

Gender and the Systemic Hypertension–Snoring Association: a Questionnaire-based Case-control Study

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Since the role of gender in the association between hypertension and snoring is unknown, we studied it while accounting for age and body mass index (BMI) as confounding variables. A questionnaire on snoring was administered to 90 hypertensive (HT) subjects (45 men and 45 women) and to 90 normotensive (NT) subjects matched for gender, age and BMI. As expected, snoring was more commonly reported by men than by women, but no significant difference was found between HT and NT men, irrespective of age. Conversely, heavy snoring was more frequently reported by HT than NT women; habitual snoring was more common among young (age < 50 years) HT than NT women; and heavy snoring was more common among older (age \geq 50 years) HT than NT women. These data suggest an effect of gender on the hypertension–snoring association: in men, snoring may be accounted for by age and BMI whether or not hypertension is present, whereas in women the natural history of snoring appears different and more severe in HT than in NT. Although the mechanism(s) responsible for the differences between men and women are obscure at present, gender may be an important variable in the systemic hypertension–snoring association. *Key words:* age, gender, hypertension, snoring

INTRODUCTION

Although the association between snoring and systemic arterial hypertension is under intense debate, its possible pathogenesis remains unclear. In most epidemiological studies, the prevalence of hypertension in populations of snorers is investigated [1–12], whereas the prevalence of self-reported snoring or other sleep disorders of breathing in hypertensive subjects is examined less frequently and with varying results [13–20]. The issue about the relationship between snoring and hypertension is complicated by two major factors—age and overweight—possibly increasing the risk for both snoring and hypertension. Although these factors are taken into consideration in almost all epidemiological studies on snorers, different conclusions are reported: snoring has been found either to be a risk factor for hypertension independently of obesity and age [1–4, 10], or to have no independent effect [5–8, 11, 12]. On the other hand, in hypertensive subjects, hypertension is not significantly associated with snoring [15, 19], while the prevalence of sleep respiratory disorders is reported either higher than [14–17] or similar to [19, 20] that observed in normotensive subjects.

Gender may also influence the relationship between snoring and hypertension, as suggested by some studies. The snoring–hypertension relationship, analysed for

snoring men and women separately [2, 3], appears stronger in women, but no information is available from these studies on sleepiness and other symptoms of sleep apnea syndromes. Another epidemiological study focusing on snoring women [10], but not including men as controls, finds a much stronger association between snoring and hypertension in women than previously reported in a study of males [4]; however, the studied women were on average heavier than the previously studied men. Most papers published on hypertensive subjects consider only men [15, 20]; in those studies in which women are included in the sample, the women are not considered separately from men and no weight-matched controls are provided [13, 14]. In summary, some data suggest that gender plays a role, possibly affecting the association between hypertension and snoring, but most studies overlook the problem, or consider it a side issue. In addition, problems such as sample size, or other methodological issues prevent a definite interpretation of the available data.

The aim of this study was to evaluate whether gender may influence the relationship between snoring and hypertension. For this purpose, we investigated if hypertensive and normotensive subjects, carefully matched for gender, age and body mass index (BMI) in a case-control study design, reported a different prevalence of snoring and other sleep apnea symptoms.

METHODS

Hypertensive men and women undergoing periodic follow-up visits to the hypertension clinics of two different hospitals in Palermo were studied. Among them, 8 men and 7 women were newly diagnosed hypertensive patients. Medical records were available with blood pressure (BP) for the other hypertensive subjects before initiation of antihypertensive treatment and the pharmacological treatment at the time of each visit. BP level before initiation of treatment was considered either as the average of four measurements taken in a resting condition in two different days, 2 weeks apart, or, when available, as the average of measurements performed during the previous 3 months and recorded in a diary. Hypertension was classified according to the WHO-ISH criteria [21] as a BP level higher than 140 mmHg systolic or 90 mmHg diastolic. The patients were interviewed before one of their visits, their height, weight and neck circumference being measured at the same time. Drugs taken by the patients at the time of the interview included alpha and beta blockers, calcium antagonists, diuretics, angiotensin converting enzyme (ACE) inhibitors, benzodiazepines. Benzodiazepines were mostly prescribed for treatment of anxiety; no other drugs were prescribed for treatment of insomnia. Normotensive subjects were recruited in the ophthalmology, orthopaedics and gynaecology outpatient clinics of the same hospitals. Subjects were classified as normotensive if they had no history of hypertension and their BP measured before the administration of the questionnaire was ≤ 140 mmHg systolic and ≤ 90 mmHg diastolic. Hypertensive and normotensive subjects were matched in a case-control fashion on the basis of the following criteria: same gender, age interval ≤ 5 years, BMI difference ≤ 3 kg/m², selection from the same hospital. Neck circumference was measured and normalized as percent of predicted neck circumference (NC%) according to the method of Davies and Stradling [22]: $NC\% = 100 * \text{neck circumference mm} / (0.55 * \text{height cm} + 310)$.

The questionnaire on snoring and sleep apnea symptoms was based on the following main questions:

1. Do you snore often?
2. Do you usually snore heavily?
3. Do you usually feel sleepy during the day on the following occasions: (a) after lunch, (b) while reading or watching TV, (c) during social activities, (d) while driving, (e) while working?
4. Do you usually wake up at night to urinate?
5. Are apneas observed during your sleep by your bed-partner?

We also enquired about smoking habits (smoking, ex smoking, non-smoking) and alcohol consumption. Subjects with an alcohol intake of >30 ml ethanol/day were excluded from the study.

Subjects who answered yes to the first two questions were considered as habitual snorers and heavy snorers, respectively. They were considered sleepy if they reported somnolence in at least one of the considered conditions except after lunch. "Don't know" was considered a negative answer.

Statistical analysis

Numerical variables (age, BMI) are reported as means \pm SD. Two-tailed paired Student's *t*-test was applied to compare age, BMI and NC% in normotensive and hypertensive subjects of the same gender, whereas an unpaired *t*-test was used to compare the same variables between the subjects of the two genders.

The chi-square test was used to evaluate differences in the frequency of somnolence and nocturia between snorers and non-snorers, or heavy snorers and remaining subjects, respectively. The same test was applied to compare snoring and heavy snoring frequency between individuals of different age, BMI and NC%. A $p < 0.05$ was considered significant.

Odds ratio and confidence limits for snoring and heavy snoring between normotensive and hypertensive subjects of the same gender were calculated according to Woolf's method.

RESULTS

Forty-five couples of matched hypertensive-normotensive individuals for each gender were studied (altogether 180 subjects). Men and women did not differ in age (men 48.8 \pm 12.0; women 49.3 \pm 10.2 years) or BMI (men 28.4 \pm 3.2; women 27.5 \pm 4.6 kg/m²), while NC% was higher in men than in women (105.7 \pm 7.6 vs 93.8 \pm 7.2%, $p < 0.001$). Almost all patients examined were under treatment for hypertension, often with two or more drugs.

Characteristics of the subjects according to gender and BP are listed in Table I. In both genders, there was no difference in age and BMI between hypertensive and normotensive subjects. NC% was similar in normotensive and hypertensive men, but was higher in normotensive than in hypertensive women ($p < 0.01$). Smokers, ex-smokers and non-smokers were similarly distributed among hypertensive and normotensive subjects within each gender. Witnessed apnoeas during sleep were reported only by 8 men and 8 women (in both genders, 4 normotensive controls and 4 hypertensive subjects).

Only four subjects gave a "don't know" answer to question 1 (one hypertensive man; one normotensive and two hypertensive women); "don't know" answers to question 2 were given by 12 subjects (1 normotensive

Table I. Characteristics of the subjects according to gender and blood pressure

	Men			Women		
	NT	HT	<i>p</i>	NT	HT	<i>p</i>
BP syst* (mmHg)	128.6 ± 14	174.6 ± 26	<0.001	120.6 ± 14	168.6 ± 28	<0.001
BP diast* (mmHg)	75.6 ± 10	102.6 ± 12	<0.001	73.6 ± 10	101.6 ± 18	<0.001
Age (years)	49.1 ± 12.0	48.6 ± 12.1	NS	49.3 ± 9.9	49.2 ± 10.6	NS
BMI (kg/m ²)	28.1 ± 3.2	28.6 ± 3.2	NS	27.4 ± 4.7	27.6 ± 4.6	NS
NC (% predicted)	105.2 ± 8.7	106.6 ± 6.3	NS	95.3 ± 6.7	92.3 ± 7.4	<0.01
Non-smokers	14	12		24	29	
Ex-smokers	15	16	NS	8	10	NS
Smokers	16	17		13	6	

HT = hypertensive; NT = normotensive.

*BP values in HT are those measured before institution of anti-hypertensive therapy.

and 1 hypertensive man; 5 normotensive and 5 hypertensive women). In summary, "don't know" answers were relatively few, and similarly distributed between normotensive and hypertensive subjects in each gender.

In the whole sample, snoring was more frequently reported by men than by women ($p < 0.01$); it was more commonly reported by subjects ≥ 50 years old than by the younger ones ($p < 0.05$), and whose NC% was $>100\%$ ($p < 0.01$) (Fig. 1). Similarly, heavy snoring was more frequently reported by men ($p < 0.01$) and was more represented among subjects ≥ 50 years old, with BMI ≥ 28 kg/m² and whose NC% was $>100\%$ ($p < 0.05$) (Fig. 2). Daytime sleepiness and nocturia were significantly more common among heavy snorers than among

the rest of the sample ($p < 0.01$ and < 0.02 , respectively); conversely, only nocturia ($p < 0.05$), not sleepiness ($0.1 > p > 0.05$), was significantly more frequent among habitual snorers than among non-snorers (Fig. 3). The relationship between snoring and somnolence was not affected by benzodiazepine intake: benzodiazepines were taken by 9.9% habitual snorers vs 15.9% non-snorers, and by 6.6% heavy snorers vs 15.3% of the other subjects.

Hypertensive heavy snorers of both genders used more drugs than normotensives, particularly beta-blockers and ACE inhibitors (Table II).

Habitual snoring was similarly reported by hypertensives and normotensives of both genders (odds ratio = 1.11 among men, 1.42 among women, Table

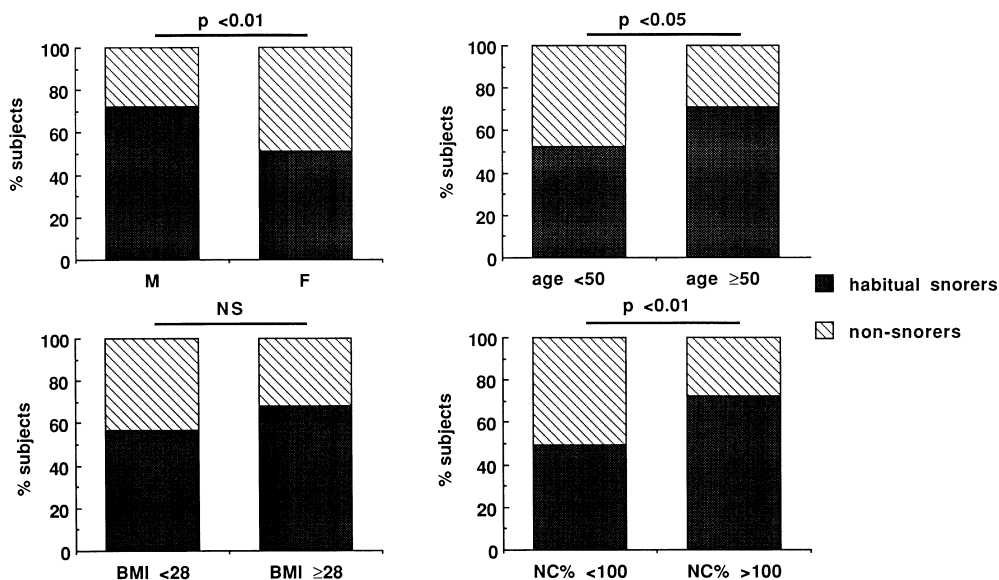


Fig. 1. Differences in the prevalence of self-reported habitual snoring among the 180 interviewed subjects according to gender, age, body mass index and neck circumference.

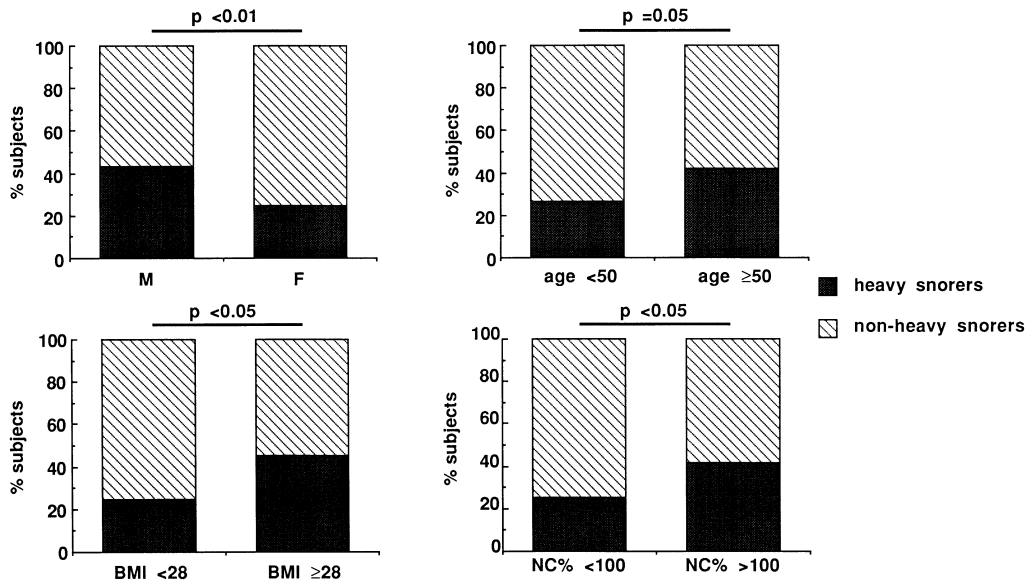


Fig. 2. Differences in the prevalence of self-reported heavy snoring among the 180 interviewed subjects according to gender, age, body mass index and neck circumference.

III); conversely, heavy snoring was more common in hypertensive than in normotensive subjects among women, but not among men (odds ratio: 2.09 among women; 1.31 among men; Table III).

The samples were also analysed according to age < and ≥50 years (Table III). Among women <50 years of age, more hypertensive than normotensive subjects reported

snoring often, with a similar proportion of hypertensive and normotensive individuals reporting snoring heavily. Conversely, among women ≥50 years a similar proportion of hypertensive and normotensive subjects reported snoring often, while more hypertensive than normotensive subjects reported snoring heavily. No difference in self-reported snoring or heavy snoring was observed

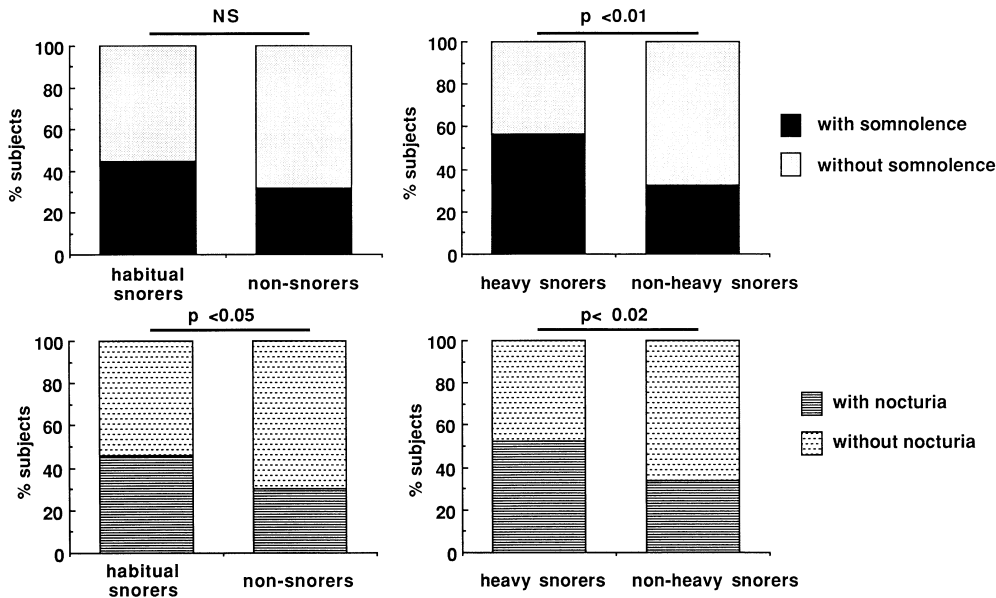


Fig. 3. Difference in the prevalence of somnolence (upper panels) and nocturia (lower panel) among habitual snorers vs non-snorers (left panels) and heavy snorers vs the subjects who either did not snore or did not snore heavily (right panels).

Table II. Number of hypertensive subjects taking different classes of drugs in each gender

	Men		Women	
	Heavy snorers <i>n</i> = 21	Others <i>n</i> = 24	Heavy snorers <i>n</i> = 14	Others <i>n</i> = 31
Beta-blockers	6	6	8	13
Ca-antagonists	8	6	3	7
ACE inhibitors	9	2	5	4
Diuretics	8	3	7	4
Other antihypert	4	2	0	5
Benzodiazepines	0	5	5	9

between hypertensive and normotensive men, either < or \geq 50 years old.

DISCUSSION

This is the first study on hypertensive subjects in which the association between arterial hypertension and snoring has been investigated in a sample including a similar number of men and women and not one exclusively or almost exclusively comprised of male individuals. Besides, each hypertensive subject was matched for gender, age and BMI with a normotensive one. Because age and BMI are the most important confounding factors complicating the interpretation of the well-known association between snoring and hypertension, our study was designed to evaluate the role of gender in the relationship between snoring and hypertension, an issue overlooked in previous studies.

Our data confirmed that snoring is strongly linked to age, body weight and neck circumference [1–4, 6, 10, 23, 24], and is more often reported by men than by women [1–3, 6, 23, 25]. The new finding was that the relationship between snoring and hypertension differed between men and women: hypertensive women reported heavy snoring

more commonly than normotensive women matched for age and BMI, whereas hypertensive and normotensive men showed no difference. Besides, a clear trend to an association between habitual snoring and hypertension was observed in women <50 years old, while hypertension was associated with heavy snoring in older women. Instead, rarely did normotensive women report habitual snoring before the age of 50, or report heavy snoring at any age. These data suggest that the natural history of snoring may differ between hypertensive and normotensive women: in the hypertensives, snoring seems first to occur at a young age, and could later become heavy; in the normotensives, snoring probably first occurs only at an advanced age, and would not become particularly intense. Among men, no relationship between snoring and hypertension was apparent at any age.

Our data are based on subjective reports of symptoms and not on instrumental recordings. Although reliability of self-reported snoring was found to be poor [26], especially among women [27, 28], we believe that our data may indicate real trends. In each couple of subjects (hypertensive and control), we matched not only gender, age and BMI, but also the hospital they attended, suggesting that sampling did not differ depending on social conditions. Therefore, we have no reason to believe that hypertensive women referred their snoring symptoms differently from the normotensive controls. In addition, similarity of results from subjects attending two different town hospitals seems to strengthen our findings. Furthermore, sleepiness and nocturia, which are known often to be associated with snoring [29–33], were more common among self-reported heavy snorers, supporting the notion that the snoring symptom was reported with accuracy by our subjects. Benzodiazepines were used less by habitual and heavy snorers than by the other subjects: therefore, the relationship between snoring and somnolence was unlikely to be mediated by benzodiazepine intake.

Anti-hypertensive drugs may have affected the occurrence and characteristics of snoring. Little is known about the effects of these drugs on respiration during sleep [34],

Table III. Differences between normotensive and hypertensive subjects for self-reported habitual and heavy snoring according to gender and age

		All men	All women	Men <50 years old	Women <50 years old	Men \geq 50 years old	Women \geq 50 years old
Habitual snoring	OR	1.11	1.42	0.94	2.83	0.63	0.69
	CI	0.44–2.77	0.61–3.26	0.27–3.29	0.88–9.12	0.18–2.25	0.40–2.48
Heavy snoring	OR	1.31	2.09	1.54	1.67	1.18	2.88
	CI	0.57–3.03	0.78–5.61	0.45–5.26	0.35–7.85	0.38–3.74	0.75–11.1

O.R. = odds ratio.

C.I. = confidence intervals.

and even less about the interaction between different drugs. The great variety of drugs taken by the hypertensive patients made it impossible to perform a statistical comparison between individuals under different treatments. In our sample, heavy snorers took more drugs than the other hypertensive subjects, particularly beta-blockers, ACE inhibitors and diuretics, but this occurred in both genders. Both an improvement and a worsening in respiration during sleep have been reported during beta-blocker therapy, whereas an improvement has been described with some ACE inhibitors [34]. In summary, the association between heavy snoring in hypertensive women did not appear as a consequence of drug intake. However, the higher use of antihypertensive drugs in heavy snorers of both genders may suggest that hypertension in subjects with upper airway obstruction during sleep could be harder to treat, as already suggested [18]. Further studies are necessary to examine this issue in detail.

More men than women smoked. This may have contributed to the higher prevalence of snoring in the male gender [23, 24, 35]. However, within each gender a similar number of smokers was represented among normotensive and hypertensive subjects. Therefore, smoking was unlikely to contribute to the higher prevalence of heavy snoring among hypertensive than normotensive women.

A limitation of this questionnaire-based study is that it could not identify the subjects where snoring was a symptom of the obstructive sleep apnea syndrome (OSAS). Snoring without apneas and OSAS may represent two different stages of a similar abnormality, whose degree of severity is influenced by ageing and increasing weight [36]. In fact, the narrowing of the upper airway during sleep, initially manifested as continuous snoring, may evolve towards complete obstruction, usually separated by heavy intermittent snoring. Among young women, most habitual snorers did not report heavy snoring; on the other hand, only self-reported heavy snoring was found to be associated with sleepiness, which is a common symptom of OSAS. This suggests that habitual light snoring could be related to milder sleep breathing disorders than heavy snoring. Therefore, even mild degrees of sleep-related breathing disorders could be significantly associated with hypertension in young women. We do not know whether these mild disorders are represented by paucisymptomatic obstructive apneas or just by snoring. Previous studies have demonstrated that snoring is a risk factor for hypertension only in subjects with OSAS [37–39]; however, the effects of age and BMI, although accurately studied, were not analysed separately for genders, so a difference between men and women could have been missed. More recently, snoring without apneas was found to be a risk factor for hypertension when associated with sleep fragmentation [40]. Unlike our investigation, the purpose of those

studies was to assess the role of snoring or sleep apnea as risk factors for hypertension, not the difference between hypertensives and normotensives in snoring symptoms.

The reason(s) why there may be a relationship between hypertension and snoring in women but not in men is unclear. We speculate that modifications in hormone levels observed in OSAS [41–43] may be present to some extent in all snorers, and interact differently with blood pressure regulation in men and women. Such interaction could result in an augmented risk for hypertension only in women.

We conclude that there is an association between hypertension and snoring in the female but not in the male gender. This association is particularly evident for heavy snoring. Heavy snoring was associated with sleepiness and nocturia, and could have been a symptom of OSAS. However, since hypertension and habitual snoring appeared associated in women <50 years of age, it is possible that in these subjects even snoring without apneas is a significant correlate of hypertension.

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