Association between Self-reported Snoring and Prediabetes among Adults Aged 40 Years and Older without Diabetes

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Abstract

Background: Several previous studies have shown that snoring is associated with glucose metabolism and the development of diabetes, but rare study has shown the association between snoring frequency and prediabetes, particularly in China. We hypothesized that individuals who snore might have a higher risk of prediabetes. This study aimed to investigate the association between self-reported snoring and prediabetes in a Chinese population.

Methods: A cross-sectional study was performed in three large communities of Beijing from December 2011 to August 2012 by recruiting individuals aged ≥40 years old. All participants were requested to complete a detailed questionnaire and undergo anthropometric measurements. A 75 g oral glucose tolerance test was performed in individuals without diabetes. Blood samples of all participants were collected; blood glucose and blood fat levels were measured. Multivariate logistic regression models were built to assess the association between snoring frequency and prediabetes.

Results: A total of 13,592 participants (female: 66.56%; mean age: 56.8 ± 7.9 years; mean body mass index: 25.5 ± 3.4 kg/m^2) were included in the final analysis. Of these, 30.9% were diagnosed with prediabetes, while 41.3% and 25.4% had occasional and habitual snoring, respectively. Habitual snoring was associated with an increased risk of prediabetes (odds ratio [*OR*]: 1.3, 95% confidence interval [*CI*]: 1.1–1.4, *P* < 0.001), after adjusting for diabetes and sleep-related confounders in the multivariable models. Habitual snoring was also associated with isolated impaired fasting glucose (IFG; *OR*: 1.3, 95% *CI*: 1.0–1.6; *P* < 0.001) and isolated impaired glucose tolerance (IGT; *OR*: 1.3, 95% *CI*: 1.2–1.5; *P* < 0.001), but not IFG + IGT (*OR*: 1.1, 95% *CI*: 0.9–1.4; *P* = 0.281). When stratified by total cholesterol (TC) levels, this association between habitual snoring and prediabetes was observed only in individuals with TC <5.6 mmol/L (*OR*: 1.4, 95% *CI*: 1.2–1.6; *P* < 0.001).

Conclusions: Habitual snoring is associated with prediabetes, but only in individuals with TC <5.6 mmol/L. Further prospective studies are needed to confirm this finding.

Key words: Cholesterol; Community; Cross-sectional Studies; Prediabetic State; Snoring

INTRODUCTION

Prediabetes, classified into two subtypes: impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT), is a risk state characterized by higher blood glucose levels than normal but which does not meet the diagnostic criteria for diabetes.[1] Individuals with prediabetes develop diabetes at an average annual risk of about 5–10%.[2,3] Moreover, comparing with the high epidemiological status of chronic diabetic complications in diabetes patients, they also have an increased risk for microvascular (chronic kidney disease, neuropathies, and diabetic retinopathy) and macrovascular diseases (cardiovascular diseases).[4-8] The prevalence of prediabetes in China is 15.5%, accounting for 148.2 million adults with prediabetes, indicating a high socioeconomic burden.[9,10]

Snoring affects approximately 5–60% of the population with deteriorating sleep quality reported by different studies.[11,12] Although the mechanism is unclear, a growing

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number of studies have shown that snoring is associated with glucose metabolism and development of diabetes.[13-16] In two similar prospective studies with 10-year follow-up, Elmasry *et al.*[14] and Al-Delaimy *et al.*[15] found that snoring was independently associated with increased incidence of Type II diabetes in 2668 men aged 30–69 years old and 69,852 women aged 40–65 years old, respectively. However, only a few studies have directly discussed the relationship between snoring and prediabetes, particularly in China. Therefore, we hypothesized that Chinese individuals who snore might have a higher risk of prediabetes. A cross-sectional study assessing the association between snoring and prediabetes was performed in a cohort of adults without diabetes, aged ≥40 years old, who were from three different communities of Beijing.

METHODS

Participants

The present study was accomplished from December 2011 to August 2012 in the Gucheng, Jindingjie, and Laoshan communities of Beijing. According to the exclusion criteria, people who had difficulty in moving, conversation, and bad compliance were excluded from this study. Overall, using a cluster sampling method, 19,308 inhabitants aged ≥40 years old were recruited with signed informed consent (135 people who aged <40 years old were excluded). This study was approved by the Ethics Committee of the Chinese People's Liberation Army (PLA) General Hospital.

Data collection

All participants underwent this study in the Community Health Service Center of the three communities, where their fasting blood sample was obtained by venipuncture after overnight fasting for at least 10 h. And then, a 75 g oral glucose tolerance test (OGTT) was performed on the individuals without self-reported diabetes to obtain the 2 h postload blood sample. The collected blood samples were subsequently analyzed on an automatic analyzer (Cobas 8000 Modular Analyzer Series; Roche Diagnostics, Basel, Switzerland) to obtain measurements of fasting blood glucose (FBG), 2 h postload blood glucose (PBG), serum triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein-cholesterol (LDL-C) in the Laboratory of Chinese PLA General Hospital. The upper limit values of TC, TG, and LDL-C were 5.6, 3.4, and 1.7 mmol/L, respectively.

Before the second venipuncture after OGTT, participants were interviewed by well-trained physicians for obtaining baseline data through a standardized questionnaire including sociodemographic information (i.e., gender, age, occupation, and education), lifestyle (i.e., smoke, alcohol consumption, and sleep habit), depression status, and medical history (i.e., stroke, myocardial infarction, and hypertension [HTN]). Snoring, quality of sleep, and night sleep duration were self-reported by answering items on a questionnaire. Snoring frequency was ascertained by the following question, "In the past 12 months, how often did you snore during the night sleeping?", and the options for responses were "never", "occasionally", and "habitual", which was defined as "never or nearly never", "1–2 nights per week", and "≥3 nights per week", respectively. The quality of sleep was classified as "good", "bad sleeper with no hypnotics", and "bad sleeper with hypnotics". The duration of night sleep was calculated by answering the question, "what time do you go to bed at night, and get up at morning, in the past 7 days?" and also recorded in the questionnaire.

The anthropometric measurements, including height (kg), weight (m), hip circumference (HC; cm), and waist circumference (WC; cm), were obtained for every participant. Body mass index (BMI) calculated as weight/height (kg/m^2) was divided into three categories: BMI <24 kg/m^2, 24 ≤BMI <28 kg/m^2, and BMI ≥28 kg/m^2.

After at least 5 min of rest, blood pressure was measured three times in the seated position using an Omron HEM-9000AI device (OMRON, OmronCompany, China). The systolic blood pressure (SBP) and the diastolic blood pressure (DBP) were calculated as the average of three measurements in the analysis.

Definition of variables

According to data from the questionnaire and the recorded values of FBG and PBG, people with self-reported diabetes ($n = 2544$), people with newly-diagnosed ($n = 2122$) diabetes (defined by FBG ≥7.0 mmol/L or PBG ≥11.1 mmol/L), people with missing blood glucose values ($n = 141$), and people who were unaware of whether they snored during sleep ($n = 909$) were excluded. The remaining subjects were included in the final statistical analysis, and classified into two groups: (1) normal glucose regulation, defined by FBG <6.1 mmol/L and PBG <7.8 mmol/L; and (2) prediabetes, including three subgroups: isolated impaired fasting glucose (iIFG, defined by FBG of 6.1–7.0 mmol/L and PBG <7.8 mmol/L), isolated impaired glucose tolerance (iIGT, defined by FBG <6.1 mmol/L and PBG of 7.8–11.1 mmol/L), and IFG + IGT (defined as FBG of 6.1–7.0 mmol/L and PBG of 7.8–11.1 mmol/L).[1]

Education status was divided into three types according to the educational duration: <6 years, 6–9 years, and >9 years. The status of smoking, alcohol, and tea consumption was recorded as yes/no. Depression status was quantified by the Patient Health Questionnaire-9, and the subjects who scored ≥10 were defined as having moderate or severe depression.[17] Family history of diabetes (FHD) was defined as any history of diabetes in the first-degree relatives (parents, siblings, and children). History of cardiovascular disease was defined as any self-reported occurrences of stroke, myocardial infarction, or coronary heart disease. HTN was defined as self-reported history of HTN or SBP ≥140 mmHg (1 mmHg = 0.133 kPa) or DBP ≥90 mmHg.

Statistical analysis

The continuous and categorical variables are presented as mean ± standard deviation (SD) and *n* (percentages),

respectively. To compare variables among different groups, Pearson test and analysis of variance (ANOVA) were used for the continuous and categorical variables, respectively. Single factor analysis was used to screen all possibly related confounders to prediabetes.

Three multivariate logistic regression models were built to examine the effects of self-reported snoring on prediabetes and its subgroups (iIFG, iIGT, and IFG + IGT) by calculating the odds ratio (*OR*) and 95% confidence intervals (*CIs*). Model 0 was not adjusted for any confounding factors, while Model 1 was adjusted for age, gender, and BMI. Model 2 was further adjusted for education status (≤6 years, 6–9 years, and >9 years), WC, HC, waist-to-hip ratio (WHR), smoking status (yes/no), alcohol consumption (yes/no), tea consumption (yes/no), TC, TG, HDL-C, LDL-C, depression status (yes/no), CVD, HTN, FHD (yes/no), and sleep-related variables (sleep quality and duration of night sleep).

An interaction test was used to assess if there were interactive variables between self-reported snoring and prediabetes. Next, the data were stratified by potential variables, and the multivariate logistic regression models described above were operated again. All analyses were performed using Empower (R; X and Y Solutions, Inc., Boston, MA, USA). A $P < 0.05$ (two-sided) was considered statistically significant for all analysis.

RESULTS

The baseline characteristics of participants in the entire cohort and categorized by the self-reported snoring frequency are shown in Table 1. A total of 13,592 participants, including 4545 men and 9047 women, aged 56.8 ± 7.9 years old, were included in the final analysis. Within them, 30.9% were diagnosed with prediabetes, while 41.3% and 25.4% were occasional and habitual snorers, respectively. With increasing snoring frequency, participants tended to be older, heavier, have higher prevalence of prediabetes, blood pressure, FBG, PPG, and TG, and include more men, smokers, habitual consumers of alcohol and tea, individuals of FHD, but have shorter duration of night sleep and lower HDL-C [Table 1].

In the multivariate analysis, occasional and habitual snoring were significantly associated with the risk of prediabetes in the Model 0 (occasional snoring: *OR* = 1.2, 95% *CI*: 1.1–1.3; *P* < 0.001; habitual snoring: *OR* = 1.6, 95% *CI*: 1.5–1.8; *P* < 0.001) which adjusted for no confounding factors, and Model 1 (occasional snoring: *OR* = 1.1, 95% *CI*: 1.0–1.2; *P* = 0.030; habitual snoring: *OR* = 1.4, 95% *CI*: 1.3–1.5; *P* < 0.001), which adjusted for the traditional risk factors (age, gender, BMI) of diabetes. However, only the association between habitual snoring and prediabetes remained significant in the model 2 after further adjustments for other diabetes-related factors and sleep-related factors (*OR* = 1.3, 95% *CI*: 1.1–1.4; *P* < 0.001) [Figure 1a].

When stratifying for prediabetes subgroups, the association with habitual snoring was established for iIFG

(Model 0: *OR* = 1.8, 95% *CI*: 1.5–2.3; *P* < 0.001; Model 1: *OR* = 1.4, 95% *CI*: 1.1–1.8; *P* = 0.002), iIGT (Model 0: *OR* = 1.6, 95% *CI*: 1.4–1.8; *P* < 0.001; Model 1: *OR* = 1.4, 95% *CI*: 1.3–1.6; *P* < 0.001), and IFG + IGT (Model 0: *OR* = 1.7, 95% *CI*: 1.4–2.0; *P* < 0.001; Model 1: *OR* = 1.3, 95% *CI*: 1.0–1.5; *P* = 0.029), and the association with occasional snoring was observed only for iIGT (Model 0: *OR* = 1.2, 95% *CI*: 1.1–1.3; *P* < 0.001; Model 1: *OR* = 1.1, 95% *CI*: 1.0–1.3; *P* = 0.012). While the association was preserved in iIFG (*OR*: 1.3, 95% *CI*: 1.0–1.6; *P* < 0.001) and iIGT (*OR*: 1.3, 95% *CI*: 1.2–1.5; *P* < 0.001) after adjusting more confounders in Model 2, the associations of occasional snoring with IFG, IGT, and IFG + IGT as well as habitual snoring with IFG + IGT were no longer significant [Figure 1b-1d].

The interactions between snoring frequency and all confounders mentioned above were tested. A trend for interaction ($P_{interaction} = 0.006$) was observed between snoring frequency and TC. In the subsequent multivariate analysis of TC-stratified subgroups (TC ≥5.6 mmol/L defined as hypocholesterolemia), the association of snoring frequency with prediabetes was observed only between habitual snoring and prediabetes in the non hypocholesterolemia subgroup using Model 2, but not in the hypocholesterolemia subgroup [Table 2].

DISCUSSION

In this cross-sectional study of 13,592 participants without diabetes who aged 40 years and older and were from three communities of Beijing, we found that self-reported habitual snoring was associated with a 30% increased risk of prediabetes, after adjusting for the diabetes and sleep-related confounders in the multivariable models, as well as its subtypes (iIFG and iIGT, but not IFG + IGT). When stratified by TC, this association between habitual snoring and prediabetes increased to 40% in individuals with nonhypercholesterolemia, but disappeared in individuals with hypercholesterolemia.

Several studies in the past have shown the relationship between snoring and diabetes,[14-16] but few studies have demonstrated an association between snoring and prediabetes. Using multivariate analysis, the NHANES study with 5685 individuals aged ≥20 years old concluded that participants with occasional and frequent snoring had higher odds of prediabetes (*OR* = 1.24, 95% *CI*: 1.04–1.47; and *OR* = 1.21, 96% *CI*: 1.02–1.43, respectively) than those who never snored.[18] Compared to this study, we found slightly higher odds (*OR* = 1.3, 95% *CI*: 1.1–1.4) of habitual snoring with prediabetes and disappearance of the association between occasional snoring, which may be explained by the racial differences between American and Chinese populations, and higher number of participants (*n* = 13,592) who were older (≥40 years) in our study. In addition, we adjusted sleep-related factors (sleep quality and duration) in the multivariable model.

Table 1: Baseline characteristics of participants who aged ≥40 years old from three communities of Beijing with different snoring frequency

Characteristics	Total (*N* = 13,592)	Snoring frequency			Statistical value	*P**
		Never (*n* = 4521)	Occasional (*n* = 5617)	Habitual (*n* = 3454)		
Age (years)	56.8 ± 7.9	56.4 ± 8.3	56.9 ± 7.8	57.3 ± 7.5	13.8	<0.001
Men, *n* (%)	4545 (33.4)	1069 (23.6)	1819 (32.4)	1657 (48.0)	273.2	<0.001
Education status (years), *n* (%)					1.4	0.021
<6	875 (6.4)	86 (1.9)	75 (1.3)	46 (1.3)	–	–
6–9	4405 (32.4)	217 (4.8)	289 (5.1)	162 (4.7)	–	–
>9	8297 (61.1)	1386 (30.7)	1843 (32.8)	1176 (34.1)	–	–
Current smoker, *n* (%)	2610 (19.2)	597 (13.2)	1037 (18.5)	976 (28.3)	147.7	<0.001
Alcohol drinker, *n* (%)	3897 (28.7)	944 (20.9)	1610 (28.7)	1343 (38.9)	158.2	<0.001
Tea drinker, *n* (%)	8410 (61.9)	2697 (59.7)	3472 (61.8)	2241 (64.9)	11.2	<0.001
Depressive scores	1.8 ± 17.3	1.8 ± 15.7	1.9 ± 21.2	1.9 ± 11.3	0.1	0.946
DNS (h)	7.5 ± 1.1	7.5 ± 1.1	7.5 ± 1.1	7.4 ± 1.1	6.3	0.003
Sleep quality, *n* (%)					4.5	0.003
Good sleeper	11,792 (87.1)	3959 (87.9)	4814 (86.0)	3019 (87.8)	–	–
Bad sleeper without hypnotics	1692 (12.5)	520 (11.5)	762 (13.6)	410 (11.9)	–	–
Bad sleeper with hypnotics	54 (0.4)	25 (0.6)	21 (0.4)	8 (0.2)	–	–
FHD, *n* (%)	3170 (23.3)	990 (21.9)	1314 (23.4)	866 (25.1)	5.5	0.004
Prediabetes, *n* (%)	4205 (30.9)	1209 (26.7)	1703 (30.3)	1293 (37.4)	53.7	0.001
BMI (kg/m²)	25.5 ± 3.4	24.6 ± 3.2	25.5 ± 3.4	26.7 ± 3.4	397.8	<0.001
WC (cm)	83.2 ± 8.9	80.5 ± 8.6	83.3 ± 8.8	86.5 ± 8.6	472.1	<0.001
HC (cm)	94.4 ± 6.9	92.9 ± 6.5	94.7 ± 7.0	95.7 ± 7.0	176.4	<0.001
SBP (mmHg)	130.5 ± 16.5	128.2 ± 16.8	130.5 ± 16.3	133.5 ± 16.2	103.5	<0.001
DBP (mmHg)	75.6 ± 9.7	74.2 ± 9.5	75.7 ± 9.6	77.2 ± 10.0	101.0	<0.001
HTN, *n* (%)	5482 (40.4)	1560 (34.6)	2176 (38.8)	1746 (50.7)	111.6	<0.001
CVD, *n* (%)	12,376 (91.1)	4170 (92.2)	5155 (91.8)	3051 (88.3)	21.4	<0.001
FBG (mmol/L)	5.4 ± 0.5	5.3 ± 0.5	5.4 ± 0.5	5.5 ± 0.5	68.4	<0.001
PBG (mmol/L)	6.8 ± 1.7	6.7 ± 1.7	6.8 ± 1.7	7.0 ± 1.8	48.6	<0.001
HbA1c (%)	5.76 ± 0.47	5.74 ± 0.48	5.75 ± 0.47	5.82 ± 0.46	32.1	<0.001
ALT (mmol/L)	21.1 ± 14.3	19.9 ± 12.9	21.1 ± 15.9	22.8 ± 13.8	21.0	<0.001
AST (mmol/L)	21.6 ± 29.7	22.5 ± 48.4	20.9 ± 11.6	21.3 ± 8.3	1.8	0.170
Cr (mmol/L)	67.7 ± 18.0	65.5 ± 13.8	67.8 ± 20.6	70.3 ± 17.9	70.7	<0.001
TC (mmol/L)	5.2 ± 1.3	5.2 ± 1.0	5.2 ± 1.0	5.2 ± 1.0	0.6	0.883
TG (mmol/L)	1.5 ± 1.1	1.4 ± 1.0	1.6 ± 1.3	1.7 ± 1.2	55.3	<0.001
HDL-C (mmol/L)	1.5 ± 0.4	1.6 ± 2.3	1.4 ± 0.5	1.4 ± 0.5	110.3	<0.001
LDL-C (mmol/L)	3.2 ± 0.8	3.2 ± 0.8	3.2 ± 0.8	3.2 ± 0.9	2.3	0.122

Data are presented as mean ± SD or *n* (%). *Compared between different snoring frequency groups. –: Not applicable. DNS: Duration of night sleep; FHD: Family history of diabetes; BMI: Body mass index; WC: Waist circumference; HC: Hip circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HTN: Hypertension; CVD: Cardiovascular disease; FBG: Fasting blood glucose; PBG: Postload blood glucose; HbA1c: Hemoglobin A1c; ALT: Alanine transaminase; AST: Aspartate transaminase, Cr: Creatinine; TC: Total cholesterol; TG: Triglycerides; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; SD: Standard deviation.

Snoring was associated with increased fasting and PBG levels in a few previous studies with individuals who were free of diabetes.[19-22] However, other studies have also shown no significant association between snoring and fasting or PBG levels.[13,23] In our study, snoring was associated with increased risks of iIFG and iIGT subgroups. Considering that iIFG is predominantly associated with hepatic insulin resistance while iIGT is often associated with muscle insulin resistance, we speculated that habitual snoring might have a link to both hepatic and muscle insulin resistance. However, it was surprising that there was no association between snoring and IFG + IGT subgroup which could be explained by the cross-sectional nature of this study.

During the development of diabetes, fasting and postload glucose levels are anomalous, accompanied with an increase in insulin resistance and decrease in β-cell function,[24,25] which are also accounted for the physiopathology of prediabetes.[10] The pathology by which snoring increases the prediabetes risk may be the triggering of metabolic processes involving insulin action. Many studies have confirmed this viewpoint. A study of 11,815 participants without diabetes aged ≥20 years old in the National Health and Nutrition Examination Survey found that snoring frequency was positively associated with increased concentrations of insulin.[23] An analysis of data from 5888 participants of the cardiovascular health study found that snoring, one symptoms of sleep-disordered breathing,
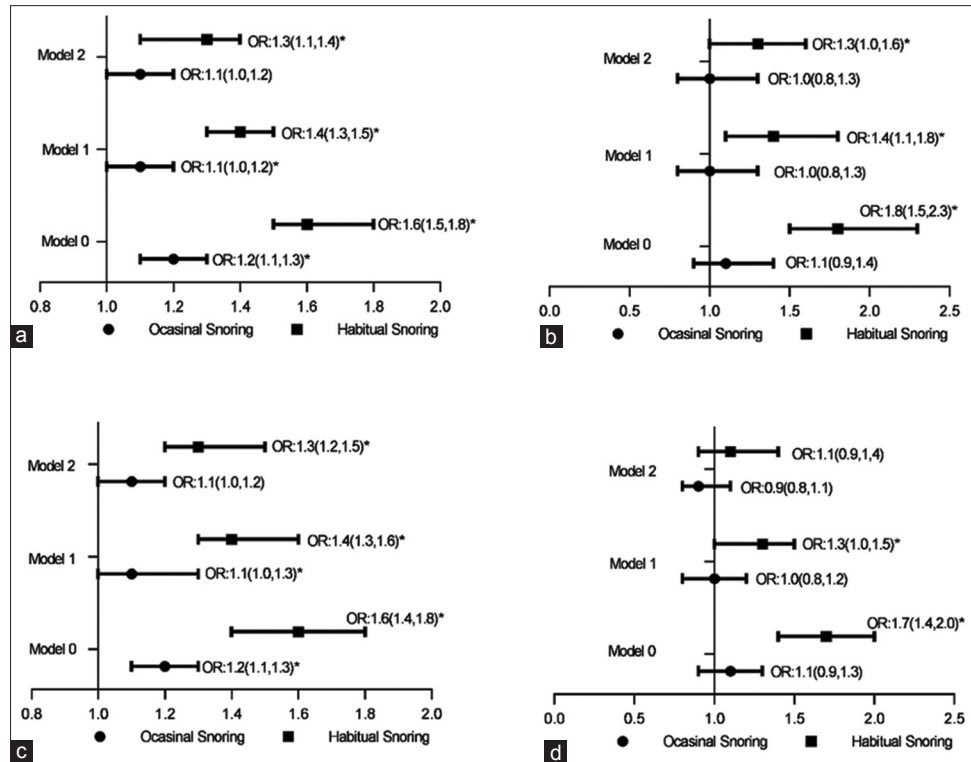
Figure 1: The association of self-reported snoring frequency with prediabetes (a); iIFG (b); iIGT (c); IFG + IGT (d). Model 0: Adjusted for no confounding factors; Model 0: Adjusted for no confounding factors; Model 1: Adjusted for age, gender, and BMI; Model 2: Adjusted for age, gender, BMI, education, WC, HC, WHR, smoke, alcohol drinker, tea drinker, total cholesterol, serum triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, depression status, cardiovascular disease, hypertension, family history of diabetes, sleep quality, and duration of night sleep. *$P < 0.05$. iIFG: Isolated impaired fast glucose; iIGT: Isolated impaired glucose tolerance; IFG: Impaired fasting glucose; IGT: Impaired glucose tolerance; BMI: Body mass index; WC: Waist circumference; HC: Hip circumference; WHR: Waist-to-hip ratio.

Table 2: Multivariate logistic regression models assessing the association between snoring frequency and prediabetes stratified by total cholesterol

Model	Snoring frequency	Prediabetes					
		Nonhypocholesterolemia			Hypocholesterolemia		
		OR	95% CI	P	OR	95% CI	P
Model 0	Never	1.0	–	–	1.0	–	–
	Occasional	1.2	1.1–1.4	<0.001	1.1	1.0–1.3	0.078
	Habitual	1.8	1.6–2.0	<0.001	1.4	1.2–1.7	<0.001
Model 1	Never	1.0	–	–	1.0	–	–
	Occasional	1.1	1.0–1.3	0.030	1.1	0.9–1.2	0.444
	Habitual	1.5	1.3–1.7	<0.001	1.2	1.0–1.5	0.017
Model 2	Never	1.0	–	–	1.0	–	–
	Occasional	1.1	1.0–1.2	0.110	1.0	0.9–1.2	0.684
	Habitual	1.4	1.2–1.6	<0.001	1.1	0.9–1.3	0.238

Hypocholesterolemia: TC ≥5.6 mmol/L. Model 0: Adjusted for no confounding factors; Model 1: Adjusted for age, gender, and BMI; Model 2: Adjusted for age, gender, BMI, education, WC, HC, WHR, smoke, alcohol drinker, tea drinker, TC, serum TGs, HDL-C, LDL-C, depression status, CVD, HTN, family history of diabetes, sleep quality, and duration of night sleep. –: Not applicable. *OR*: Odds ratio; *CI*: Confidence intervals; BMI: Body mass index; HTN: Hypertension; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; WHR: Waist-to-hip ratio; WC: Waist circumference; HC: Hip circumference; TG: Triglyceride; TC: Total cholesterol; CVD: Cardiovascular disease.

was associated with higher lower insulin sensitivity, which was estimated by the Gutt index.[13] Other researches[21,22] also produced the same conclusion that snoring frequency was positively associated with an increase in insulin secretion and resistance. Continuous positive airway pressure (CPAP) therapy is a widely-used treatment in snoring patients. Guo et al.[26] found that CPAP therapy may improving both blood glucose and insulin sensitivity in patient with diabetes and sleep apnea-hypopnea syndrome. Several mechanisms can interpret these associations. Upper airway obstruction caused by habitual snoring could lead to intermittent hypoxia and sleep fragmentation, which may activate the sympathetic

nervous and hypothalamic-pituitary-adrenal axis and increase the catecholamine and cortisol levels respectively, finally resulting in insulin sensitivity and glucose tolerance.[27-32] The activation of pro-inflammatory cytokines induced by hypoxia also plays a role in the development of prediabetes caused by snoring.[33,34]

Dyslipidemia, including TC is known to be a high-risk factor of prediabetes and diabetes. We could not clearly explain the mechanism for the association between snoring and dyslipidemia, but sleep restriction caused by snoring may increase the levels of cortisol and ghrelin, enhance sympathetic response and reduce leptin levels, which could regulate appetite and energy expenditure.[31,35] Our data show that snoring was associated with prediabetes in individuals with nonhypercholesterolemia rather than hypercholesterolemia. This may suggest that the effect of habitual snoring on prediabetes becomes readily measurable only when it is not overshadowed by stronger factors such as hypercholesterolemia.

Strengths of the present study includes the large samples size and the association between snoring and prediabetes were made by TC subgroup analysis. It should be noted that this study had limitations. First, the cross-sectional nature of this study could only find the occasional association; further prospective studies are needed to verify the association between snoring frequency and prediabetes. Second, the status of snoring was obtained from self-reported, only part from their family members, which might underestimate the frequency of snoring. Third, self-reported snoring frequency but not precise clinical measures, such as polysomnography, could result in some statistical error. Although polysomnography could reduce variability in the analysis, it was unavailable for a large epidemiological study.

In conclusion, we found that in individuals free of diabetes, aged ≥40 years old, habitual snoring was associated with prediabetes independent of confounders such as gender, age, BMI, WC, and many other variables. This association was observed only in participants without hypercholesterolemia. Hence, self-reported snoring maybe useful as a low-cost and noninvasive indicator in the screening of individuals who are prone to prediabetes.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med 1998;15:539-53. doi: 10.1002/(sici)1096-9136(199807)15:7<539:aid-dia668>3.0.co;2-s.
2. Forouhi NG, Luan J, Hennings S, Wareham NJ. Incidence of type 2 diabetes in England and its association with baseline impaired fasting glucose: The Ely study 1990-2000. Diabet Med 2007;24:200-7. doi: 10.1111/j.1464-5491.2007.02068.x.
3. Nathan DM, Davidson MB, DeFronzo RA, Heine RJ, Henry RR,
Pratley R, *et al.* Impaired fasting glucose and impaired glucose tolerance: Implications for care. Diabetes Care 2007;30:753-9. doi: 10.2337/dc07-9920.
4. Weng JP, Bi Y. Epidemiological status of chronic diabetic complications in China. Chin Med J 2015;128:3267-9. doi: 10.4103/0366-6999.171350.
5. Plantinga LC, Crews DC, Coresh J, Miller ER 3rd, Saran R, Yee J, *et al.* Prevalence of chronic kidney disease in US adults with undiagnosed diabetes or prediabetes. Clin J Am Soc Nephrol 2010;5:673-82. doi: 10.2215/CJN.07891109.
6. Tesfaye S, Boulton AJ, Dyck PJ, Freeman R, Horowitz M, Kempler P, *et al.* Diabetic neuropathies: Update on definitions, diagnostic criteria, estimation of severity, and treatments. Diabetes Care 2010;33:2285-93. doi: 10.2337/dc10-1303.
7. Gabir MM, Hanson RL, Dabelea D, Imperatore G, Roumain J, Bennett PH, *et al.* Plasma glucose and prediction of microvascular disease and mortality: Evaluation of 1997 American Diabetes Association and 1999 World Health Organization criteria for diagnosis of diabetes. Diabetes Care 2000;23:1113-8. doi: 10.2337/diacare.23.8.1113.
8. Brunner EJ, Shipley MJ, Witte DR, Fuller JH, Marmot MG. Relation between blood glucose and coronary mortality over 33 years in the Whitehall study. Diabetes Care 2006;29:26-31. doi: 10.2337/diacare.29.01.06.dc05-1405.
9. Yang W, Lu J, Weng J, Jia W, Ji L, Xiao J, *et al.* Prevalence of diabetes among men and women in China. N Engl J Med 2010;362:1090-101. doi: 10.1056/NEJMoa0908292.
10. Gu DF, Shi YL, Chen YM, Liu HM, Ding YN, Liu XY, *et al.* Prevalence of chronic kidney disease and prediabetes and associated risk factors: A community-based screening in Zhuhai, Southern China. Chin Med J 2013;126:1213-9. doi: 10.3760/cma.j.issn.0366-6999.20123504.
11. Suwanprathes P, Won C, Komoltri C, Nana A, Kotchabhakdi N, Guilleminault C. Epidemiology of sleep-related complaints associated with sleep-disordered breathing in Bangkok, Thailand. Sleep Med 2010;11:1025-30. doi: 10.1016/j.sleep.2010.04.007.
12. Chuang LP, Hsu SC, Lin SW, Ko WS, Chen NH, Tsai YH. Prevalence of snoring and witnessed apnea in Taiwanese adults. Chang Gung Med J 2008;31:175-81.
13. Strand LB, Carnethon M, Biggs ML, Djoussé L, Kaplan RC, Siscovick DS, *et al.* Sleep disturbances and glucose metabolism in older adults: The cardiovascular health study. Diabetes Care 2015;38:2050-8. doi: 10.2337/dc15-0137.
14. Elmasry A, Janson C, Lindberg E, Gislason T, Tageldin MA, Boman G. The role of habitual snoring and obesity in the development of diabetes: A 10-year follow-up study in a male population. J Intern Med 2000;248:13-20. doi: 10.1046/j.1365-2796.2000.00683.x.
15. Al-Delaimy WK, Manson JE, Willett WC, Stampfer MJ, Hu FB. Snoring as a risk factor for type II diabetes mellitus: A prospective study. Am J Epidemiol 2002;155:387-93. doi: 10.1093/aje/155.5.387.
16. Wu HB, Wang H, Hu RY, Zhong JM, Qian YJ, Wang CM, *et al.* The association between sleep duration, snoring and prevalent type 2 diabetes mellitus with regard to gender and menopausal status: The CKB study in Zhejiang rural area, China. Acta Diabetol 2017;54:81-90. doi: 10.1007/s00592-016-0918-1.
17. Zheng Y, Wang A, Pan C, Lu J, Dou J, Lu Z, *et al.* Impact of night sleep duration on glycemic and triglyceride levels in Chinese with different glycemic status. J Diabetes 2015;7:24-30. doi: 10.1111/1753-0407.12186.
18. Alshaarawy O, Teppala S, Shankar A. Markers of sleep-disordered breathing and prediabetes in US adults. Int J Endocrinol 2012;2012:902324. doi: 10.1155/2012/902324.
19. Facco FL, Grobman WA, Kramer J, Ho KH, Zee PC. Self-reported short sleep duration and frequent snoring in pregnancy: Impact on glucose metabolism. Am J Obstet Gynecol 2010;203:142.e1-5. doi: 10.1016/j.ajog.2010.03.041.
20. Troxel WM, Buysse DJ, Matthews KA, Kip KE, Strollo PJ, Hall M, *et al.* Sleep symptoms predict the development of the metabolic syndrome. Sleep 2010;33:1633-40.
21. Shin C, Kim J, Kim J, Lee S, Shim J, In K, *et al.* Association of habitual snoring with glucose and insulin metabolism in nonobese Korean adult men. Am J Respir Crit Care Med 2005 1;171:287-91. doi: 10.1164/rccm.200407-906OC.

22. Meslier N, Gagnadoux F, Giraud P, Person C, Ouksel H, Urban T, *et al*. Impaired glucose-insulin metabolism in males with obstructive sleep apnoea syndrome. Eur Respir J 2003;22:2122-33. doi: 10.1183/09031936.03.00089902.

23. Ford ES, Wheaton AG, Chapman DP, Li C, Perry GS, Croft JB. Associations between self-reported sleep duration and sleeping disorder with concentrations of fasting and 2-h glucose, insulin, and glycosylated hemoglobin among adults without diagnosed diabetes. J Diabetes 2014;6:338-50. doi: 10.1111/1753-0407.12101.

24. Defronzo RA. Banting lecture. From the triumvirate to the ominous octet: A new paradigm for the treatment of type 2 diabetes mellitus. Diabetes 2009;58:773-95. doi: 10.2337/db09-9028.

25. Tabák AG, Jokela M, Akbaraly TN, Brunner EJ, Kivimäki M, Witte DR. Trajectories of glycaemia, insulin sensitivity, and insulin secretion before diagnosis of type 2 diabetes: An analysis from the Whitehall II study. Lancet 2009;373:2215-21. doi: 10.1016/s0140-6736(09)60619-x.

26. Guo LX, Zhao X, Pan Q, Sun X, Li H, Wang XX, *et al*. Effect of continuous positive airway pressure therapy on glycemic excursions and insulin sensitivity in patients with obstructive sleep apnea-hypopnea syndrome and type 2 diabetes. Chin Med J 2015;128:2301-6. doi: 10.4103/0366-6999.163382.

27. Xie A, Skatrud JB, Puleo DS, Morgan BJ. Exposure to hypoxia produces long-lasting sympathetic activation in humans. J Appl Physiol (1985) 2001;91:1555-62.

28. Nonogaki K. New insights into sympathetic regulation of glucose and fat metabolism. Diabetologia 2000;43:533-49. doi: 10.1007/s001250051341.

29. Hjalmarsen A, Aasebø U, Birkeland K, Sager G, Jorde R. Impaired glucose tolerance in patients with chronic hypoxic pulmonary disease. Diabetes Metab 1996;22:37-42.

30. Follenius M, Brandenberger G, Bandesapt JJ, Libert JP, Ehrhart J. Nocturnal cortisol release in relation to sleep structure. Sleep 1992;15:21-7.

31. Larsen JJ, Hansen JM, Olsen NV, Galbo H, Dela F. The effect of altitude hypoxia on glucose homeostasis in men. J Physiol 1997;504(Pt 1):241-9. doi: 10.1111/j.1469-7793.1997.241bf.x.

32. Stamatakis KA, Punjabi NM. Effects of sleep fragmentation on glucose metabolism in normal subjects. Chest 2010;137:95-101. doi: 10.1378/chest.09-0791.

33. Alberti A, Sarchielli P, Gallinella E, Floridi A, Floridi A, Mazzotta G, *et al*. Plasma cytokine levels in patients with obstructive sleep apnea syndrome: A preliminary study. J Sleep Res 2003;12:305-11.

34. Punjabi NM, Shahar E, Redline S, Gottlieb DJ, Givelber R, Resnick HE; Sleep Heart Health Study Investigators. Sleep-disordered breathing, glucose intolerance, and insulin resistance: The sleep heart health study. Am J Epidemiol 2004;160:521-30. doi: 10.1093/aje/kwh261.

35. Taheri S, Lin L, Austin D, Young T, Mignot E. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. PLoS Med 2004;1:e62. doi: 10.1371/journal.pmed.0010062.