestyle factors (drinking alcohol, smoking, and exercise), and witnessed sleep apnea, we compared least-square means of mean and maximum IMT at baseline, and after two and four years using general linear models. Further, we applied mixed-effects modeling to assess the effect of the covariation between IMTs that were observed at different time-points on the same subjects as well as the fixed effect of snoring and time on the change in IMT. Multivariate mixed-effects logistic regression analysis was used to estimate covariate-adjusted odds ratios (ORs) of the prevalence of elevated IMT and plaque, after adjustment for witnessed sleep apnea and other covariates. Since our data showed a gender difference in the mean IMTs and the prevalence of plaque and the association between snoring and IMT, we applied gender-specific analyses to the present study. Statistical analyses were performed with SAS 9.2 software (SAS Institute Inc., Cary, NC, USA).

3. Results

The sample was divided into three groups – habitual, occasional, and non-snorers. Table 1 compares characteristics and mean and maximum IMTs between the three groups with different snoring frequencies as assessed at baseline by gender. Habitual snorers were significantly older than the other two groups in women, whereas in men occasional snorers were the youngest of the three snoring groups. The age differences were, however, small. Even after we excluded subjects with known cardiovascular disease or stroke and those on medications for diabetes and hyperlipidemia in the present study, both habitual and occasional snorers had significantly higher cardiovascular risk factors, namely BMI, BP, triglycerides, HDL-cholesterol (lower values), and glucose, compared with non-snorers, in both genders. Non-snorers tended to drink less alcohol and exercise more than subjects who reported snoring in men, although not in women. Baseline mean and maximum IMTs were also compared between the three groups with different frequencies of snoring (Table 1). In men, there were no significant differences in mean and maximum IMTs at baseline between groups who snored and those who did not. In women, after adjusting for conventional cardiovascular risk factors and witnessed sleep apnea, both mean and maximum IMTs were significantly higher in habitual snorers and occasional snorers, compared with non-snorers by pairwise comparisons (Table 1).

Changes over the four-year follow-up period were then examined. Figure 1 shows the change in adjusted mean and maximum IMTs over four years in three groups with different snoring frequencies in men (A) and women (B). *P*-values, derived from mixed-effects linear regression analyses, indicate that both mean and maximum IMTs increased with time ($P_{\text{time}} < 0.0001$) and snorers showed elevated IMT across time in women ($P_{\text{snoring}} = 0.017$ in mean IMT and 0.002 in maximum IMT). In time-point-specific pairwise comparisons, both mean and maximum IMTs in habitual and occasional snorers were significantly higher than those in non-snorers at year 4 as well as at baseline (Fig. 1B); the statistical significance was not present at year 2 for either measure. The changing patterns of both mean and maximum IMT over four years, however, were not different between the three snoring groups in women ($P_{\text{interaction}} = 0.64$ in mean IMT and 0.67 in maximum IMT). In women, surprisingly, maximum IMT seemed to decrease from baseline to year 2 and then increase again at year 4, even though the changes were not statistically significant. In men, it was also shown that mean and maximum IMTs significantly increased during four years ($P_{\text{time}} < .0001$), but there was no significant difference in IMT both across baseline and over time between the groups with different snoring frequency (Fig. 1A). A complementary analysis comparing OR of the top quartile of the IMTs versus the lowest quartile (Supplementary Table 2) was also performed. In the further analysis, habitual snoring in women also showed a 1.8- and 2.8-fold excess risk for top quartile of maximum IMT at baseline and year 2, respectively, compared with the lowest group.

The presence of elevated IMT (maximum IMT ≥ 1.0 mm) was then examined. Table 2 compares the prevalence of elevated IMT between the three snoring groups at each time-point and estimated ORs for elevated IMT after adjustment for covariates. In women, the prevalence of elevated IMT was significantly higher in habitual snorers than occasional snorers and non-snorers at all three time points, although the difference tended to attenuate

over time (Table 2). After adjustment for covariates and witnessed sleep apnea, the estimated ORs also indicate that both habitual and occasional snoring in women were associated with 80% and 60% increased risk for elevated IMT, respectively, at baseline only. At years 2 and 4, the ORs for elevated IMT in habitual snorers and occasional snorers declined. In men, there was no statistically significant difference between groups in the prevalence of elevated IMT.

Figure 2 represents the presence of plaque between snoring groups at each time-point in men (A) and women (B). Multivariate mixed-effects logistic regression showed that the prevalence of plaque significantly increases with time in both men ($P_{\text{time}} < 0.0001$) and women ($P_{\text{time}} = 0.001$). However, the independent effect of snoring on the prevalence of plaque across time ($P_{\text{snoring}} = 0.07$ in men and 0.26 in women) and changes over four years ($P_{\text{interaction}} = 0.07$ in men and 0.85 in women) was not significant in both genders (Fig. 2).

4. Discussion

The present four-year follow-up study found cross-sectional difference in carotid IMT between female snorers and non-snorers at baseline, but not in men. The ORs of the prevalence of elevated IMT (maximum IMT > 1.0 mm) showed that both habitual and occasional snoring in women were associated with 80% and 60% increased risk for the elevated IMT, respectively, at baseline only. The complementary analysis using quartiles also suggests that cross-sectional association of snoring with elevated IMT occurs only in early time-points in women. The increase of IMT and development of plaque over four years, however, did not differ by snoring groups in both genders.

The most definitive study on the relationship between snoring and carotid atherosclerosis in human subjects was reported by Lee and colleagues in 2008 [14]. They showed, using a cross-sectional in-laboratory study in adult volunteers, that heavy snoring without severe OSA was independently associated with the presence of plaque on carotid arteries (OR, 10.5; 95% CI, 2.1–51.8), but not femoral arteries, suggesting a local effect of snoring on adjacent vessels [14]. An epidemiological study with a cross-sectional design also found that prevalence of plaque in carotid bifurcation was significantly higher in self-reported snorers, compared with non-snorers. [15] The plausible effect of snoring on carotid atherosclerosis has been supported by a recent hypothesis stating that repeated vibrations induced by snoring might increase local inflammatory responses [10,11] and might also cause vessel damage in carotid arteries by transmission of vibration energy [12,13]. In a rat model, vibrations applied to the tail increased intimal thickening [13]. Amatoury and colleagues' animal study using a rabbit model also found that snoring-induced vibration energy was transmitted, increasing around the carotid artery wall and in the carotid sinus, which might result in progression of carotid atherosclerosis [12]. However, there is still a lack of evidence in human subjects, and it is controversial whether snoring itself does lead to carotid atherosclerosis, independent of OSA. Recently, a cross-sectional population-based study reported that there was no association between frequency of self-reported snoring and carotid stenosis [16].

To the best of our knowledge, the present study is the first prospective cohort study evaluating the association between snoring and carotid atherosclerosis. We found that the difference in carotid IMT among three different snoring groups was significant at baseline only, and only in women, not in men. Although the independent contribution of snoring in explaining IMT variance seems very small ($R^2 < 1\%$), the difference of 0.02 mm in mean and maximum IMTs between habitual snorers and non-snorers may have clinical significance as well as statistical significance. From the prospective Carotid Atherosclerosis Progression Study, Lorenz and colleagues have reported that hazard ratios for the incidence of stroke, myocardial infarction, and death are increased by 9–13% per 0.1 mm increment of carotid IMT [24]. However, the changing patterns of carotid IMTs over a period of four years in the present study did not differ in either gender in groups that snored and groups that did not.

That we found no association with snoring frequency in men either at baseline or with follow-up and in women only at baseline but not follow-up would argue against snoring having an independent effect on carotid atherosclerosis. It is conceivable, however, that the effect of snoring on the carotid blood vessels appears at a relatively early age; in older adults other factors, such as obesity and hypertension, affect the presence of carotid atherosclerosis more than does snoring. Unfavorable cardiovascular risk factors including high serum cholesterol level, high BP, and smoking are closely associated with increased carotid IMT [25,26]. Those factors, which become worse with increasing age, could dilute the effect of snoring on carotid IMT over time. These covariates were controlled for in our analyses. The follow-up period of four years might also be too short to reveal the effect of snoring on carotid atherosclerosis. Previous studies, which reported that self-reported snoring might contribute to cardio/cerebrovascular diseases, tended to follow up their subjects for 10 or more years [27,28]. Carotid atherosclerosis is known to be a slowly progressive disease [29]. Because little is known about the independent effect of snoring on carotid atherosclerosis, longer prospective studies are needed. In addition, there might be ethnic differences. The study by Lee et al. was in Caucasians [14], whereas the study reported here is in Asians. In some previous studies ethnic differences in the prevalence and correlates of carotid atherosclerosis were observed [30–31]. Woodard et al. demonstrated that the presence of carotid plaques was associated with aortic and coronary artery calcification in White women, but not African-American women [31]. Another study compared the relationship between coronary calcium and carotid atherosclerosis in four different ethnic groups of White, Black, Hispanic, and Chinese [32]. They reported that coronary calcium is less strongly associated with carotid atherosclerosis in Blacks than in other ethnic groups, suggesting further investigations to determine whether coronary calcium carries the same risk information in different ethnic groups [32]. The ethnic difference in the impact of individual risk factors on carotid atherosclerosis has not been widely investigated, and studies including Asians are scarce. Future prospective observations on the effect of snoring on carotid atherosclerosis need to be performed in different ethnic groups.

In the present study, the significant difference in IMT at baseline appeared in women only, not in men. The basis for this gender difference is unknown but could conceivably result from different patterns of fat distribution in neck, affecting transmission of vibration to the

carotid arteries. Although gender differences in association with snoring and carotid atherosclerosis have not yet been fully examined, there are some studies showing an independent association between carotid atherosclerosis and cardiovascular risk factors such as metabolic syndrome in women only [33,34]. Other studies also found that decreases in HDL and increase in triglyceride levels have greater impact on coronary heart disease risk in women, compared with men [35,36]. They suggested that gender differences could be partly attributed to the confounding effect of unhealthy profiles on atherosclerosis in men. It has been known that conventional cardiovascular risk factors, such as elevated cholesterol, hypertension, and smoking, increase more rapidly in men than in women from their thirties or forties [37]. Similarly, in the present study, even male participants who did not snore were more likely to have elevated BP, glucose, and cholesterol than female snorers and female non-snorers (Table 1). Figure 2 shows that the incidence rate of plaque throughout four years in non-snorers was almost identical to the rate in habitual snorers. Those elevated cardiovascular risk factors may attenuate the relationship of snoring with subclinical atherosclerosis.

In addition to the short-term follow-up period, the present study has other limitations. First, snoring was assessed by questionnaire only. Although self-reported snoring has been used widely in large epidemiological studies [3–5], frequency of snoring might be underestimated. However, misclassification in the existence of snoring is an unlikely differential in the present study. To compensate for this limitation, we examined test–retest reliability on the snoring question and the result demonstrated high reproducibility ($\kappa = 0.73$). For further investigations on whether the vibration induced by snoring can accelerate carotid atherosclerosis, however, objective snoring measurements, such as loudness or frequency of snoring sound, using microphones will be needed. The study by Lee et al. that showed a strong association with carotid atherosclerosis and snoring used objective quantitative measures of the amount of snoring and OSA [14]. It is known that OSA is associated with increased carotid IMT [38,39] and a higher risk of strokes [40]. Although the present study cannot exclude that individuals who snored had OSA, we adjusted for repeated episodes of witnessed sleep apnea in all multivariate analyses. Finally, the present study measured IMT in common carotid arteries only, not at bifurcation or internal and external arteries. Previously some studies have reported that plaques at the bifurcation area of the carotid arteries are more likely to be associated with snoring or other cardiovascular disease rather than plaque in common carotid arteries [15,41]. In other studies plaques in other segments such as common or internal carotid arteries have been revealed to have predictive values for stroke [24,40,41].

In conclusion, the presence of self-reported snoring did not accelerate subclinical change in carotid atherosclerosis during a four-year follow-up, although baseline differences in IMT between female snorers and non-snorers were significant. Additional longer-term studies with objective assessment of snoring and the presence of sleep-disordered breathing are needed to indicate whether snoring does contribute to atherosclerosis of the carotid vessels. Given the high prevalence of snoring, this is an important public health question.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Significant difference in carotid intima-media thickness between female snorers and nonsnorers at baseline.
- No difference in the changes in intima-media thickness over 4 years by snoring groups.
- No cross-sectional and prospective difference in the presence of plaque between snorers and nonsnorers in both genders.

Fig. 1.

Change in mean and maximum carotid intima-media thickness (IMT) over four years among groups with different frequency of snoring in men (A) and women (B). P -values were derived from multivariate mixed-effect linear regression models. P_{time} and P_{snoring} indicate the effect of time on change in IMT over four years and the effect of snoring group on IMT across time, respectively; $P_{\text{interaction}}$ indicates significance of whether the change in IMT over time differs by snoring groups. *Adjusted for age, body mass index, blood pressure, triglyceride, medication for hypertension, current smoking (men only), and witnessed sleep apnea. **IMT in habitual and occasional snorers is significantly ($P < 0.05$) different from that of non-snorers at the particular time-point by year-specific pairwise comparisons. [Fig. 1. (A), right-hand graph, y-axis label: should be 'Adjusted']

(A)

(B)

Fig. 2.

Change in the prevalence of plaque between snoring groups in men (A) and women (B). *P*-values were derived from multivariate mixed-effect linear regression models. *P*_{time} and *P*_{snoring} indicate the effect of time on change in intima-media thickness (IMT) over four years and the effect of snoring group on IMT across time, respectively, and *P*_{interaction} indicates significance of whether the change in IMT over time differs by snoring groups.

Table 1

Comparison of general characteristics and intima-media thickness of carotid arteries at baseline between groups with different frequency of snoring.

	Men			P-value ^a	Women			P-value
	Habitual snorers (n = 443)	Occasional snorers (n = 835)	Non-snorers (n = 346)		Habitual snorers (n = 282)	Occasional snorers (n = 759)	Non-snorers (n = 464)	
Age (years)	52.3 ± 7.2 ^b	51.4 ± 6.7	52.5 ± 7.6 ^b	0.02	54.6 ± 7.8 ^{b,c}	52.1 ± 7.1 ^c	51.1 ± 7.4	<0.0001
Body mass index (kg/m ²)	25.1 ± 2.6 ^{b,c}	24.4 ± 2.6 ^c	23.6 ± 2.4	<0.0001	25.7 ± 3.2 ^{b,c}	24.3 ± 2.8 ^c	23.6 ± 2.6	<0.0001
Systolic blood pressure (mmHg)	116.5 ± 14.4 ^b	113.9 ± 13.4 ^c	113.8 ± 14.2	0.003	111.4 ± 14.4 ^c	109.6 ± 15.7 ^c	106.2 ± 13.7	<0.0001
Diastolic blood pressure (mmHg)	79.5 ± 10.3	77.5 ± 9.7 ^c	77.0 ± 9.9	0.0004	73.4 ± 9.4 ^c	72.3 ± 9.8 ^c	70.4 ± 9.1	<0.0001
On hypertension medication (%)	17	14	11	0.07	27	15	10	<0.0001
Fasting total cholesterol (mg/dL)	195.9 ± 32.6	195.5 ± 33.4	191.4 ± 32.2	0.11	201.4 ± 33.2	198.1 ± 34.6	197.1 ± 35.4	0.26
Fasting triglyceride (mg/dL)	162.2 ± 138.7 ^{b,c}	151.0 ± 98.6	137.3 ± 87.5	0.007	130.6 ± 73.8 ^{b,c}	118.9 ± 73.7	108.5 ± 61.7	0.0002
Fasting HDL-cholesterol (mg/dL)	42.2 ± 9.3 ^{b,c}	43.8 ± 10.7	44.3 ± 9.6	0.007	46.3 ± 10.3 ^{b,c}	47.1 ± 9.8	48.7 ± 10.8	0.003
Fasting glucose (mg/dL)	95.9 ± 18.3 ^{b,c}	93.4 ± 13.3	92.8 ± 14.5	0.005	90.9 ± 14.6 ^{b,c}	87.8 ± 9.5	86.9 ± 16.1	0.0002
Smoking (%)	36	31	35	0.19	1	2	2	0.14
Drinking alcohol (%)	77	75	68	0.007	33	28	27	0.22
Regular exercise (%)	44	54	51	0.004	58	57	55	0.67
Witnessed sleep apnea (%)	54	19	0	–	20	4	0	–
Intima-media thickness (mm) ^d								
Mean	0.710 ± 0.004	0.711 ± 0.003	0.711 ± 0.005	0.93	0.705 ± 0.005 ^c	0.702 ± 0.004 ^c	0.694 ± 0.005	0.05
Maximum	0.917 ± 0.005	0.918 ± 0.004	0.917 ± 0.006	0.97	0.910 ± 0.006 ^c	0.907 ± 0.006 ^c	0.896 ± 0.006	0.03

HDL, high-density lipoprotein.

Values are mean ± SD unless otherwise indicated.

^a P-values were derived from analysis of variance or χ^2 -test.

^b Significantly ($P < 0.05$) different from occasional snorers.

^c Significantly ($P < 0.05$) different from non-snorers.

^d Adjusted for age, body mass index, blood pressure, triglyceride, glucose, smoking (men only), drinking, medication on hypertension, and witnessed sleep apnea.

Table 2
Adjusted odds ratios of elevated IMT for different snoring groups by stratified analysis using multivariate mixed-effect modeling.

Snoring group	Elevated IMT (maximum IMT ≥ 1.0 mm)							
	Baseline			Year 2			Year 4	
	Prevalence (%)	OR ^a	95% CI	Prevalence (%)	OR ^a	95% CI	Prevalence (%)	OR ^a 95% CI
Men								
Habitual snorers	20	1.11	0.72–1.70	26	1.20	0.78–1.84	37	0.85 0.59–1.23
Occasional snorers	17	1.25	0.84–1.84	20	0.99	0.66–1.46	36	1.00 0.72–1.39
Non-snorers	16	1.00		21	1.00		38	1.00
	<i>P</i> = 0.36			<i>P</i> = 0.06			<i>P</i> = 0.89	
Women								
Habitual snorers	24	1.80	1.13–2.87	21	1.55	0.94–2.57	35	1.21 0.80–1.83
Occasional snorers	16	1.60	1.07–2.38	13	1.12	0.73–1.73	29	1.30 0.94–1.81
Non-snorers	10	1.00		10	1.00		22	1.00
	<i>P</i> < 0.0001			<i>P</i> = 0.0006			<i>P</i> = 0.002	

IMT, intima-media thickness; OR, odds ratio; CI, confidence interval.
^aAdjusted for age, body mass index, blood pressure, triglyceride, medication for hypertension, current smoking (men only), and witnessed sleep apnea.