Snoring and the Risk of Ischemic Brain Infarction

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To determine if a history of snoring is a risk factor for brain infarction, I conducted a case–control study of risk factors for ischemic stroke using 177 consecutive male patients aged 16–60 (mean 49) years with acute brain infarction. For each patient I chose an age-matched (±6 years) male control. Arterial hypertension, coronary heart disease, snoring (habitually or often), and heavy drinking (>300 g/wk) were risk factors in the stepwise multiple logistic regression analysis. The odds ratio of snoring for brain infarction was 2.13. By McNemar's test this association increased strongly if a history of sleep apnea, excessive daytime sleepiness, and obesity were all present with snoring (odds ratio 8.00). My study indicates that snoring may be a risk factor for ischemic stroke, possibly because of the higher prevalence of an obstructive sleep apnea syndrome among snorers than nonsnorers. (*Stroke* 1991;22:1021–1025)

Recent epidemiological studies have revealed that a history of habitual snoring is associated with arterial hypertension and coronary heart disease.[1–8] Snoring has also been suggested as a risk factor for brain infarction,[9,10] especially for strokes occurring during sleep or shortly after awakening.[11] Heavy snoring is associated with the obstructive sleep apnea syndrome, which has several harmful effects on the cardiovascular system.[12–19]

Several confounding factors can be involved in the association between snoring and brain infarction because many potential risk factors for stroke are also associated with snoring and sleep apnea.[20] In addition to arterial hypertension and coronary heart disease, these include age,[7,8,21,22] obesity,[3,4,7,8,22–25] smoking,[4,7,22] and alcohol consumption.[22,26–31]

The purpose of my study was to define the roles of snoring and sleep apnea as risk factors for brain infarction, controlling for potentially confounding variables.

Subjects and Methods

I studied 177 consecutive male patients aged 16–60 years admitted to the Meilahti University Hospital in Helsinki. Brain infarction was always confirmed by a neurologist and in 171 cases (96.6%) by neuroradiological examinations. For each patient, I chose an age-matched (±6 years) male control from a series of patients admitted to the same hospital for acute reasons other than brain infarction and without any history of ischemic cerebrovascular disease. Patients and controls were examined, seeking potential risk factors for brain infarction including a history of snoring and symptoms of sleep apnea.

A detailed medical history was obtained from the patients and the controls, from their hospital notes, and from clinical and laboratory examinations during follow-up. I collected the data about arterial hypertension (previous antihypertensive medication or blood pressure values remaining at least 150/100 mm Hg during follow-up), coronary heart disease (previous myocardial infarction and/or typical angina pectoris requiring medication), and diabetes mellitus (antidiabetic medication or special diet because of impaired glucose tolerance known previously or diabetic blood glucose recordings during follow-up).

Sleeping habits, smoking, and alcohol consumption were assessed always using the same standardized questionnaire. The reliability of the data on snoring from the questionnaire has been assessed previously.[25] The history of snoring was categorized as "always or almost always" (habitual snoring), "often," "occasionally," or "never." Those who reported snoring habitually or often were defined as "snorers," and the rest of the patients and controls were defined as "nonsnorers." If a patient or control could not clarify his snoring status with certainty, a cohabiting person was interviewed. The frequency of alcohol consumption was categorized as "daily or almost daily," "1–3 times/wk," "1–3 times/mo," or "never or occasionally." The questionnaire was primarily directed at clarifying the frequency of drinking. However, in 156 patients (88.1%) and 153 controls (86.4%) it was also possible to estimate the consumption of alcohol in

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TABLE 1. Frequencies and Categorical Groups of Potential Risk Factors for Ischemic Brain Infarction in 177 Patients and 177 Controls

Risk factor	Patients No.	Patients %	Controls No.	Controls %
Arterial hypertension*	62	35.0	26	14.8
Coronary heart disease†	51	29.0	21	11.9
Diabetes mellitus	30	16.9	13	7.3
Body mass index‡				
>27.0 kg/m²	66	37.7	59	33.3
≤27.0 kg/m²	109	62.3	118	66.7
Snoring§				
Habitually	50	29.1	27	15.7
Often	40	23.3	28	16.3
Occasionally	54	31.4	85	49.4
Never	28	16.3	32	18.6
Smoking‖				
>10 cigarettes/day	77	45.0	61	35.3
1–10 cigarettes/day	20	11.7	26	15.0
Never smoked or stopped smoking	74	43.3	86	49.7
Alcohol consumption				
Frequency¶				
Daily or almost daily	28	16.2	22	12.6
1–3 times/wk	52	30.1	47	27.0
1–3 times/mo	54	31.2	54	31.0
Never or occasionally	39	22.5	51	29.3
Quantity#				
>300 g/wk	17	10.9	5	3.3
>150–300 g/wk	21	13.5	16	10.5
>0–150 g/wk	82	52.6	109	71.2
0 g/wk	36	23.1	23	15.0

*n=176 for controls.
†n=176 for patients.
‡n=175 for patients.
§n=172 for patients and controls.
‖n=171 for patients, 173 for controls.
¶n=173 for patients, 174 for controls.
#n=156 for patients, 153 for controls.

grams per week. Body mass index in kilograms per square meter was also calculated.

After tabulating the data by using BMDP,[32] the univariate risk factors for brain infarction among matched case–control pairs were determined by using McNemar's test; the risk of brain infarction is given by the odds ratio (OR) calculated as the proportion of discordant pairs (s/t),[33] where s and t indicate the number of pairs with only the case (s) or only the control (t) exposed to a risk factor. The 95% confidence interval (CI) of the OR was then calculated with the aid of tables based on the binomial distribution.[33,34] To establish the independent contribution of individual risk factors, stepwise multiple logistic regression analyses were carried out with brain infarction as a dependent variable. To obtain individual ORs from all the analyses, the independent variables were dichotomized from selected cutoff points. Arterial hypertension, coronary heart disease, diabetes mellitus, and snoring were dichotomized as yes versus no, smoking as >10 cigarettes/day versus ≤10 cigarettes/day (including nonsmokers), body mass index as >27.0 kg/m² versus ≤27.0 kg/m², and alcohol consumption as >1–3 times/mo versus ≤1–3 times/mo (including abstainers) or >300 g/wk versus ≤300 g/wk (including abstainers).

Results

Mean age of the 177 stroke patients was 49.0 (standard deviation [SD] 9.3, median 52, range 16–60) years, and that of the 177 age-matched controls was also 49.0 (SD 9.7, median 50, range 16–65) years. The symptoms and clinical presentation of 16 patients (9.0%) suggested cardiogenic embolic infarction. In 135 patients (76.3%) infarction was localized in the carotid and in 42 (23.7%) in the vertebrobasilar artery territory. The frequencies and categorical groups of potential risk factors for brain infarction in the patients and controls are presented in Table 1.

In 30 patients (16.9%) and 32 controls (18.1%) the history of sleeping habits was ascertained from co-

TABLE 2. Risk Factors for Ischemic Brain Infarction Among 177 Male Patients and 177 Age- and Sex-Matched Controls by McNemar's Test

Risk factor	Discordant case–control pairs +/−	Discordant case–control pairs −/+	Odds ratio	95% confidence interval
Arterial hypertension	56	20	2.80	1.65–4.93
Coronary heart disease	44	14	3.14	1.69–6.21
Diabetes mellitus	28	11	2.55	1.23–5.67
Body mass index >27.0 kg/m²	42	34	1.24	0.77–2.00
Snoring habitually or often	58	25	2.32	1.43–3.87
Smoking >10 cigarettes/day	50	35	1.43	0.91–2.27
Alcohol consumption				
>1–3 times/mo	50	38	1.32	0.85–2.06
>300 g/wk*	14	5	2.80	0.95–9.93

+/−, discordant case–control pair with only case exposed to risk factor; −/+, discordant case–control pair, with only control exposed to risk factor.
*n=135 matched pairs with known quantity of weekly alcohol consumption in grams.

TABLE 3. Independent Risk Factors for Ischemic Brain Infarction by Stepwise Multiple Logistic Regression Analysis in 177 Male Patients and 177 Age- and Sex-Matched Controls

Risk factor	Odds ratio	95% confidence interval
Arterial hypertension	2.89	1.56–5.34
Coronary heart disease	2.95	1.53–5.70
Snoring habitually or often	2.13	1.29–3.52
Heavy drinking (>300 g/wk)	6.80	1.86–24.9

Other risk factors tested were diabetes mellitus, obesity (body mass index >27 kg/m^2), smoking >10 cigarettes/day, and frequent drinking (>1–3 times/mo).

habiting friends or relatives. In five cases in each group reliable data about sleeping habits were not obtainable, leaving 167 age-matched case–control pairs with data on snoring.

The univariate risk factors for brain infarction among the matched case–control pairs were coronary heart disease, arterial hypertension, diabetes mellitus, and snoring (Table 2). In the stepwise multiple logistic regression analysis heavy drinking (>300 g/wk), coronary heart disease, arterial hypertension, and snoring proved to be independent risk factors (Table 3). The frequency of drinking was also used as a variable for alcohol consumption, but it did not remain in the logistic model as a significant risk factor.

The association between snoring and brain infarction was found among all patient subgroups tested (i.e., among subgroups with strokes of probable cardiogenic and atherothrombotic origin and among those with infarction in the carotid and vertebrobasilar territories). The association was strongest between snoring and cardiogenic embolism (from logistic model: OR 4.71, 95% CI 1.42–15.6).

In addition to snoring habitually or often, 40 patients (23.3%) and 17 controls (9.9%) were reported to have apnea-like breathing disturbances during sleep. Nine patients (5.2%) and two controls (1.2%) were strongly suspected of having an obstructive sleep apnea syndrome because of the constellation of snoring with apneic periods, excessive daytime sleepiness, and obesity (body mass index of >27 kg/m^2). The risk of suffering a stroke associated with an increasing likelihood of obstructive sleep apnea is presented in Table 4. After excluding apnea, obesity, and excessive daytime sleepiness, the history of snoring as such did not increase the risk of brain infarction significantly (OR 1.22), whereas the most likely obstructive sleep apnea syndrome was clearly associated with brain infarction (OR 8.00) (Table 4).

To eliminate the potential bias caused by a theoretical influence of earlier strokes on the occurrence of snoring and sleep apnea among stroke victims,[35,36] I excluded patients with previous strokes (n=18, 10.2%) and repeated the analyses including only patients with first strokes. This did not affect the results.

Discussion

In the present study, 52.3% of the patients were snorers, and the OR of snoring habitually or often for brain infarction was 2.13. Thirty-two percent of the controls were snorers, which tallies with the expected occurrence of snoring in the male population.[6,7] In a prospective study of 4,388 men aged 40–69 years[10] the relative risk for combined coronary heart disease and/or stroke between habitual or frequent snorers and nonsnorers was 2.38. There were 16 stroke cases among 1,294 snorers in contrast to none among 480 nonsnorers.

In addition to coronary heart disease and stroke, snoring has been associated with arterial hypertension.[1–8] Coronary heart disease and hypertension are strong predictors of brain infarction. Alcohol consumption and obesity could also have a confounding effect on the results because these two factors are known to be associated with snoring and sleep apnea.[3,4,7,8,22–28] Alcohol intoxication and heavy drinking have been suggested as risk factors for stroke, especially among young and middle-aged men.[29–31] In the multiple logistic regression analyses, however, none of these potential confounding variables affected the role of snoring as a risk factor, nor did the other risk factors tested.

The mechanisms by which snoring could increase the risk of brain infarction are unknown. One explanation could be the higher prevalence of obstructive sleep apnea among habitual snorers than among

TABLE 4. Increasing Risk of Ischemic Brain Infarction by Increasing Suspicion of Obstructive Sleep Apnea Syndrome Among 167 Age-Matched Pairs of Patients and Controls With Known Data on Sleeping Habits by McNemar's Test

Snoring	Apnea	Excessive daytime sleepiness	Obesity	Discordant case–control pairs +/−	Discordant case–control pairs −/+	Odds ratio	95% confidence interval
+	−	−	−	22	18	1.22	0.63–2.42
+	+ or −	+ or −	+ or −	58	25	2.32	1.43–3.87
+	+	+ or −	+ or −	34	13	2.62	1.35–5.40
+	+	+	+ or −	17	6	2.83	1.07–8.78
+	+	+	+	8	1	8.00	1.07–356.1

Obesity, body mass index >27 kg/m^2; +, symptom present; −, symptom not present; +/−, discordant case–control pair with only case exposed to all symptoms indicated by +; −/+, discordant case–control pair with only control exposed to all symptoms indicated by +.

occasional snorers. The obstructive sleep apnea syndrome, in turn, is known to be associated with cardiac arrhythmias[12–16] and a decreased cardiac index.[17] Consistent with these previous observations, snoring was particularly associated with cardiogenic embolism in the present study (OR 4.71). Marked hypotensive periods have been noticed in association with sleep apnea,[18,19] which also may increase the risk of ischemic stroke by hemodynamic mechanisms, especially among patients with severely stenotic atherosclerotic lesions in the cervical arteries.

In detailed analyses by subgroups, the association of snoring with stroke was most clearly connected to symptoms of an obstructive sleep apnea syndrome. In such an analysis the history of snoring as such, without other symptoms indicating obstructive sleep apnea, was not associated with an increased risk of brain infarction. The suspected prevalence of an obstructive sleep apnea syndrome among the controls (1.2%) tallies well with other Scandinavian estimates of its frequency in the male population.[8,25] On the contrary, the frequency of a suspected obstructive sleep apnea syndrome among stroke patients in this study (5.2%) seems higher than expected, although similar estimates have been reported from Italy.[21]

The frequency of a self-reported apnea-like breathing pattern during the night was not significantly influenced by different habits of alcohol consumption in this study. None of those with a suspected obstructive sleep apnea syndrome was a heavy drinker. However, when only snorers were included in the analyses, there were seven heavy drinkers among the patients and none among the controls. Accordingly, while heavy drinking was an independent risk factor for stroke, one part of the increased risk could be explained by the likelihood of alcohol consumption aggravating snoring and apnea among the snorers.[27,28]

Vertebrobasilar ischemia triggered repetitively by periods of obstructive sleep apnea has recently been documented.[37] Sleep apnea could also be a consequence of brain infarction, especially if the lesion is located in the territory of the vertebrobasilar circulation.[35,36] For this reason the analyses were also carried out after excluding patients with earlier stroke, but this did not affect the results.

The reliability of data on snoring obtained by questionnaire has been assessed previously.[25] Based on all-night sleep recordings with monitoring of respiration, body movements, oxygen saturation, and snoring sounds, self-reported habitual snorers seemed to be true heavy snorers. On the other hand, 13% of self-reported never snorers were not aware of their snoring.[25] A history of snoring obtained by questionnaire seems to be valid and by no means an overestimation. Men giving their own sleeping history are less likely to report habitual snoring and more likely to classify themselves as nonsnorers than those consulting their bed partners.[3] In the present study such a bias could be avoided because the history of sleeping habits was confirmed by a cohabiting relative as often in the patient group as in the control group.

In conclusion, there seems to be an association between a history of snoring and brain infarction. The mechanism of this association remains unknown, but one possible explanation is the higher prevalence of an obstructive sleep apnea syndrome among snorers than among those who snore only occasionally.

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