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Letter to the Editor

Habitual snoring and risk of stroke: A meta-analysis of prospective studies

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Habitual snoring (HS), which is defined as snoring more than three nights per week, occurs among approximately 33% of the general population [1]. Emerging evidence suggests that this increase in HS problems may be due to hypertension [2], diabetes mellitus [3], metabolic syndrome [4], and intima-media thickness (IMT) [5]. In addition, there was mounting evidence for an association between HS and cardiovascular and all-cause mortality [6–8]. However, the role of HS in stroke is still uncertain.

Recently, a prospective study found that self-reported snoring was associated with an increase risk of future cardiovascular disease among older adults [9]. However, it remains unclear whether HS independently increases stroke risk, or whether this relationship is confounded by traditional stroke risk factors, the latest published meta-analysis of 8 cohort studies showed a significant positive relationship between self-reported HS and stroke (pooled relative risk = 1.26, 95% confidence interval: 1.11–1.43) [10]. The results showed that habitual snoring was significantly associated with risk of stroke, and the association was stronger in men than in women. This investigation has much practical implication regarding the prevention of stroke.

Snoring is the most important and cardinal manifestations of obstructive sleep apnea (OSA) [11]. Our previous meta-analysis of 10 cohort studies also found a significant association between OSA and the risk of stroke after adjustment of established cardiovascular risk factors (pooled relative risk = 2.10, 95% confidence interval: 1.50–2.93) [12]. Our results were consistent with that of Li et al. [10]. However, the previous meta-analysis found insufficient evidence in the subgroup meta-analyses by stroke subtypes (total stroke versus ischemic stroke versus hemorrhagic stroke), geographical area (United States versus Europe), and duration of follow-up (<10 versus ≥10 years). Thus, to obtain a more comprehensive estimate of the putative influence of habitual snoring on stroke, we conducted a meta-analysis of prospective studies.

This meta-analysis was planned, conducted and reported according to the standards of quality for reporting meta-analyses [13]. We carried out a systematic search to December 2014 using the PubMed, Embase, and ISI Web of Science databases using the following keywords: snoring, snorer, self-reported snoring, stroke, coronary heart disease, coronary artery disease, myocardial infarction, myocardial ischemia, cerebrovascular disorders, cardiovascular disease, heart failure, prospective studies, cohort studies, longitudinal studies, and follow-up studies. There were no language restrictions. Citations selected from the initial search were subsequently screened for eligibility. Studies were included in this meta-analysis if they fulfilled the following criteria: (1) the study of adult patients had a cohort design; (2) the exposed subject was a patient with self-reported habitual snoring; (3) the reported quantitative estimates of the multivariate adjusted relative risks (RRs) and 95% confidence intervals (CIs) for stroke outcomes associated with self-reported habitual snoring, hazard ratio was considered equivalent to RRs. Studies were excluded if they met the following criteria: (1) the study design did not include a cohort (for example, cross-sectional and retrospective case–control studies); and (2) the unadjusted RRs and 95% CIs were reported (for example, just adjusted age or sex).

When the studies did not have stroke subgroup (such as ischemic stroke, hemorrhagic stroke) specific data, we used data from the included studies as an equivalent to total stroke. The RRs were pooled using the random-effects model [14]. All statistical tests were performed in STATA software (version 11.0; Stata Corporation LP, College Station, Texas). *P* values were 2-sided and $P < 0.05$ was considered statistically significant.

The detailed steps of our literature search are shown in Fig. 1. Six cohort studies met the inclusion criteria [6,15–19]. Characteristics of the selected studies were listed in Table 1. The multivariable adjusted RRs of stroke in relation to HS from each study and the combined RR are presented in Fig. 2. Participants with HS, compared with non-snorers,

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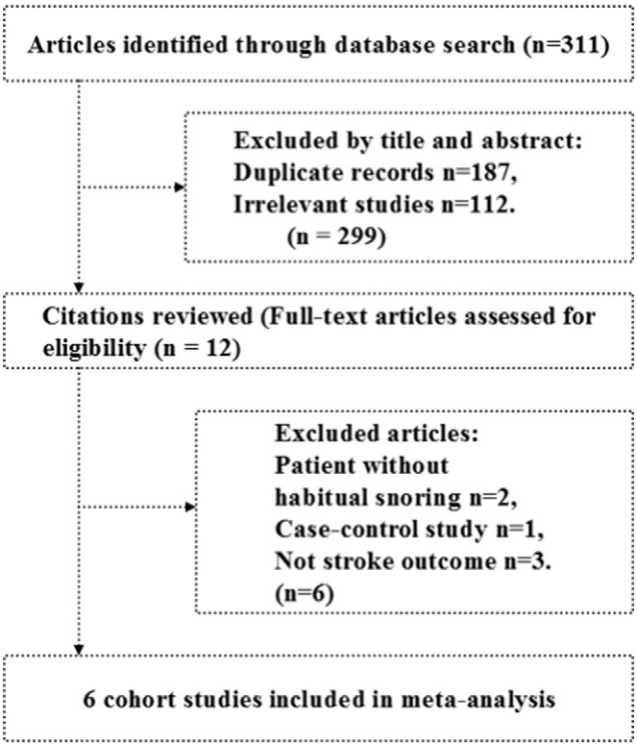

Fig. 1. The process of study selection.

experienced a significant increased risk for development of stroke based on six studies [6,15–19] (combined RR, 1.25; 95% CI, 1.11–1.42). The pooled estimate of multivariate RRs based on two studies [15,17] was 1.48 (95% CI: 1.08–2.04) among men and 1.21 among women (95% CI: 1.05–1.40) [16,19]. The forest plots of multivariable RRs and 95% CI for stroke and HS are showed in Fig. 2. Moreover, we conducted subgroup analyses to further elucidate the effect of HS on stroke risk. Fig. 3 showed the pooled RR for stroke stratified by stroke subgroup, geographical region, and duration of follow-up. Of 6 studies, in most subgroups, HS was associated with an increased risk of stroke. The increased risk was more evident in several strata of study characteristics (Fig. 3).

The current meta-analysis of 6 cohort studies confirmed a modest but statistically significant positive association between HS and risk of stroke after adjustment of established cardiovascular risk factors. Proposed biological mechanisms for HS in stroke also remain to be elucidated, although clinical studies have shown that HS is associated with hypertension, IMT and plaque [2,5], it may link the development of atherosclerosis with the pathogenesis of stroke event. On the other hand, snoring is strongly associated with OSA and may represent early stages of the OSA continuum, it may be an early marker of OSA, an established as a risk factor for stroke [19]. In spite of this, many individuals that snore do not have OSA. Future research should strive to identify the relative impact of sleep symptoms versus true disorders on stroke outcomes and could explore whether effective treatment of HS may prevent or improve the course of stroke.

Conflict of interest statement

None.

Acknowledgments

ZYT and ML conceived and designed the experiments. KL, XWZ and WSH analyzed the data. ML and KL wrote the paper. ML, XWZ and WSH performed the literature search and the data extraction. All authors saw and approved the final version of the manuscript. We thank the editors of the International Journal of Cardiology for editing the manuscript.

Table 1
Characteristic of included prospective studies.

Author	Publication, (year)	Country/ population	Sex	Sample size (n)	Event (n)	Follow-up, (year)	Age, (year)	Outcome assessment	Exposure categories	HR or RR	Adjusted variables
Koskenvuo et al. [15]	1987	Finland/Europe	M	4388	42	3	40–69	ICD-8 and hospital records	Frequent/occasional or none	1.40 (0.82, 2.38) for ischemic stroke	Age, BMI, history of HT, smoking, alcohol, adjustment age for mortality
Jennum et al. [6]	1994	Denmark/Europe	F M	804	60	6	70	ICD-8 and hospital records	Snorer/Non	1.26 (0.71, 2.29)	Sex, tobacco, alcohol, BMI, social class, PA, DBP, HDL
Hu et al. [16]	2000	United States	F	71779	398	8	40–65	ICD-8 and hospital records	Regularly/never	1.35 (0.91, 1.99); 1.42 (0.88, 2.29) for ischemic stroke; 1.80 (0.85, 3.83) for hemorrhagic stroke	Age, time, BMI, cigarette, menopausal, history of MI, diabetes, and HC, alcohol, vitamin, PA, sleep positions and hours
Elwood et al. [17]	2006	UK/Europe	M	1874	107	10	55–69	ICD-10	Frequent/none	1.53 (1.01, 2.23) for ischemic stroke	Age, social class, smoking habit, alcohol consumption, BMI, neck circumference
Yeboah et al. [18]	2011	United States	F M	5338	76	7.5	45–84	By a committee and death certificate	Regularly/never	1.24 (0.73, 2.13)	Age, sex, race, BMI, smoking, diabetes, TC, HDL, SBP, BP medication, stain, benzodiazepine, alcohol use
Sands et al. [19]	2013	United States	F	42244	993	14.8	50–79	By medical records and death certificate	Frequent/none	1.19 (1.02, 1.40) for ischemic stroke	Age, race, education, income, smoking, PA, alcohol, depression, diabetes, BP, BMI, WHR, HC

ICD: International Classification of Diseases; CVD: cardiovascular disease; IHD: ischemic heart disease; MI: myocardial infarction; F: female; M: male; HR: hazard risk; RR: relative risk; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; WHR: waist-to-hip ratio; BP: blood pressure; HT: hypertension; HC: hypercholesterolemia; TC: total cholesterol; HDL: high density lipoprotein; PA: physical activity.

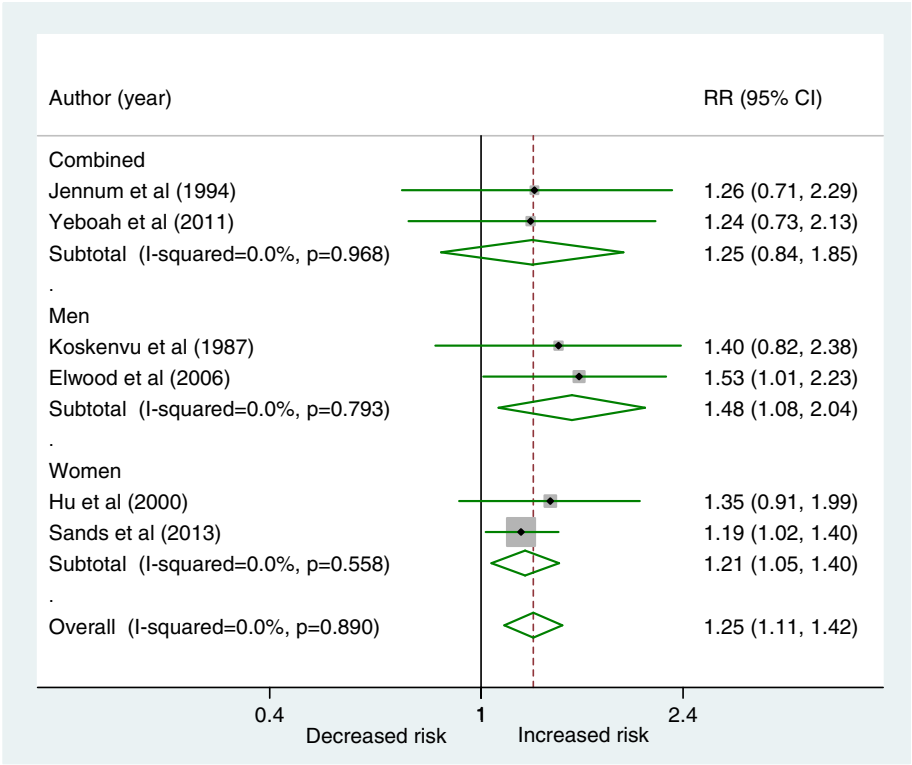

Fig. 2. Random effects analysis of fully adjusted studies for the association between HS and stroke. Combined: studies which did not have sex specific data. HS: habitual snoring.

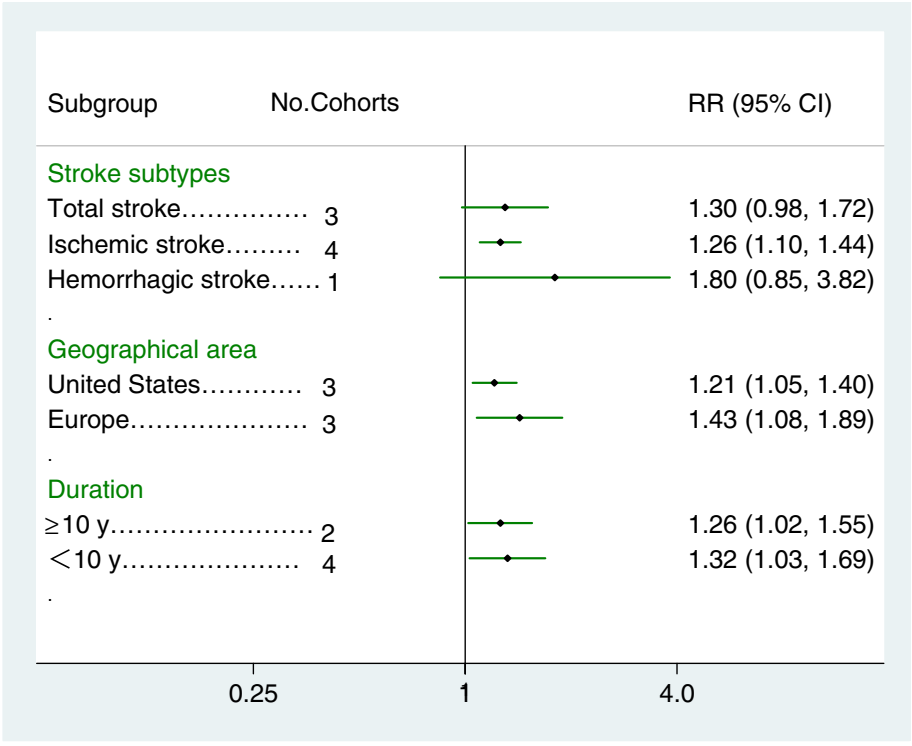

Fig. 3. Analyses of subgroups relating HS to stroke. HS: habitual snoring.

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