

Sleep apnoea is a common occurrence in women

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ABSTRACT

Obstructive sleep apnoea is primarily regarded as a male disorder, presenting with snoring, daytime sleepiness and cardiovascular disease. We aimed to determine the frequency of sleep apnoea among women in the general population.

We investigated 400 women from a population-based random sample of 10,000 women aged 20-70 years. They answered a questionnaire and performed overnight polysomnography.

Obstructive sleep apnoea (apnoea-hypopnoea index ≥ 5) was found in 50% (95% CI 45-55%) of women aged 20-70 years. Sleep apnoea was related to age, obesity and hypertension but not to daytime sleepiness. Severe sleep apnoea (apnoea-hypopnoea index ≥ 30) was scored in 14% (95% CI 8.1-21%) of women aged 55-70 years and in 31% (95% CI 12-50%) of obese women with a body-mass index of $>30 \text{ kg/m}^2$ aged 50-70 years. Sleep apnoea with daytime sleepiness and sleep apnoea with hypertension were observed as two different phenotypes of obstructive sleep apnoea.

Obstructive sleep apnoea occurs in 50% of women aged 20-70 years. 20% of women have moderate, and 6% severe sleep apnoea. Sleep apnoea in women is related to age, obesity and hypertension but not to daytime sleepiness. When searching for sleep apnoea in women, women with hypertension or obesity should be investigated.

KEY WORDS

Daytime sleepiness, Epidemiology, Hypertension, Phenotypes, Polysomnography, Sleep apnoea syndromes, Women's Health

INTRODUCTION

Obstructive sleep apnoea is primarily regarded as a male disorder. Sufferers snore and experience daytime sleepiness and run an increased risk of hypertension, stroke and early death [1-9]. Nasal continuous positive airway pressure (CPAP) and oral appliances in the form of mandibular advancement devices during sleep reduce apnoeas, daytime sleepiness and blood pressure [2, 10-14].

A mean of five or more apnoeas and hypopnoeas per hour of sleep according to overnight polysomnography with continuous respiratory monitoring and sleep staging using EEG is the diagnostic criterion for sleep apnoea [2]. In 1993, Young et al. reported that 9% of middle-aged American woman had sleep apnoea and that 2% were also sleepy during the daytime [15]. There are, however, only a few epidemiological studies in women and the frequency of sleep apnoea in women is still uncertain, especially when using modern diagnostic equipment and new scoring recommendations [15-19]. Oronasal thermistors were used in previous prevalence studies and not nasal pressure sensors which are now recommended when diagnosing sleep apnoea [2, 20]. Our knowledge of snoring, daytime sleepiness, hypertension, age and obesity in women with sleep apnoea is also limited.

We aimed to determine the frequency of sleep apnoea among women in the population and associated factors.

METHODS

Subjects

In April 2000, a postal questionnaire was sent to 10,000 randomly selected women aged more than 20 years from the general population in the Municipality of Uppsala, Sweden, in the

population-based study entitled “Sleep and Health in Women” [21]. The response rate was 71.6% for all women. It was 72.9% in women aged 20-44 years, 74.8% in women aged 45-54 years, 77.8% in women aged 55-70 years and 55.0% in women aged 70 years and more. The questionnaire included the following question on snoring: “How often do you snore loudly and disturbingly”, with the following five alternative answers: “never”, “seldom”, “sometimes”, “often” and “very often “. Participants reporting loud and disturbing snoring “often” or “very often”, which occurred in 7.6%, were characterized as habitual snorers [22].

Full-night polysomnographic recordings were obtained in 400 non-pregnant women aged 20-70 years from November 2001 to February 2004. Excluded from polysomnography were 5 women in the snoring group who were treated for sleep apnoea. Women were randomly selected from responders in phase 1, with over-sampling of habitual snorers, and comprised 230 habitually snoring women and 170 women from the complete sample [23, 24]. Another 177 women from the randomly selected group, and 121 women from the snoring group declined polysomnography and they were replaced with other women from each group by random.

The written informed consent of all the participants was obtained and the study protocol was approved by the Ethics Committee at the Medical Faculty at Uppsala University.

Procedures

Overnight ambulatory polysomnography (Embla, Flaga hf, Iceland) included continuous recordings of electroencephalograms (C3-A2, C4-A1), electro-oculograms, electromyograms (submental and bilateral anterior tibialis muscles), air flow with a three-port oro-nasal thermistor and a nasal flow pressure sensor, respiratory effort from piezo-electric belts (Resp-

EZ, EPM Systems, Midlothian, VA, USA), finger pulse oximetry (Embla A10 flex Sensor), electrocardiograms (V5) and a body position sensor. Sensors were attached by nurses in the evening and the recordings were then performed unattended at home. Data loss occurred in six of 400 home studies and these women were re-examined within a short period.

All recordings were scored manually (CS). An obstructive apnoea was defined as the cessation of airflow in both nasal pressure and oro-nasal thermistor for at least 10 seconds with continuing abdominal and thoracic movements according to the American Academy of Sleep Medicine [2]. An obstructive hypopnoea was defined as a 50% reduction in both oro-nasal thermistor and nasal pressure for at least 10 seconds, compared with baseline, accompanied by abdominal and thoracic movements in combination with an arousal or an oxygen desaturation of 3% or more [2]. Central apnoeas were scored at the cessation of both oro-nasal thermistor and nasal pressure for 10 seconds without respiratory movements. Sleep was scored in 30-second epochs according to Rechtschaffen and Kales [25]. The obstructive apnoea-hypopnoea index was defined as the mean number of obstructive apnoeas and hypopnoeas per hour of sleep. Sleep apnoea was considered when the apnoea-hypopnoea index was 5 or more. Moderate sleep apnoea was considered when the apnoea-hypopnoea index was 15 - < 30 and severe sleep apnoea when the apnoea-hypopnoea index was 30 or more [2].

Height and weight were measured in the morning after polysomnography. Body-mass index (BMI) was defined as the weight in kilograms divided by the square of the height in meters. Systolic and diastolic blood pressure was measured in the supine position after 15 minutes' rest during the daytime. Subjects with systolic blood pressure of > 140 mmHg and/or diastolic blood pressure of > 90 mmHg were invited for measurements on two other days and the mean

of the measurements was calculated. Hypertension was defined as the ongoing treatment of physician-diagnosed hypertension or systolic blood pressure of > 140 mmHg and/or diastolic blood pressure of > 90 mmHg.

A questionnaire was administered during the day before polysomnography. It included questions on snoring, daytime sleepiness, smoking and alcohol. Habitual snoring was considered at a response of “often” or “very often” to the question “How often do you snore loudly and disturbingly?” The alternative responses were “never”, “seldom”, “sometimes”, “often” or “very often”. Apnoea witnessed by a bed partner was considered at a response of “sometimes”, “often” or “very often”.

Daytime sleepiness was scored according to the Epworth Sleepiness Scale (ESS) [26]. Responders are asked to rate their likelihood of dozing in eight different situations on a 4-point scale. The summary score varies from 0 to 24. Excessive daytime sleepiness was considered at an ESS score of ≥ 10 .

Current smoking was defined as smoking one or more cigarettes a day. Alcohol dependence was defined using the cut down, annoyed by criticism, guilty about drinking and eye-opener drinks questionnaire (CAGE) [27]. Subjects who answered yes to at least two of the four questions were defined as being alcohol dependent.

Statistical analysis

Weighting was applied because the individuals were sampled with unequal probability due to the over-sampling of habitually snoring women. Present non-snoring women and habitually snoring women were weighted to the source population of 6,515 non-snoring women and 536

habitually snoring women respectively. All the results were weighted to the source population, in order to present data on sleep from women in the general population. The data are presented as weighted means or proportions (95% confidence interval (CI)). Univariate and multivariate logistic regression was performed. All calculations were based on weighted data.

RESULTS

Polysomnographic recordings were made in all 400 women. Six women underwent a second polysomnography due to poor quality in the first recordings. The final analysis included 399 women, as one was excluded because she did not fall asleep during the recording. We had no minimal total sleep time for inclusion. The shortest total sleep time was 155 minutes and the longest was 569 minutes. The weighted mean characteristics of the included women are given in Table 1, while the weighted sleep characteristics are given in Table 2.

The weighted mean obstructive apnoea-hypopnoea index among women 20-70 years of age was 8.9 (95% CI 7.8-10) events/h and 50% (95% CI 45-55%) of women had obstructive sleep apnoea with an apnoea-hypopnoea index of ≥ 5 . Overweight, age, hypertension, witnessed apnoea and snoring were related to sleep apnoea, while daytime sleepiness, alcohol dependence and smoking were not (Table 3).

Obstructive sleep apnoea was found in 24% (95% CI 45-55%) of women aged 20-44 years, in 56% (95% CI 47-65%) of women aged 45-54 years and in 75% (95% CI 67-82%) of women aged 55-70 years (Table 3). In the whole population, sleep apnoea occurred in 80% (95% CI 70-90%) of women with hypertension and in 84% (95% CI 72-95%) of obese women with a

body-mass index above 30 kg/m². The frequency of sleep apnoea in the population in relation to age and body-mass index is given in Figures 1, 2.

Severe sleep apnoea (apnoea-hypopnoea index ≥ 30) occurred in 0.1% (95% CI 0.0-0.6%) of women aged 20-45 years, in 4.6% (95% CI 0.8-8.5%) of women aged 45-54 years and in 14% (95% CI 8.1-21%) of women aged 55-70 years. As many as 31% (95% CI 12-50%) of obese women aged 55-70 years had severe sleep apnoea.

Hypertension and daytime sleepiness were observed as two different phenotypes in women with sleep apnoea. Hypertension occurred in 25% and daytime sleepiness in 34% of women with obstructive sleep apnoea (apnoea-hypopnoea index ≥ 5). Only 3.6% of women with sleep apnoea had the combination of both daytime sleepiness and hypertension. Obstructive sleep apnoea was independently related to hypertension among women without sleepiness with an OR of 3.7 (95% CI 1.3-10) after adjustments for age, BMI, alcohol dependence and smoking (Table 4). The frequency of hypertension increased with the severity of sleep apnoea in univariate analysis (Figure 3, Table 4), but not in multivariate analysis because of the interaction with BMI.

Snoring was associated with sleep apnoea (Table 3). Sleep apnoea was, however, more frequently observed than habitual snoring and as many as 46% (95% CI 50-51%) of women who did not report that they snored habitually had an apnoea-hypopnoea index of 5 or more (Table 3).

Central sleep apnoea with a central apnoea-hypopnoea index of ≥ 5 occurred in 1.3% (95% CI 0.2-2.4%) of women. All the women with central sleep apnoea also had obstructive sleep apnoea.

DISCUSSION

Unexpectedly, we found that as many as 50% (95% CI 45-55%) of women in the general population fulfilled the criterion for sleep apnoea, with more than five apnoeas and hypopnoeas per hour of sleep. Sleep apnoea occurred in 80% (95% CI 70-90%) of women with hypertension and in 84% (95% CI 72-95%) of obese women. Severe sleep apnoea occurred in 14% (95% CI 8.1-21%) of women aged 55-70 years and in 31% (95% CI 12-50%) of obese women aged 55-70 years. Sleep apnoea was related to age, obesity, hypertension, witnessed apnoea and snoring but not to daytime sleepiness, alcohol dependence or smoking.

Daytime sleepiness and hypertension were observed as two different phenotypes of sleep apnoea. Thirty-four percent of the present women with sleep apnoea were sleepy during the daytime, 25% had hypertension and only 3.6% suffered from the combination of both sleepiness and hypertension. Hypertension was independently related to obstructive sleep apnoea in women without daytime sleepiness.

Snoring and daytime sleepiness are the main reasons for men and women to seek medical attention for sleep apnoea. However, daytime sleepiness was not related to sleep apnoea in the present women and most women with sleep apnoea did not snore. Habitual snoring occurred in 7.6% of the present sample. It was associated with sleep apnoea, but habitual snoring was not as common as sleep apnoea. A previous study also reports that severe sleep apnoea occurs in non-snoring women [15].

The sleep apnoea syndrome is defined as an apnoea-hypopnoea index of over 5, in combination with excessive daytime sleepiness [2, 20]. Daytime sleepiness is also a main

indication for the treatment of sleep apnoea [10, 11, 13]. Previous epidemiological studies report that the majority of women with an apnoea-hypopnoea index of over 5 do not complain of daytime sleepiness [15, 17-19] and that sleep apnoea is not related to excessive daytime sleepiness [17-19]. In 1993, using positive answers to three questions on hypersomnolence, Young et al. reported that 23% of women with sleep apnoea were tired during the daytime [15]. Using the Epworth Sleepiness Scale, we also found that the vast majority of women with sleep apnoea were not tired during the daytime. Daytime sleepiness was not related to sleep apnoea in the present women, in mild, moderate or severe sleep apnoea. Instead, obesity, hypertension and older age were key signs of sleep apnoea in women. It is possible that sleep apnoea has not been observed as a public health problem in women, as they have other signs of sleep apnoea than men.

In 1993, Young et al. reported that 9% of state-employed women had an apnoea-hypopnoea index over 5 [15]. Duran et al. from Spain, Kim et al. from Korea and Ip et al. from China report a frequency of sleep apnoea in women of 4% to 28% [17-19]. The above studies used a two-phase investigation system with a postal questionnaire or telephone enquiry to a large group of women and polysomnograms to a limited group. We used modern equipment, new diagnostic criteria and included women from the population and observed a much higher prevalence of sleep apnoea in women than that reported previously. Air flow was measured in the present study using both a nasal pressure cannula and an oronasal thermistor [2, 20]. Hypopnoeas have previously been defined in different ways and a reduction in air flow of 50%, followed by a desaturation of 4%, has often been used. The new recommendations, which were used in the present study, include desaturations of at least 3% instead of 4% after a reduction in air flow of 50% [2, 20]. Different inclusion criteria and different populations at another time point can possibly also explain some of the differences.

It is known that the prevalence of sleep apnoea increases with age, but the relevance of sleep apnoea defined as an apnoea-hypopnoea index of > 5 without symptoms in older ages is uncertain. The exact cut-off for the apnoea-hypopnoea index as a risk factor for cardiovascular disease in older ages is also unknown. However, recent long-term follow-up data from the Wisconsin Sleep Cohort and the Sleep Heart Health Study observed that severe sleep apnoea with an apnoea-hypopnoea index of > 30 is associated with a marked increase in mortality in the population [28-30]. Young et al. followed 1522 men and women in Wisconsin during a period of 18 years and observed a tripling in the risk of all-cause mortality adjusted for age, gender, BMI and other factors among subjects with severe sleep apnoea vs. no sleep apnoea [28]. Punjabi et al. followed 6441 men and women for 8.2 years in the Sleep Heart Health Study [29]. Men with severe sleep apnoea younger than 70 years ran double the risk of death. Corresponding women had a similar odds ratio of 1.76 that did not reach significance, which could be due power problems, since fewer women with severe sleep apnoea and fewer women than men died during the follow-up.

We found that about 4.6% of women aged 45-55 years and as many as 14% of women aged 55-70 years and 31% of obese women aged 55-70 years have severe sleep apnoea with an apnoea-hypopnoea index of > 30 . It is necessary to identify these women with unrecognized severe sleep apnoea as they probably run an increased risk of early death, without adequate treatment for obstructive sleep apnoea. We used different polysomnographic technology and different scoring criteria compared with the Wisconsin Sleep Cohort and the Sleep Heart Health Study and found a higher prevalence of severe sleep apnoea and it is therefore not certain that the present women with severe sleep apnoea share the same risk of death [28, 29].

Smoking and alcohol consumption are often considered as risk factors for sleep apnoea despite limited evidence, especially in women. It is well known that alcohol consumption before going to bed worsens sleep apnoea in men [31] and that smoking is related to snoring in men and women [22, 32]. Drinking > 23 grams of alcohol a day was related to oxygen desaturations and snoring in a study of Japanese women [33]. Smoking was related to sleep apnoea and alcohol to sleep apnoea in men but not in women in the Wisconsin Sleep Cohort [34, 35]. However, many epidemiological studies do not report any association between obstructive sleep apnoea and smoking or alcohol [18, 19, 36, 37]. In support of these studies, we did not find any association between obstructive sleep apnoea and smoking or drinking alcohol in women.

The limitations of the present study include data on snoring since women may snore despite a negative answer because they are single, have problems with awake bed-partners' observations or lack a "don't know answer" to the question on snoring. We used modern diagnostic equipment, including nasal airflow, new definitions for apnoea and hypopnoea and performed polysomnography at home, which is a strength but also a limitation when comparing the present results with older studies. Daytime sleepiness was scored using the Epworth Sleepiness Scale, as it is frequently used. There are, however, many limitations, including the subjective nature, and it might be less applicable in women as it includes questions on car driving and women drive less than men [38]. There is a need for the identification of specific symptoms of sleep apnoea in women. We investigated women only and we cannot compare women with men, which is another limitation in the present study, especially when it comes to compare our results with previous epidemiological studies.

In conclusion, obstructive sleep apnoea occurs in 50% of women aged 20-70 years. 20% of women have moderate, and 6% severe sleep apnoea. Sleep apnoea in women is related to age, obesity and hypertension but not to daytime sleepiness. When searching for sleep apnoea in women, women with hypertension or obesity should be investigated.

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Table 1. Weighted mean characteristics of participating women

Subjects	Mean or % (95% confidence interval)
Age (years)	48 (46-49)
Body mass index (kg/m ²)	25 (25-26)
Hypertension (%)	15 (11-19)
Current smoking (%)	16 (13-30)
Alcohol dependence (%)	5.6 (3.0-8.0)

Table 2. Sleep characteristics

	Weighted mean (95% confidence interval)
Total sleep time (min)	392 (472-481)
Stage 1 (% of TST)	8 (7.8-8.8)
Stage 2 (% of TST)	63 (62-63)
Stage 3-4 (% of TST)	10 (9.8-11)
REM (% of TST)	19 (18-20)

TST=total sleep time

Table 3. Frequency of obstructive apnoea-hypopnoea index (AHI) and associated factors

	AHI		
	≥ 5	≥ 15	≥ 30
All, 20-70 years old (%)	50 (45-55)	20 (17-25)	5.9 (3.7-8.3)
20-44 years old (%)	24 (18-31)	4.2 (1.0-7.4)	0.1 (0.0-0.6)
45-54 years old (%)	56 (47-65)	17 (11-24)	4.6 (0.8-8.5)
55-70 years old (%)	75 (67-82)	43 (34-52)	14 (8.1-21)
p-value	< 0.001	< 0.001	0.008
BMI < 25 kg/m ² (%)	39 (32-45)	9.0 (5.1-13)	0.1 (0.0-0.6)
BMI 25-29.9 kg/m ² (%)	55 (46-63)	26 (18-33)	9.2 (0.4-14)
BMI \geq 30 kg/m ² (%)	84 (72-95)	54 (39-69)	19 (7.1-30)
p-value	< 0.001	< 0.001	< 0.001
No hypertension (%)	44 (39-49)	17 (13-21)	4.0 (1.9-6.1)
Hypertension (%)	80 (70-90)	39 (26-51)	14 (4.8-22)
p-value	< 0.001	< 0.001	0.002
Non-snorers (%)	46 (40-51)	18 (14-22)	6.1 (3.5-8.7)
Snorers (%)	66 (53-79)	34 (21-47)	6.3 (0.0-13)
p-value	0.007	0.009	0.96
No witnessed sleep apnea (%)	46 (41-52)	17 (13-21)	3.8 (1.8-5.6)
Witnessed sleep apnea (%)	65 (46-84)	40 (21-59)	12 (0.0-25)
p-value	0.053	0.002	0.036
ESS < 10 (%)	48 (42-54)	20 (15-25)	6.2 (3.2-9.2)
ESS \geq 10 (%)	48 (39-57)	18 (11-25)	2.7 (0.0-5.4)
p-value	0.99	0.64	0.13
Non-smokers (%)	48 (42-53)	19 (15-24)	5.0 (2.5-7.3)
Smokers (%)	51 (38-64)	20 (9.6-30)	5.3 (0.0-11)
p-value	0.62	0.93	0.88
Alcohol dependent: No (%)	48 (43-53)	19 (15-23)	5.2 (2.9-7.5)
Alcohol dependent: Yes (%)	46 (23-69)	24 (4.0-43)	1.8 (0.0-8.0)
p-value	0.82	0.57	0.49

Values are presented as the weighted mean in per cent and 95% confidence intervals.

BMI=Body mass index, ESS=Epworth sleepiness scale

Table 4. Associations between risk factors and hypertension

	Unadjusted OR (95% CI)	p-value	Adjusted OR¹ (95% CI)	p-value
AHI < 5, ESS < 10 (controls)	1		1	
AHI < 5, ESS ≥ 10	1.32 (0.40-4.31)	0.65	1.33 (0.35-5.12)	0.65
AHI > 5, ESS ≥ 10	2.18 (0.74-6.41)	0.16	0.73 (0.19-2.70)	0.63
AHI > 5, ESS < 10	8.24 (3.56-19.1)	< 0.001	3.66 (1.30-10.3)	0.014
AHI >15,ESS <10*	11 (4.27-28)	<0.001	4.5 (0.43-48)	0.209
AHI >30,ESS <10*	16 (4.6-56)	<0.001	3.06 (0.09-101)	0.531
Age	1.10 (1.07-1.14)	< 0.001	1.08 (1.03-1.12)	0.001
BMI	1.32 (1.22-1.43)	< 0.001	1.29 (1.18-1.42)	<0.001
Alcohol dependence	3.13 (1.21-8.07)	0.018	7.16 (2.14-23.9)	0.001
Current smoking	1.23 (0.60-2.52)	0.58	2.01 (0.60-5.10)	0.14

¹ Adjusted for all the factors in the table. * Analysed in a separate with AHI <5, ESS<10 as controls. AHI=apnoea-hypopnoea index, ESS= Epworth sleepiness scale, BMI=body mass index

FIGURE LEGENDS

Figure 1. Prevalence (%) of sleep apnoea (apnoea-hypopnoea index ≥ 5) in women in relation to age and body mass index

Figure 1

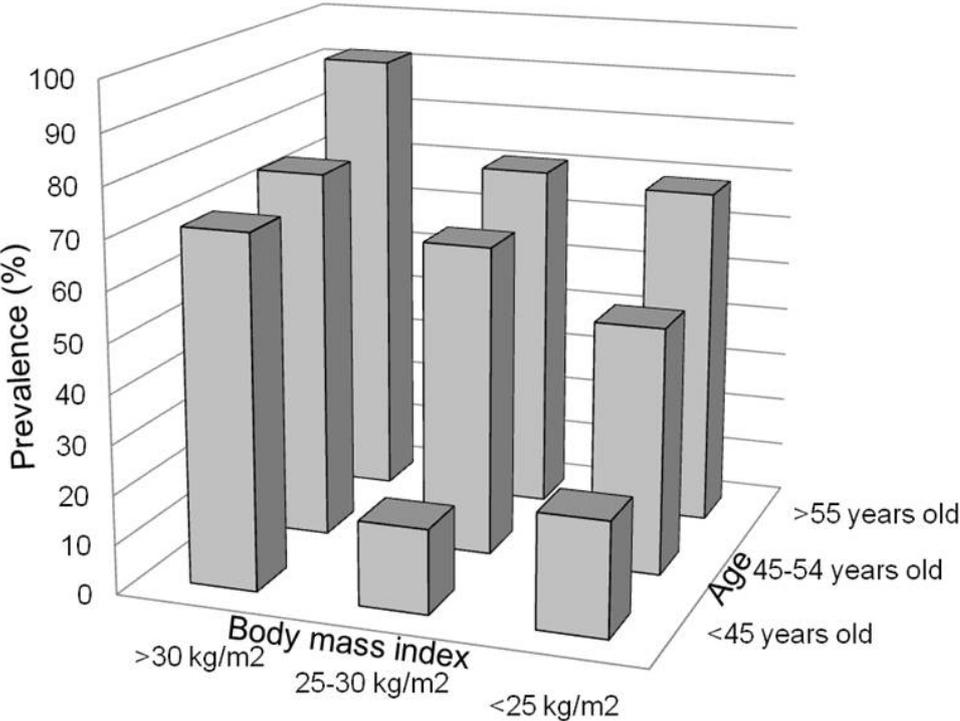


Figure 2. Mean number of apnoeas and hypopnoeas per hour of sleep (apnoea-hypopnoea index) in women in relation to age and body mass index

Figure 2

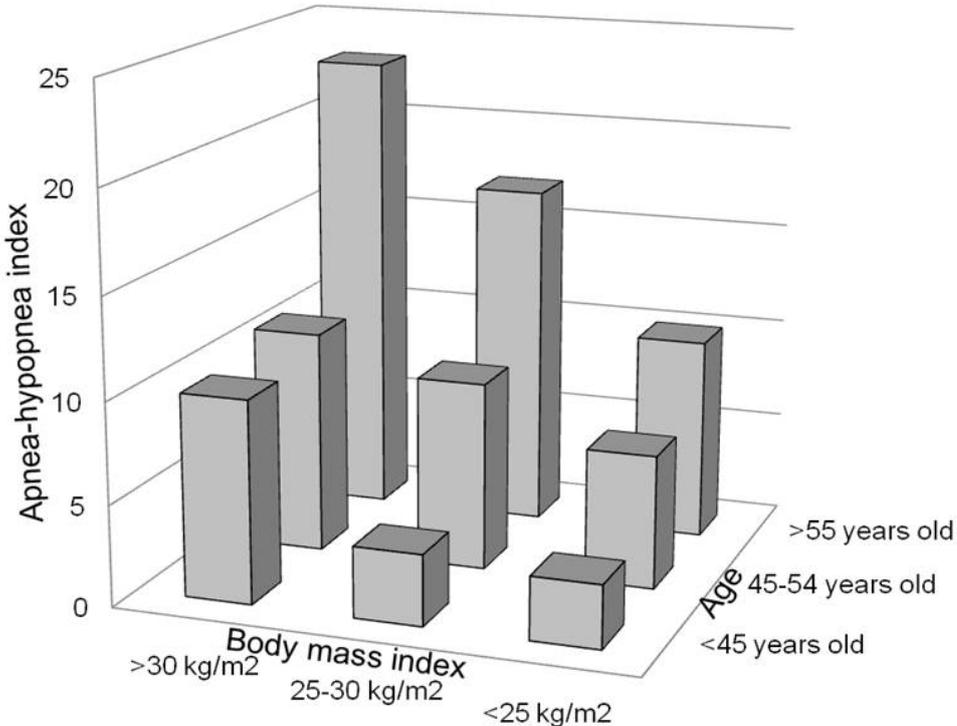


Figure 3. Prevalence (%) of hypertension (HT) and excessive daytime sleepiness (EDS) with regard to the apnoea-hypopnoea index (AHI)

Figure 3

