Risk Factors

Snoring and Risk of Cardiovascular Disease in Women

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OBJECTIVES   To examine prospectively the association between snoring and incidence of cardiovascular disease (CVD) in women.

BACKGROUND   Whether snoring increases risk of CVD remains unclear; most previous studies have been small, not prospective and limited to men.

METHODS   Seventy-one thousand seven hundred seventy-nine female nurses 40 through 65 years of age and without previously diagnosed CVD or cancer at baseline in 1986 were followed up for eight years. Frequency of snoring was assessed using mailed questionnaires at baseline.

RESULTS   During eight years of follow-up, we documented 1,042 incident cases of major CVD events (644 coronary heart disease [CHD] and 398 stroke). Compared with nonsnorers, the age-adjusted relative risks (RRs) of CVD were 1.46 (95% confidence interval 1.23 to 1.74) for occasional snorers and 2.02 (1.62 to 2.53) for regular snorers. The age-adjusted RRs of CHD were 1.43 (1.15 to 1.77) for occasional snorers and 2.18 (1.65 to 2.87) for regular snorers. The age-adjusted RRs of stroke were 1.60 (1.21 to 2.12) and 1.88 (1.29 to 2.74), respectively. After further adjustment for smoking, body mass index (BMI) and other covariates, the positive association between snoring and CVD was attenuated but remained statistically significant (RRs of CVD were 1.20 [1.01 to 1.43] for occasional snorers and 1.33 [1.06–1.67] for regular snorers.

CONCLUSIONS   These data suggested that snoring is associated with a modest but significantly increased risk of CVD in women, independent of age, smoking, BMI and other cardiovascular risk factors. While further study is needed to elucidate the biological mechanism underlying this association, snoring may help clinicians identify individuals at higher risk for CVD. (J Am Coll Cardiol 2000;35:308–13) © 2000 by the American College of Cardiology

In some, but not all, epidemiologic studies, regular snoring has been associated with increased risk of hypertension (1,2), ischemic heart disease (2–4) and stroke (5–7). The mechanisms are largely unknown, but probably mediated by obstructive sleep apnea because heavy snoring almost invariably accompanies sleep apnea (8). Sleep apnea may independently increase risk of systemic hypertension (9). In addition, sleep apnea causes hypoxemia, which promotes atherosclerosis in experimental studies (10).

However, most snorers do not have sleep apnea. Whether snoring itself increases risk of hypertension and cardiovascular disease (CVD) remains controversial (8,11,12). Most previous epidemiological studies of snoring and CVD used cross-sectional or case-control designs and, therefore, may be prone to bias because snoring and sleep apnea can be a consequence of stroke (13). The sole prospective cohort study of snoring and CVD, which involved only three years of follow-up, was conducted among men (3). Therefore, we investigated the association between snoring and incidence of major CVD during eight years of follow-up among women enrolled in the Nurses' Health Study.

METHODS

Study population. The Nurses' Health Study cohort was established in 1976 when 121,700 female registered nurses, married and aged 30 to 55 years and residing in 11 large U.S. states, completed a mailed questionnaire on their medical history and lifestyle. Every two years, follow-up questionnaires have been sent to update information on potential risk factors and to identify newly diagnosed cases of coronary and other diseases. On the 1986 questionnaire, we asked the following: 1) indicate total hours of actual sleep in a 24-h period (from 5 h or less to 11+); 2) what is your usual sleeping position? (on back, on side, on front); 3)

Abbreviations and Acronyms

BMI = body mass index
CHD = coronary heart disease
CI = confidence interval
CVD = cardiovascular disease
MI = myocardial infarction
RR = relative risk

do you snore? (regularly, occasionally and never). We included the 71,779 women 40 to 65 years old and without diagnosed CVD or cancer in 1986, the baseline year for these analyses.

All the nurses were married in 1972. We reassessed their marital status in 1980 (married, divorced or widowed). In 1992, we asked the participants whether they lived with their spouses or partners.

Ascertainment of end points. The primary end points for this study were incident cardiovascular events (defined as nonfatal myocardial infarction [MI] or fatal coronary heart disease [CHD] and fatal and nonfatal stroke) that occurred after the return of the 1986 questionnaire but before June 1, 1994. We requested permission to review medical records from women who reported having a nonfatal MI or stroke on a follow-up questionnaire. Study physicians with no knowledge of the self-reported risk factor status reviewed the records. Nonfatal MI was confirmed if data in the record met the criteria of the World Health Organization of symptoms plus either diagnostic electrocardiographic changes or elevated cardiac enzyme levels (14). Infarctions that required hospital admission and for which confirmatory information was obtained by interview or letter, but for which no medical records were available, were designated as probable (17%). We included all confirmed and probable cases in the analyses because results were the same after excluding probable cases. Stroke was confirmed by medical records according to the criteria of the National Survey of Stroke (15), requiring a constellation of neurologic deficits, sudden or rapid in onset, lasting 24 h or more; events were further subclassified as hemorrhagic stroke (subarachnoid or intraparenchymal), ischemic stroke (thrombotic or embolic) or stroke of unknown cause.

Deaths were reported by next of kin and the postal system or ascertained through the National Death Index. We estimate that follow-up information for the deaths was over 98% complete (16). Fatal CHD was confirmed by hospital records or autopsy or if CHD was listed as the cause of death on the death certificate and evidence of previous CHD was available. We designated as presumed fatal CHD cases those cases in which CHD was the underlying cause on the death certificate but no records were available. These cases constituted about 14.7% of fatal CHD cases. We also included sudden deaths (defined as death within 1 h of onset of symptoms; 12.3% of fatal CHD). Analyses limited to

confirmed cases yielded very similar results, although with wider confidence intervals (CI). Fatal strokes were coded using the same criteria as nonfatal cases, but we accepted autopsy evidence as well as the death certificate listing of cause.

Statistical analysis. Person-time for each exposure category (never snoring, occasional snoring and regular snoring) was accumulated, and incidence rates were calculated by dividing the number of events by person-time of follow-up in each category. The relative risk (RR) was computed as the rate in a specific category of the exposure divided by that in the reference category (nonsnorers) with adjustment for age. In multivariate analyses using pooled logistic regression (17), we simultaneously included age (five-year interval), smoking status (never, past, current smoking of 1 to 14, 15 to 24 and $\geq$25 cigarettes per day), body mass index (BMI) (quintiles), alcohol consumption (0, 1 to 4, 5 to 14, 15+ g/day), physical activity (weekly energy expenditure in metabolic equivalent hours) (18), menopausal status (premenopausal, postmenopausal without hormone replacement, postmenopausal with past hormone replacement, postmenopausal with current hormone replacement), parental history of premature MI, history of diabetes or hypercholesterolemia, number of sleeping hours per day and usual sleeping position. We did not control for history of hypertension in the primary analyses, because snoring has been associated with risk of hypertension, and thus, the development of hypertension may be an intermediate step for the association between snoring and CVD. In secondary analyses, we also adjusted for hypertension, as well as for the duration of rotating night shift assessed in 1988 (0, 1 to 5, 6 to 14, 15+ years), which has previously been associated with the risk of CHD in the Nurses' Health Study (19).

RESULTS

During eight years of follow-up (551,541 person years), we documented 644 incident cases of CHD and 398 incident cases of stroke. At baseline, 5% of women reported sleeping five hours or less a day, 26% 6 h, 41% 7 h, 24% 8 h and 5% 9 h or more. About 81% of women reported usually sleeping on their side, 7% on their back and 11% on their front; 25% of women reported never snoring, 65% reported occasional snoring and 10% regular snoring.

All participants were married in 1972; in 1980, the majority of women (84%) remained married. The prevalence of regular snoring was slightly higher among those who were divorced or widowed (11%) than those who remained married (9%). In 1992, 74% of women reported living with their spouses or partners. The prevalence of regular snoring was similar between those living with spouses or partners (9%) and those not living with spouses or partners (10%).

Women who reported snoring regularly were more likely to sleep on their back, smoke cigarettes, use alcohol and have longer duration of night shift work (Table 1). They

Table 1. Baseline Characteristics and Risk Factors for Cardiovascular Disease According to Self-Reported Snoring at Baseline in 1986

	Frequency of Snoring		
Characteristics	Never (25%)	Occasionally (65%)	Regularly (10%)
Average # hours of sleeping/day	7.0	7.0	7.0
Usual sleep position (%)			
On side	80	82	81
On back	6.3	6.5	8.3
On front	12.0	11.0	10.0
% of women			
History of hypertension	18.3	24.5	33.5
History of diabetes	2.1	3.4	5.7
History of hypercholesterolemia	9.6	11.9	14.8
Current smoking	15.8	22.5	27.1
Parental history of MI	13.4	14.3	15.8
Multivitamin supplement use	44.4	42.1	39.4
Vitamin E supplement use	17.0	15.8	14.4
Night shift ≥5 yrs*	16.2	18.2	21.7
Mean			
Age (yrs)	50.4	52.8	53.5
Body mass index (kg/m^2)	23.0	24.4	26.8
Alcohol intake (g/day)	5.9	6.6	6.7
Physical activity (METS/week)	15.6	13.9	11.1
Saturated fat intake (% energy)	11.6	11.7	12.0
Polyunsaturated fat (% energy)	6.1	6.1	6.2
Trans fat (% energy)	1.7	1.7	1.7
Dietary cholesterol (mg/1,000 kcal)	149	151	156

Data were directly standardized to the age distribution of the entire study population.
METs = metabolic equivalents; MI = myocardial infarction.
*Reported in 1988.

tended to be slightly older, heavier and less physically active and had a substantially higher prevalence of hypertension, diabetes and hypercholesterolemia at baseline. Dietary fat and cholesterol intakes did not differ appreciably across categories of snoring.

After adjustment for age, both occasional and regular snoring were associated with significantly increased risk of CVD (Table 2). Compared with never snorers, the RRs of CVD were 1.46 (95% CI 1.23 to 1.74) for occasional snorers and 2.02 (1.62 to 2.53) for regular snorers. The age-adjusted RRs of fatal CVD (including fatal MI and stroke) were 1.61 (1.10 to 2.38) and 2.07 (1.25 to 3.43), respectively. Snoring was associated with increased risk of CHD, total stroke, ischemic stroke and hemorrhagic stroke in the age-adjusted analysis.

After further adjusting for smoking, BMI and other covariates, the positive associations for CVD were attenuated but remained statistically significant (multivariate RRs were 1.20 [1.01 to 1.43] for occasional snorers and 1.33 [1.06 to 1.67] for regular snorers). After additional adjustment for history of hypertension, multivariate RRs of CVD were 1.20 (1.01 to 1.42) for occasional snorers and 1.30 (1.03 to 1.64) for regular snorers. Further adjustment for

duration of shift work, marriage status and whether they lived with a partner or spouse did not change these RRs. Because snoring was strongly related to obesity (Table 1), we were concerned about potential residual confounding by BMI. However, when the analyses were repeated by including deciles of BMI rather than quintiles in the model, the results remained virtually the same. After adjustment for snoring, neither the number of sleeping hours per day nor usual sleep positions was significantly associated with risk of CVD (data not shown). In further analyses, we observed a positive association between snoring and CVD across different strata of BMI and smoking.

DISCUSSION

In this prospective study of women, we observed a modest but significant positive association between snoring and incidence of CVD. After accounting for age, smoking, BMI and other cardiovascular risk factors, occasional snorers had 20% (95% CI 1% to 43%) increase in risk of CVD compared with nonsnorers, while regular snorers had 33% (6% to 67%) increase in risk.

Table 2. Relative Risks (95% Confidence Intervals) of Coronary Heart Disease and Stroke According to Self-Reported Snoring at Baseline in 1986

	Frequency of Snoring		
	Never	**Occasionally**	**Regularly**
Total cardiovascular events (coronary heart disease + stroke)**			
# cases	162	729	151
Person-years	143,719	356,530	51,292
Age-adjusted	1.0	1.46 (1.23–1.74)	2.02 (1.62–2.53)
Multivariate	1.0	1.20 (1.01–1.43)	1.33 (1.06–1.67)
Fatal cardiovascular events			
# cases	31	156	30
Age-adjusted	1.0	1.61 (1.10–2.38)	2.07 (1.25–3.43)
Multivariate	1.0	1.33 (0.90–1.96)	1.35 (0.80–2.26)
Coronary heart disease			
# cases	102	441	101
Age-adjusted	1.0	1.43 (1.15–1.77)	2.18 (1.65–2.87)
Multivariate*	1.0	1.11 (0.89–1.39)	1.33 (1.00–1.77)
Total stroke			
# cases	60	288	50
Age-adjusted	1.0	1.60 (1.21–2.12)	1.88 (1.29–2.74)
Multivariate	1.0	1.42 (1.07–1.89)	1.35 (0.91–1.99)
Ischemic stroke			
# cases	38	176	37
Age-adjusted	1.0	1.51 (1.06–2.14)	2.14 (1.36–3.37)
Multivariate	1.0	1.31 (0.91–1.88)	1.42 (0.88–2.29)
Hemorrhagic stroke			
# cases	16	79	13
Age-adjusted	1.0	1.77 (1.03–3.03)	1.97 (0.94–4.11)
Multivariate	1.0	1.71 (0.99–2.95)	1.80 (0.85–3.83)

*Models include the following: age (five-year category); time period (four periods); body mass index (five categories); cigarette smoking (never, past and current smoking of 1 to 14, 15 to 24 and ≥25 cigarettes per day); menopausal status (premenopausal, postmenopausal without hormone replacement, postmenopausal with past hormone replacement, postmenopausal with current hormone replacement); parental history of myocardial infarction before 60 years of age; alcohol consumption (four categories); multivitamin and vitamin E supplement use; physical activity (METS, in quintiles); average number hours of sleeping (5 h, 6, 7, 8, ≥9); usual sleep positions (on side, on back, on front); history of diabetes; history of hypercholesterolemia.
  METs = metabolic equivalent hours.

Strengths and limitations. The high rate of follow-up reduced potential bias due to loss to follow-up. Furthermore, snoring and covariates were assessed prospectively, eliminating possible bias due to retrospective recall which may be present in case-control and cross-sectional analyses. Since CVD may cause snoring (13), we excluded women with cardiovascular end points at baseline. Women who reported snoring regularly had a somewhat less healthy risk profile (Table 1). After we controlled for smoking, BMI and other covariates, the RRs were substantially attenuated, reflecting confounding effects of these variables. However, a significant positive association between snoring and CVD persisted. Also, in stratified analyses by BMI and smoking, the excess risk associated with snoring remained in all subgroups.

Information on snoring and other potential risk factors was self-reported by female nurses. The reliability of snoring data was not validated in this population, but similar questions about frequency of snoring have been validated in other populations (20), in which self-reported habitual snoring appeared to be reliable according to all-night sleep recordings with monitoring of respiration, body movements, oxygen saturation and snoring sound. Since all our participants were registered, married nurses at entry with a demonstrated interest in medical research, the possibility of underreporting of snoring should be small relative to that in general populations. Nevertheless, some misclassification of the snoring variable was inevitable. Perhaps some women were unaware of their snoring. However, the prevalence of snoring did not appear to vary appreciably with marital status or living arrangement in our cohort. Also, because snoring was assessed prospectively, any misclassification of

snoring frequency would be nondifferential with respect to CVD, which, if present, would result in underestimation of the effects of snoring.

Previous studies. Our findings among women are, in general, consistent with previous studies of men. In a prospective study of 4,388 men (3), 149 men were newly diagnosed with ischemic heart disease, and 42 men were diagnosed with stroke during three years of follow-up. After adjusting for age, BMI, smoking and other cardiovascular risk factors, the RRs comparing men who reported snoring habitually or frequently with nonsnorers were 1.71 for ischemic heart disease and 2.08 for ischemic heart disease and stroke combined. In a cross-sectional study of 3,847 men and 3,664 women, Koskenvuo et al. (2) found a significant association of self-reported habitual snoring with risk of angina pectoris in men (RR = 2.01) but a weak association in women (RR = 1.23). Several case-control studies have reported a positive association of snoring with risk of coronary disease or stroke (5,6,21), but the direction of the association has been questioned because snoring can be a consequence of CVD (8).

Biological mechanisms. The adverse effect of snoring on risk of CVD may be mediated through obstructive sleep apnea (22). In a series of heavy snoring patients (23), most had increased apnea frequencies consistent with sleep apnea syndrome. Sleep apnea has been directly associated with MI (22) and stroke (5). Apnea is associated with hypoxemia, which may accelerate atherosclerosis in coronary and intracranial arteries (10). Also, sleep apnea may adversely affect hematologic factors, such as decreasing fibrinolytic activity (24). In addition, because of cyclical increase in sympathetic output and systemic and pulmonary artery pressures due to hemodynamic responses to obstructive apnea (9,25), sleep apnea may directly cause systemic hypertension, a strong risk factor for both CHD and stroke.

Because most snorers do not have sleep apnea, it is unclear whether simple snoring without frank sleep apnea may also increase the risk of CVD. In a cross-sectional study among 580 adults from the Wisconsin Sleep Cohort Study, Young et al. (26) found that simple snoring was significantly associated with elevated blood pressure, independent of age, gender and BMI; the magnitude of the association was smaller than that for more severe sleep-disordered breathing. The authors suggest that simple snoring represents the beginning of the sleep-disordered breathing continuum, which ranges from partial airway collapse and mildly increased upper-airway resistance to complete airway collapse and severe obstructive sleep apnea lasting 60 s or more (27). Our study, like most of previous epidemiologic studies, cannot distinguish the effects of simple snoring from snoring with sleep apnea on the risk of CVD. However, we observed a significant increase in risk of CVD, albeit small, among occasional snorers who were most likely to be simple snorers. These results support the notion that snoring

without sleep apnea may represent the beginning of the sleep-disordered breathing continuum.

Conclusions. Our data suggest that snoring is associated with a modest but significantly increased risk of CVD in women, independent of age, smoking, obesity and other cardiovascular risk factors. While further study is needed to elucidate the biological mechanism underlying this association, snoring may help clinicians identify individuals at higher risk for CVD.

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