Prevalence of sleep apnoea and snoring in hypertensive men: a population based study

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Background: Several studies have reported an association between sleep disordered breathing (SDB) and hypertension (HT) but there is still a debate as to whether this is an effect of confounders. Some researchers have found an age dependent relationship between SDB and HT with higher risk at lower ages. A case-control study was performed in hypertensive men and non-hypertensive male controls matched for age and body mass index to assess whether there is an independent association between SDB and HT. If so, we further wanted to investigate whether this effect is age dependent.

Methods: An overnight sleep study was performed in a population based, age stratified sample of 102 hypertensive men aged 43–82 years and 102 non-hypertensive controls.

Results: Hypertensive subjects had a significantly higher prevalence of SDB than non-hypertensive subjects (apnoea-hypopnoea index (AHI): 10.8 ± 7.3; desaturation index (DI): 8.5 ± 5.2; AHI >10: 37% ± 24%, p<0.05; DI >10: 29% ± 12%; lowest desaturation: mean (SD) 81.9 (7.3) vs 84.7 (6.1), p<0.01). After adjusting for neck circumference and physical inactivity, DI and lowest desaturation were still independent predictors of HT with adjusted odds ratios of 2.3 (95% CI 1.0 to 5.3) and 0.94 (95% CI 0.89 to 0.99), respectively. When the subjects were split into two groups according to age (<60 and ≥60 years), the influence of DI >10 on HT was strongest in the younger men (adjusted OR 4.3 (95% CI 1.0 to 19.3) vs 2.1 (95% CI 0.7 to 6.5)) and the association between minimum oxygen saturation (SaO2) and HT reached statistical significance in the younger men only.

Conclusion: SDB is more prevalent in men with HT than in controls. DI >10 and lowest desaturation are independent predictors of HT irrespective of confounders. The results indicate that the influence of SDB on HT is more pronounced in younger and middle aged men than in those above 60 years.

Obstructive sleep apnoea (OSA) is common in the community. In a middle aged population 24% of men and 9% of women suffer from OSA when defined as at least five respiratory pauses per hour of sleep. About 20% of subjects with OSA report daytime sleepiness and thereby fulfill the treatment criterion for obstructive sleep apnoea syndrome (OSAS). The importance of investigating the association between sleep related breathing disorders and cardiovascular disease is stressed by reports of a high prevalence of sleep apnoea among patients with hypertension (HT) and coronary artery disease, as well as an increased mortality in patients with sleep apnoea. Whether this is a true causal relationship or whether it is partly or completely caused by confounding is still a matter of debate.

Several studies have reported an association between OSA and HT, but no independent relationship has been found by others. The inconsistencies in the results are probably due to differences in the methods used and populations studied, including failure to control for confounding factors such as age, sex, and obesity.

In some epidemiological studies the association between snoring and HT and between sleep apnoea and HT was age dependent, with an increased risk in younger people.

METHODS

Study population

The aim of this study was to determine whether the prevalence of snoring and respiratory events (apnoeas, hypopnoeas and desaturations) during sleep was different in hypertensive men than in controls matched for age and body mass index (BMI). If so, we further wanted to analyse whether this difference is age dependent. A population based, age stratified case-control study with overnight sleep study was performed.

In 1984 a random sample of 4021 men aged 30–69 years drawn from the population registry of the city of Uppsala, Sweden were sent a postal questionnaire which was answered by 3201 (79.6%). In a 10 year follow up study in 1994 the 2975 men still alive from the responders in 1984 received a new questionnaire. After two reminders, 2668 men (89.6%) aged 40–79 years had returned acceptably answered questionnaires. Based on these answers, 270 men were classified as hypertensive and 2277 as non-hypertensive. To avoid the age distribution being too skewed, age stratification was performed with 10 year age strata. The aim was to include 120 hypertensive subjects and 120 non-hypertensive controls (30+30 subjects aged 40–49, 40+40 aged 50–59, 30+30 aged 60–69, and 20+20 in the 70–79 age stratum). Because of the relative lack of hypertensive subjects in the lower age strata, we were only able to include 26 hypertensive men aged 40–49 years. A total of 116 hypertensive men and 116 non-hypertensive controls were enrolled in the sleep study. The age stratification was made from the age in 1994. Age data presented here are for the age at the date of the sleep study.

Definition of hypertensive and non-hypertensive subjects

Based on the answers to the 1994 questionnaire, the subjects were classified as hypertensive if they (1) answered “yes” to the question “Do you have high blood pressure?” or (2) reported attending regular medical check ups for hypertension and (3) reported using any antihypertensive medication. Non-hypertensive subjects were defined as those who answered “no” to the question on blood pressure and who reported no regular medical check ups for hypertension. When performing the calculations, the blood pressure at the visit as well as responses to the updated questionnaire at the visit were considered.
Subjects classified as hypertensive were enrolled randomly within each age stratum. For each subject with hypertension, four non-hypertensive controls matched for BMI and age were sampled. As soon as a hypertensive subject had been included, one of the four non-hypertensive subjects was asked to participate. If he disagreed, the next control person was contacted and asked to participate. Subjects who lived too far away from the city of Uppsala or who were not expected to manage the home monitoring were excluded.

Procedure
The sleep studies were performed between March 1996 and February 1998. At the first visit the subjects came to the sleep laboratory to meet a nurse and additional questionnaires were filled in. The nurse was unaware of the category to which the subject belonged. The participants were instructed how to install the monitoring devices and all subjects underwent a whole night recording, reported that they now had criteria for classification as a hypertensive, or who had a mean systolic BP ≥160 or diastolic BP ≥95 based on the three repeated measurements, were excluded from the study.

Questionnaires
Daytime sleepiness was assessed using the Epworth Sleepiness Scale (ESS). Alcohol dependence was defined as a positive response to at least two of the four questions in the CAGE questionnaire. Previous and current smoking habits were assessed by six questions. Smoking was defined as being a regular smoker for at least 6 months and the participants were categorised into non-smokers, previous smokers, and current smokers. Physical activity was estimated by a question with four different categories of increasing level of physical activity ranging from category 1 (low level of physical activity): “Spending most of the time in front of the TV, reading and other sedentary activities” to category 4 (high level of physical activity): “Regular hard exercise or competition in sports like running, skiing, swimming, football or similar several times a week”; subjects were asked to place themselves in one of these categories.

Monitoring snoring and sleep related respiration
All subjects underwent an overnight sleep study in their own homes using the Eden-Tec monitoring system. The details and validity of this device have been described previously.23 The monitoring system is a portable four channel recorder measuring nasal/oral airflow (thermistry), chest wall impedance, oxygen saturation (finger pulse oximetry), and snoring. Snoring was measured using a microphone attached to the neck at the level of the upper right corner of the cricothyroid cartilage. Sampling was performed at 10 Hz and all sounds of more than 90 dB were recorded. Sleep time was estimated by use of a subject diary in conjunction with visual assessment of the overnight tracing. A minimum of 4 hours of estimated sleep was required. Due to this restriction, 14 first night records were rejected but were accepted after a second study night. Apart from snoring sounds, all events were scored
manualy by one of the authors (AE) who was blind to the subject's classification.

Desaturation was defined as a decrease in oxygen saturation of at least 4%. Apnoea was defined as a cessation of oronasal airflow for at least 10 seconds and hypopnoea as a 50% or more reduction in oronasal airflow for at least 10 seconds, followed by either a desaturation or a compensatory increase in chest wall impedance of at least 50%. There was no distinction between central and obstructive apnoeas. The total sum of apnoeas and hypopnoeas was divided by the estimated sleep time to obtain the apnoea-hypopnoea index (AHI) and desaturatiion index (DI) was calculated in the same manner. The snoring index (SI) was defined as (total time with snoring >90 dB/estimated total sleep time) × 100.

All the participants gave their informed consent and the study was approved by the ethics committee at the Medical Faculty at Uppsala University.

Statistical methods
Statistical analysis was performed using StatView for Windows 5.0 (SAS Institute Inc, Cary, North Carolina, USA) and Stata 6.0 (Stata Corporation, College Station, Texas, USA). The results are presented as mean (SD) values. A p value of <0.05 was regarded as statistically significant. To achieve normal distribution, continuous variables were log transformed. Correlations between continuous variables were calculated using linear regression. For comparison between continuous variables in hypertensive and non-hypertensive subjects, the paired t test was used and the results presented as mean differences and 95% confidence intervals (95% CI). The method proposed by Gardner and Altman was used for comparison of matched proportions.24 Conditional logistic regression was used to analyse the relation between sleep disordered breathing (SDB) parameters and HT and results are presented as odds ratios (OR) with 95% confidence interval. To test the influence of confounders on the associations between the SDB parameters and HT, potential confounders (waist/hip ratio, neck circumference, smoking, physical inactivity, and alcohol dependence) were added one by one into the conditional logistic regression model. Confounders that changed the OR by 10% or more were then included in the final multiple conditional logistic regression models.

RESULTS
At the time of the sleep study 10 of the men enrolled as non-hypertensive controls either fulfilled the criteria for the hypertensive group or had a mean systolic BP ≥160 or diastolic BP ≥95 on the three repeated measurements and were hence excluded from the final analyses. Another four non-hypertensive subjects were excluded because they had a BP ≥160/95 at the first visit and did not come back for another measurement. Two subjects who had reported HT in the 1994 questionnaire but had stopped taking antihypertensive medication at the time of this study who no longer attended for regular medical attention and had a systolic BP <160 and diastolic BP <90 at the nurse examination were also excluded. The final analyses were therefore performed on 102 matched pairs.

Characteristics of the study population
The mean (SD) period since being diagnosed as hypertensive in the study group was 12.7 (9.8) years. At the time of the sleep study five of the hypertensive subjects were receiving no antihypertensive medication, 52 were on monotherapy, 35 were being treated with two antihypertensive drugs, and 10 with three drugs or more. The most frequently used antihypertensive treatment was β blockers (n=53, 52%), followed by angiotensin converting enzyme (ACE) inhibitors (n=36, 35%), calcium channel antagonists (n=35, 34%), and diuretics (n=20, 20%).

The general characteristics of the participants are presented in table 1. The neck circumference was significantly larger in the hypertensive group and the subjects in this group were more often physically inactive, but there were no significant differences in any of the other potential confounders.

The mean (SD) score on the ESS was 6.7 (4.0). This did not significantly correlate with AHI (r=0.01, p=0.8), DI (r=0.01, p=0.9), or with the SI (r=-0.02, p=0.9). The mean ESS score did not significantly differ between the groups (table 1).

Monitoring results
Overall, the mean (SD) AHI was 9.0 (10.8). AHI was significantly related to age (r=0.22, p=0.002), BMI (r=0.26, p=0.0002), neck circumference (r=0.33, p<0.0001), and to the waist/hip ratio (r=0.26, p=0.0002). The mean (SD) DI was 6.9 (9.7) and, as expected, there was a strong correlation with AHI (r=0.86, p<0.0001).

The hypertensive subjects had a higher mean AHI, DI, and SI and a lower mean minimum SaO2 than the control subjects (table 2). The prevalence of AHI ≥10 and DI ≥10 was also higher in the hypertensive group than in the control group. At least 10% of the hypertensive subjects had a DI ≥10, while 10% and 2% of the control subjects had a DI ≥10 and SI ≥10 respectively. This difference was significant only for the interval 10–<20 (15% v 5%, difference 10%, 95% CI 1 to 18; fig 1).

The hypertensive and non-hypertensive subjects were further compared for the prevalence of sleep apnoea of different severity. Using AHI as a marker for severity of SDB, the difference between the groups was most pronounced when using a threshold value of >30 (12% v 2%, difference 10%, 95% CI 3 to 17). When DI was used as a marker of severity, all DI intervals tested (10–<20, 20–<30, >30) were more prevalent in the hypertensive group although the difference was significant only for the interval 10–<20 (15% v 5%, difference 10%, 95% CI 1 to 18; fig 1).
Effect of age
As DI > 10 and lowest desaturation were significantly related to HT even when confounders were taken into account, these associations were analysed separately in subjects aged <60 years (50 hypertensive and 50 non-hypertensive) and ≥60 years (52 hypertensive and 52 non-hypertensive). As shown in table 3, lowest desaturation was significantly related to HT only in the younger age group. Also, for DI > 10, the adjusted OR for HT was higher in the younger men, although the association was not significant in any of the age groups.

DISCUSSION
The main findings of this population based study were that SDB is more prevalent in hypertensive men than in controls. When DI > 10 or lowest desaturation were used as markers of SDB, this difference was present also after adjustment for the influence of important confounders. The association between SDB and HT was most pronounced in younger men.

The results confirm the findings of previous smaller studies in which hypertensive and non-hypertensive subjects have been compared for the prevalence of SDB. Fletcher and coworkers compared 46 hypertensive men taken off medication with 34 age and weight matched normotensive control subjects. An AHI >10 was found in 30% of the hypertensive subjects and 9% of the controls. In 50 patients from a HT clinic Kales et al30 diagnosed sleep apnoea (defined as >30 apnoeas/night) in 30% of hypertensive patients and in none of the age and sex matched (but not BMI matched) controls. In volunteers investigated by whole night polysomnography and 24 hour BP monitoring, Worsnop et al31 found an AHI >5 in 38% of both the 34 treated and the 34 untreated hypertensive subjects, but in only 4% of the 25 normotensive subjects. The differences between the groups were only partly explained by BMI, age, and sex. Isaksen and Svanborg17 reported OSA in 56% of 16 treated but uncontrolled hypertensive subjects compared with 19% of 16 treated and controlled subjects matched for BMI, age, and sex.19

When the association between SDB and HT has been studied in sleep laboratory cohorts, the results have been more conflicting with an independent association being reported by some but not by others.4–9 In the cited studies, however, other sleep clinic patients with lower AHI or no apnoeas were used as controls, which means that the control groups included an unknown number of patients who might have raised blood pressure due to upper airway resistance syndrome or sleep fragmentation of other causes. In the study by Rauscher et al17 where no independent association was found between number of apnoeas and hypopnoeas during sleep at baseline and the incidence of HT during the next 4 years. The study population comprised 709 employed men and women aged 30–60 years at baseline who were all investigated by polysomnography. Their data strongly support the hypothesis

The role of age in SDB seems to be complex. Young28 has previously suggested an heuristic model with sleep apnoea as both an age related disorder seen at lower ages and an age dependent condition in the elderly, with a potential overlap in the 60–70 year age range. This hypothesis was supported by the results of a population based study of the prevalence and severity of OSAS in men aged 20–100 years by Bixler et al29 who found that the prevalence of sleep apnoea tended to increase with age. On the other hand, the maximum prevalence of OSAS, defined as an AHI of > 10 and the presence of daytime symptoms, was in the middle age group (45–64 years).

As far as we are aware, this is the first case-control study where differences between hypertensive and non-hypertensive subjects have been compared separately for different age groups. Even though SDB was more common in hypertensive than in non-hypertensive subjects at all ages, the difference was most pronounced or reached statistical significance in the younger age group only, indicating that the strength of the association between SDB and HT is strongest in younger individuals. This is in accordance with previous epidemiological studies where the association between snoring and HT has been analysed for different age groups, and where both cross sectional24 and prospective data25 indicate a stronger relationship in younger subjects. Also, in a sleep laboratory cohort of 599 patients with documented HT, Grote et al26 found that the respiratory distress index and age were the only independent predictors of uncontrolled HT in patients aged 50 years or less while BMI was the only predictor in older patients. Bixler et al29 recently reported the results of a study which analysed the interrelationship between SDB, HT, age, and BMI in 1741 men and women who all underwent polysomnography. SDB and even snoring were found to be independently associated with HT in both men and women, and the relationship was strongest in young subjects, especially those of normal weight. An important difference between their study and the study reported here is that their population was sampled on the basis of risk factors for SDB. In our study the hypertensive subjects were randomly sampled from the general population and inclusion was based on the prevalence of HT without taking any symptoms of SDB into consideration.

Because of the cross sectional design of our study, it is not possible to state whether the association between SDB and HT is due to a cause-effect relationship with SDB causing HT. From the data obtained we cannot rule out the reverse—that is, the possibility that respiratory pauses during sleep could be caused by cardiovascular disease. There is, however, increasing evidence that HT is caused by SDB and not the reverse. Peppard et al32 reported prospective data from the Wisconsin Sleep Cohort Study where a dose-response relationship was found between number of apnoeas and hypopnoeas during sleep at baseline and the incidence of HT during the next 4 years. The study population comprised 709 employed men and women aged 30–60 years at baseline who were all investigated by polysomnography. Their data strongly support the hypothesis

### Table 3 Independent risk factors for hypertension

<table>
<thead>
<tr>
<th>Adjusted odds ratio (95% CI)*</th>
<th>Age 40–59 years</th>
<th>Age ≥60 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI &gt;10</td>
<td>1.01 (0.95 to 1.07)</td>
<td>1.02 (0.98 to 1.10)</td>
</tr>
<tr>
<td>AHI ≥10</td>
<td>1.8 (0.5 to 6.5)</td>
<td>1.5 (0.6 to 3.5)</td>
</tr>
<tr>
<td>DI &gt;10</td>
<td>1.03 (0.98 to 1.10)</td>
<td>1.02 (0.97 to 1.07)</td>
</tr>
<tr>
<td>DI ≥10</td>
<td>4.3 (1.0 to 19.3)</td>
<td>2.1 (0.7 to 6.5)</td>
</tr>
<tr>
<td>Lowest desaturation (%)</td>
<td>0.9 (0.8 to 1.0)</td>
<td>0.9 (0.9 to 1.1)</td>
</tr>
<tr>
<td>SII (%)</td>
<td>1.00 (0.96 to 1.06)</td>
<td>1.01 (0.96 to 1.07)</td>
</tr>
</tbody>
</table>

AHI=apnoea-hypopnoea index; DI=desaturation index; SII=snoring index.

*Adjusted for neck circumference and physical inactivity.
that SDB is an independent risk factor for developing HT but it does not rule out a reversed causal relationship. In an epidemiologic study using snoring as a marker of SDB, Stradling et al. previously found that persistent habitual snoring is an independent predictor of developing HT over a 10 year period in men aged 30–49 years.\(^9\) In contrast, hypertensive men run no increased risk of becoming habitual snorers. More recently, Stradling et al.\(^{10}\) reported that increased mean respiratory effort during sleep, measured as oscillations in pulse transit time, was an independent predictor of a reduced nocturnal blood pressure and an increased prevalence of HT have been observed to be related to both general obesity and fat distribution.\(^{11}\) External neck circumference is increased in sleep apnoea and it has been suggested that this measurement explains most or all of the link between obesity and sleep apnoea.\(^{12}\) However, when adjusting for neck circumference in our study, DI \(\geq 10\) and lowest desaturation were still independent predictors of HT, indicating that the association between SDB and HT cannot be explained only by an interrelationship with fat distribution.

Sleep disordered breathing was defined using a cut off point of AHI \(\geq 10\) and not less than 31% of the whole population fulfilled this criterion. Even though a higher prevalence of sleep apnoea has been reported in an Australian study,\(^{3}\) the prevalence of SDB was high compared with most other population based studies. This is partly explained by the fact that the population was biased by oversampling of hypertensive subjects and, as the non-hypertensive controls were matched for BMI, there was also an oversampling of overweight subjects in the control group. Comparisons with other studies are, however, difficult since considerable differences in the reported prevalence between different studies are largely attributable to differences in event definition and measurement. However, all subjects were analysed with the same identical monitoring system and respiratory events were analysed by a researcher who was blind to study group and age. This indicates that any misclassification of participants resulting from measurement error would not have introduced a systematic bias into our results and would, if anything, have weakened the statistical association we found. The results of the comparisons between the two groups were similar when using AHI \(\geq 5\) or AHI \(\geq 20\) as cut off points (not shown). It is important to note that the clinical importance of any particular cut off point has not been adequately determined.

The difference between hypertensive and non-hypertensive subjects could have been further underestimated because of the definition for HT used here. Hypertensive subjects had established HT and most had been on antihypertensive medication for many years. A limitation of this study is that the BP was measured only once—in the morning after sleep monitoring. When using mean BP of \(\geq 140/90\) during 24 hours as a cut off point for HT, Worsnop et al.\(^{12}\) found that 38% of both treated and untreated hypertensive subjects had an AHI \(\geq 5\) compared with only 4% of the non-hypertensive subjects. It seems reasonable to assume that some of the non-hypertensive subjects in this study might have had untreated or borderline HT if 24 hour measurements had been performed.

The results from our study confirm an association between SDB and HT which is independent of the influence of confounders. The results further indicate that the association between OSA and HT is clearer in the younger age groups, and that the role of age in this connection has to be taken into account in future studies of the relationship between SDB and HT.

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