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Undiagnosed obstructive sleep apnea in hypertensive outpatients in primary care—Associations with sleep complaints, depressive symptoms and global perceived health

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ABSTRACT

Objective: 1) To describe the prevalence of undiagnosed obstructive sleep apnea (OSA) and depressive symptoms in hypertensive men and women below 65 years of age, and 2) to describe the association of OSA to subjective sleep complaints, depressive symptoms and global perceived health. Design: Cross-sectional design focusing on nursing care outcomes of obstructive sleep apnea. Setting: Four primary care health centres in Sweden. PATIENTS: 411 consecutive patients (52% women), mean age 57.9 years (SD 5.9 years), with diagnosed hypertension (BP > 140/90). Main Outcome Measures: Prevalence of OSA and depressive symptoms, and association of OSA to sleep complaints, depressive symptoms and global perceived health. RESULTS: Mild, moderate and severe OSA was seen among 29%, 16% and 14% of patients, respectively. Depressive symptoms were seen in 16% of the total group, with a higher prevalence among men, compared to women, 21% vs. 12%. No differences were found regarding blood pressure, estimated sleep need, sleep sufficiency index, insomnia symptoms, daytime sleepiness or depressive symptoms with respect to different degrees of OSA. Apnea-hypopnea index was significantly associated to perceived health after adjustment for gender and comorbidities, but when depressive symptoms and non-restorative sleep were added to the model, 33% of the variance in global perceived health was explained. Conclusion: OSA is highly prevalent among patients with hypertension in primary care and does together with sleep complaints and depressive symptoms have a negative impact on global perceived health. Hypertensive patients without subjective sleep complaints or depressive symptoms may still have OSA.

Keywords: Depression; Global Perceived Health; Hypertension; Nursing Care; Obstructive Sleep Apnea; Sleep Disordered Breathing; Sleep

1. INTRODUCTION

The worldwide prevalence of hypertension (HT) has been estimated to be as high as 1 billion individuals. Estimates suggest that HT is responsible for 62 percent of

cerebrovascular disease, 49 percent of ischemic heart disease (IHD), and 7.1 million deaths each year [1]. Obstructive sleep apnea (OSA) occurs in 24% of men and 9% of women when defined as at least five respiratory pauses per hour of sleep [2]. OSA is associated to various types of cardiovascular disease (e.g., stroke, IHD, heart failure, arrhythmias) and can cause an increased mortality [3]. A suggested mechanism is the increased cardiovascular stress (*i.e.*, sympathetic activation) caused by the breathing related events (*i.e.*, the apneas/hypopneas that causes hypoxia) [3]. Another suggested cause is the high and increasing prevalence of obesity [4]. Swedish data indicate an increasing obesity problem among HT patients, and, as a consequence, an increasing occurrence of OSA [5].

Global perceived health (GPH) is an important outcome in nursing care, incorporating depression, insomnia and daytime sleepiness as crucial components [6], of which all are associated with OSA in patients referred to sleep clinics, but also with poor health perceptions in the general population [7]. Simultaneous use of antidepressant and antihypertensive medications may increase the likelihood of OSA syndrome (OSAS) diagnosis [8]. Improved knowledge about the links between OSA, subjective sleep complaints, depression and GPH in hypertensive outpatients may help nurses to identify patients, as well as targets for nursing interventions. The purpose of this study was 1) to describe the prevalence of different severity levels of OSA in adults with HT in primary care, and 2) to explore the contributions of OSA to subjective insomnia and daytime sleepiness, depressive symptoms and GPH in patients with undiagnosed OSA.

2. MATERIALS AND METHODS

2.1. Design and Selection Criteria

A cross-sectional design focusing on nursing care outcomes of OSA breathing was used. After ethical approval (Dnr M29-07), all 918 eligible patients 18 - 65 years of age with diagnosed hypertension (140/90) at four primary care centres in Sweden were screened. Exclusion criteria were terminal disease, ongoing treatment for OSAS, severe psychiatric disease, dementia, alcohol/drug abuse, or difficulties reading and understanding the Swedish language.

2.2. Clinical Variables

A nurse (*i.e.*, specialized on pulmonary medicine) and a physician (*i.e.*, specialized in ear nose and throat diseases) collected all data at the hospital. The data comprised weight, height, blood pressure, subjective sleep (*i.e.*, sleep duration, estimated sleep need), medication and co-morbidities. Diagnosis of diabetes mellitus was based on a history, current treatment (oral therapy or insulin) or a fasting blood glucose value ≥7 mmol/l. IHD was defined on the basis of a history of angina pectoris and/or myocardial infarction and/or coronary angioplasty and/or coronary bypass surgery. Respiratory disease was premised on a history of asthma or chronic obstructive pulmonary disease, or on current treatment (β^2 agonists and/or inhaled corticosteroids).

2.3. Self-Rating Scales

The 11 items of the Berlin Sleep Apnea Questionnaire (BSAQ) focusing on occurrence of OSA symptoms/characteristics (*i.e.*, **part 1**; snoring, witnessed apneas, **part 2**; daytime sleepiness, **part 3**; occurrence of obesity, and HT) was used to measure the risk of having OSA [9]. If two of the three parts are showing an "occurrence" of symptoms/characteristics the patient is supposed to have a high risk of suffering from OSA. The 3 items of the Minimal insomnia symptoms scale (MISS) were used to measure difficulties initiating sleep, difficulties maintaining sleep and difficulties with non-restorative sleep [10]. The patients grade their difficulties on a scale ranging from no problems (0), to very great problems (4). The Epworth sleepiness scale (ESS) was used to measure daytime sleepiness [11]. The eight items (*i.e.*, different daily situations in which the subjects are asked to rate the likeliness of dozing or falling asleep) are rated on a scale of 0 - 3 and are summarised into a score between 0 - 24 points with a cut-off of >10 indicating excessive daytime sleepiness. The 14 items Hospital anxiety and depression scale (HAD) was used to measure depressive symptoms [12]. The scores from the seven depression items ranges from 0 - 21, the higher score the more depressive symptoms. A cut-off of ≥7 was used to indicate depressive symptoms. The first question concerning current health status from the SF-36, was used to measure GPH [13]. The participants ranked their health as 1) excellent, 2) very good, 3) good, 4) fair or 5) poor.

2.4. Recordings of Sleep Disordered Breathing

Full-night respiratory recordings were performed in the patients' homes, including monitoring of nasal-airflow, pulse oximetry, respiratory movements and body position. Data were recorded with a polygraphic equipment (Embletta, Somnologica, ResMed AB, Trollhättan, Sweden) and all recordings were scored according to the 2007 recommendations of the American Academy of Sleep Medicine [14] by the same experienced physician who was blinded to the results of the other data. The total number of apneas and hypopneas was divided by the estimated sleep time, giving the apnea-hypopnea index (AHI). An oxygen-desaturation index (ODI) was calculated in the same manner. Patients were defined as having mild (*i.e.*, AHI > 5), moderate (*i.e.*, >15) or severe

(*i.e.*, >30) OSA.

2.5. Statistical Analysis

Normally distributed variables were analysed with *t*-test, ANOVA or Pearson correlations. Mann-Whitney test, Kruskal-Wallis test, Chi-square test or Spearman rank correlations were used on non-normally distributed or dichotomous variables. To examine if AHI was independently associated with perceived health, nested linear regression analysis was used. Before entering the regression model, AHI was logarithmic transformed to normality. Adjustments were made for theoretically selected covariates (*i.e.*, gender, diabetes, IHD, respiratory disease, body mass index (BMI) and depressive symptoms) and subjective sleep complaints (*i.e.*, non-restorative sleep) with the highest correlation to perceived health. The significance level was set to $p < 0.05$. All statistical analyses were performed with the PASW statistics 18 (IBM Inc., USA).

3. RESULTS

3.1. Study Population

Of the 918 patients 12% (50 men and 59 women) were omitted from participation due to exclusion criteria's and 28% (170 men and 159 women) chose not to participate. Of the 480 patients who participated in the clinical examination 411 accepted respiratory recordings. Seventeen recordings were lost due to technical problems. Thus, the final study population consisted of 394 patients.

Population characteristics, co-morbidities and medications are given in **Table 1**.

3.2. Prevalence of OSA and Depressive Symptoms

Fifty-nine percent of the 394 patients had OSA (AHI ≥ 5). Mild, moderate and severe OSA occurred among 29%, 16% and 14% of the patients, respectively. Average ODI was twice and five times as high in the groups with moderate and severe OSA (20.0 and 45.6, respectively) compared to those with mild OSA (7.9) ($p < 0.001$) (**Table 1**). Neither systolic, diastolic blood pressure nor medication differed between the three groups of patients with OSA, or compared to patients without OSA. BMI was significantly associated with AHI ($p < 0.001$). Obesity (BMI ≥ 30) was seen in 30%, 43% and 68% of the patients with mild, moderate and severe OSA, respectively.

Diabetes was more prevalent among patients with at least mild OSA ($p = 0.04$, χ^2 3.8). Neither history of IHD nor respiratory disease was associated with severity of OSA. Prevalence of depressive symptoms in relation to severity of OSA is presented in **Table 2**. A total of 16% had a HAD score ≥ 7. A larger proportion of men than women had depressive symptoms, 21% vs. 12% ($p < 0.01$).

3.3. Association of OSA to Sleep Complaints, Depressive Symptoms and GPH

Patients with moderate or severe OSA had longer sleep duration compared to those with mild or no OSA ($p < 0.01$). The total HAD score was not associated with the degree of OSA. Patients without OSA had better GPH compared to individuals with at least mild OSA ($p < 0.01$). Depressive symptoms, non-restorative sleep, difficulties maintaining sleep, difficulties initiating sleep and BMI were the variables with the strongest correlations to perceived health. AHI and ODI were also significantly related to GPH (**Table 3**).

Table 4 shows that patients with depressive symptoms had more difficulties maintaining sleep ($p = 0.004$), non-restorative sleep ($p = 0.008$) and GPH (0.001), but no differences were seen regarding sleep duration, sleep need, difficulties initiating sleep or daytime sleepiness. AHI was significantly associated with GPH after adjustment for gender and co-morbidities (block 3, **Table 5**). After adding BMI to the model in block 4 AHI and diabetes became non-significant. Depressive symptoms and non-restorative sleep explained almost 22% of the variance in GPH.

4. DISCUSSION

An important result of relevance for nursing care was that a large proportion of hypertensive outpatients had objective evidence of OSA, but there was no association to blood pressure. Depressive symptoms were common, but not clearly related to OSA. Gender, respiratory disease, BMI, depressive symptoms and non-restorative sleep explained 33% of the variance in GPH. The prevalence of OSA in this study (59%) is larger than that found in other large community-based general population studies, which is somewhat surprising given that the average BMI in this Swedish study was lower than that in previous North American studies. For example, the Sleep Heart Health Study [15] and the Wisconsin Sleep Cohort Study [16] documented OSA prevalence rates between 22% - 46%. We included only patients with HT, which may be an explanation for the difference. Our finding is in line with Worshop *et al.* [17], which found that 38% of 68 hypertensive patients had OSA, regardless of hypertensive treatment, compared to 4% among normotensive controls. A previous study [18] of men with therapy-resistant HT found that 56% had OSA, compared with 19% in successfully treated hypertensive's matched for age and gender.

Two other previous studies [19,20] observed different rates, but different designs and other scoring criteria's

Table 1. Characteristics, medication and comorbidities across the groups for obstructive sleep apnea (n = 394).

Characteristics	AHI				
	<5 **No Obstructive Sleep Apnea** n = 160, 41%	≥5 **Mild Obstructive Sleep Apnea** n = 113, 29%	≥15 **Moderate Obstructive Sleep Apnea** n = 64, 16%	≥30 **Severe Obstructive Sleep Apnea** n = 57, 14%	p
Gender:					
Men n (%)	61 (38)	56 (50)	29 (45)	39 (68)	
Women n (%)	99 (62)	57 (50)	35 (55)	18 (32)	0.001
Age:					
mean (sd)	57.3 (6.8)	57.8 (7.6)	58.6 (5.5)	58.2 (6.1)	NS
Sleep disordered breathing					
AHI, m (sd)	2.1 (1.48)	8.8 (2.8)	21.8 (4.4)	49.3 (19.2)	0.001
ODI, m (sd)	2.0 (1.5)	7.9 (3.1)	20.0 (4.9)	45.6 (20.5)	0.001
SaO2-M, m (sd)	94.4 (7.5)	94.0 (3.9)	93.4 (1.7)	92.6 (1.7)	0.001
SaO2-N, m (sd)	88.7 (7.4)	84.2 (8.6)	78.8 (11.3)	75.0 (11.6)	0.001
Total desat, m (sd)	13.8 (12.2)	52.4 (24.0)	128.5 (48.9)	270.3 (158.8)	0.001
Time below 90%, m (sd)	0.5 (4.7)	1.4 (4.8)	6.7 (12.7)	14.6 (13.2)	0.001
Blood pressure:					
SBP, mean (sd)	138.8 (17.4)	142.5 (15.7)	140.0 (17.6)	140.0 (19.2)	NS
DBP, mean (sd)	86.5 (9.6)	87.9 (10.2)	86.0 (10.7)	89.1 (13.5)	NS
BMI:					
mean (SD)	27.0 (4.3)	29.0 (4.8)	30.1 (5.6)	31.4 (4.6)	0.001
Medication:					
CA-blockers, n (%)	27 (17)	22 (20)	14 (22)	16 (28)	NS
B-blockers, n (%)	72 (45)	49 (43)	32 (51)	29 (51)	NS
ACEI/ARB, n (%)	90 (56)	66 (58)	34 (53)	33 (58)	NS
Digoxin, n (%)	0 (0)	0 (0)	1 (0)	0 (0)	NS
Diuretics, n (%)	50 (31)	36 (32)	24 (38)	18 (32)	NS
Number of hypertensive drugs, m (sd)	1.49 (0.75)	1.53 (0.82)	1.76 (0.87)	1.74 (0.78)	NS
Hypnotics, n (%)	10 (6)	4 (3)	4 (6)	0 (0)	NS
Anti-depressant, n (%)	10 (6)	15 (13)	7 (11)	6 (11)	NS
Comorbidities:					
Diabetes, n (%)	20 (13)	22 (20)	11 (17)	14 (24)	NS
IHD, n (%)	20 (13)	14 (13)	11 (17)	13 (23)	NS
HC, n (%)	40 (26)	33 (30)	20 (31)	21 (37)	NS
RD, n (%)	10 (6)	6 (5)	4 (6)	4 (7)	NS
TIA/Stroke, n (%)	3 (2)	2 (2)	0 (0)	3 (5)	NS

The AASM criteria were used when patients were categorized into OSA groups based on apnea-hypopnea index <5, ≥5, ≥15 or ≥30. Significant p-values are bolded. Key: ACEI—Angiotensin converting inhibitor; ARB—Angiotensin receptor blockers; AHI—Apnea-hypopnea index; B-blockers—Beta blockers; BMI—Body mass index; DBP—Diastolic blood pressure; HC = Hypercholesterolemia, IHD—Ischaemic heart disease; ODI— Oxygen desaturation index; RD—Respiratory disease; SaO2-M—Mean saturation, SaO2-N—Nadir saturation, SBP—Systolic blood pressure; SD— standard deviation; TIA/stroke—Trans ischaemic attack/stroke.

were used. Sjöström *et al.* [19] found in a stratified sample of hypertensive men that 37% had AHI > 10. In a community-based case-control study, Hedner *et al.* [20] found a prevalence of 82% (AHI > 10) in middle-aged patients with both HT and diabetes. They also noted a higher prevalence of severe OSA (AHI > 30), 47% of men and 24% of women. Comparing our data with those from Hedner's sample is difficult, since the metabolic syndrome is one of the best predictors for OSA [21]. These high prevalence figures imply that screening of

Table 2. Self-rated sleep, daytime sleepiness, depressive symptoms and perceived health across the severity groups for obstructive sleep apnea (n = 394).

Characteristics	AHI				
	<5 **No Obstructive Sleep Apnea** n = 160, 41%	≥5 **Mild Obstructive Sleep Apnea** n = 113, 29%	≥15 **Moderate Obstructive Sleep Apnea** n = 64, 16%	≥30 **Severe Obstructive Sleep Apnea** n = 57, 14%	p
Self-rated sleep:					
Sleep duration, hours, m (sd)	6.7 (1.0)	6.5 (1.2)	7.0 (1.1)	7.0 (1.2)	NS
Estimated sleep need, hours, m (sd)	7.6 (0.7)	7.8 (0.9)	7.9 (1.1)	7.9 (0.8)	NS
Sleep sufficiency index, %, m (sd)	0.88 (0.13)	0.85 (0.14)	0.89 (0.15)	0.89 (0.16)	NS
Self-rated symptoms of obstructive sleep apnea:					
High risk on BSAQ, n (%)	92 (59)	95 (84)	58 (92)	49 (89)	0.001
Low risk on BSAQ, n (%)	63 (41)	18 (16)	5 (8)	6 (11)	0.001
Snoring, n (%)	102 (66)	97 (87)	60 (94)	53 (95)	0.001
Witnessed apneas, n (%)	13 (8)	20 (18)	18 (29)	26 (47)	0.001
Insomnia symptoms:					
Difficulties initiating sleep, n (%)	17 (11)	15 (13)	4 (6)	3 (6)	NS
Difficulties maintaining sleep, n (%)	31 (20)	28 (26)	15 (24)	7 (13)	NS
Difficulties with non-restorative sleep, n (%)	24 (15)	26 (23)	13 (21)	9 (16)	NS
Daytime sleepiness:					
Total ESS score, m (sd)	7.8 (4.4)	7.8 (4.0)	8.0 (4.7)	8.7 (4.3)	NS
ESS > 10, n (%)	53 (34)	32 (28)	21 (33)	24 (42)	NS
Depressive symptoms:					
HAD total score, m (sd)	3.7 (2.5)	4.2 (2.5)	3.9 (2.6)	4.3 (2.7)	NS
Yes (HAD ≥ 7), n (%)	19 (12)	22 (19)	9 (14)	12 (21)	NS
Perceived health:					
m (sd)	2.98 (0.85)	3.24 (0.86)	3.21 (0.68)	3.3 (0.91)	0.04

The AASM criteria were used when patients were categorized into OSA groups based on apnea-hypopnea index <5, ≥5, ≥15 or ≥30. Significant p-values are bolded. Key: BSAQ—Berlin Sleep Apnea Questionnaire, ESS—Epworth sleepiness scale, HAD—Hospital Anxiety and depression Scale.

Table 3. Correlations between demographics, sleep apnea variables, sleep complaints, depressive symptoms and perceived health in patients with hypertension (n = 394).

Variables	Perceived health	p
Gender	0.03	NS
Apnea hypopnea index	0.16	0.02
Oxygen desaturation index	0.17	0.001
SaO2-M	− 0.10	NS
SaO2-N	− 0.12	0.02
Total desaturations	0.13	0.009
Time below 90%	0.08	NS
Systolic blood pressure	0.04	NS
Diastolic blood pressure	− 0.05	NS
Body mass index	0.27	0.001
Diabetes	0.14	0.005
Ischemic heart disease	0.15	0.005
Respiratory disease	0.16	0.002
Total night sleep hours	− 0.04	NS
Estimated sleep need	0.21	0.001
Sleep sufficiency index	− 0.20	0.001
Difficulties initiating sleep	0.23	0.001
Difficulties maintaining sleep	0.25	0.001
Non-restorative sleep	0.42	0.001
ESS score	0.12	0.02
HAD score	0.38	0.0001

Key: ESS—Epworth sleepiness scale, HAD—Hospital anxiety and depression scale, SaO2-M—Mean saturation, SaO2-N—Nadir saturation.

Table 4. Self-rated sleep, insomnia symptoms, daytime sleepiness and perceived health in patients with hypertension (n = 394) with respect to degree of depressive symptoms.

Characteristics	No Depressive symptoms HAD < 7 n = 332, 84%	Depressive symptoms HAD ≥ 7 n = 62, 16%	p
Gender:			
Men, n (%)	146 (44)	39 (63)	
Women, n (%)	186 (56)	23 (37)	0.008
Age, mean (SD)			
Self-rated sleep:			
Total night sleep, hours, m (sd)	6.75 (1.06)	6.64 (1.3)	NS
Estimated sleep need, hours, m (sd)	7.73 (0.86)	7.82 (0.80)	NS
Sleep sufficiency index, %, m (sd)	0.88 (0.13)	0.85 (0.17)	NS
Insomnia symptoms:			
Difficulties initiating sleep, n (%)	27 (8)	12 (19)	NS
Difficulties maintaining sleep, n (%)	60 (18)	21 (34)	0.004
Difficulties with non-restorative sleep, n (%)	53 (16)	19 (31)	0.008
Daytime sleepiness:			
Total score, m (sd)	7.9 (4.2)	8.4 (4.7)	NS
ESS > 10, n (%)	107 (82)	23 (18)	NS
Perceived health:			
m (sd)	3.0 (0.84)	3.7 (0.74)	0.001

Key: AHI—Apnea-hypopnea index; ESS—Epworth sleeiness scale, DS—Depressive symptoms.

OSA in patients with HT in primary care should be performed. OSA-related apneas and desaturations are important both for self-rated sleepiness (*i.e.*, due to increased number of awakenings and a disturbed sleep structure) and for cardiovascular disease (*i.e.*, by sympathetic activation and increased levels of catecholamine's, causing inflammation, arterial stiffness and atherosclerosis) [22]. Continuous positive airway pressure, often initiated and managed by nurses, can reduce cardiovascular morbidity and mortality [23,24], particularly in adherent patients with severe OSAS.

Blood pressure reductions have been found especially in sleepy patients [25-27] with frequent desaturations, but also when hypertension is severe, untreated or refractory [22]. Surprisingly, we found no association between OSA severity and blood pressure, GPH, or self-rated sleepiness in contrast to previous studies where a dose-response relationship was found between night-time blood pressure and increasing AHI [16,22]. However, this may be due to the fact that our patients were already regularly followed and controlled, mostly successfully, at nurse-led outpatient clinics for hypertension. Furthermore, we found that more than 50% of those with severe OSA (*i.e.*, AHI ≥ 30) scored <10 on the ESS, thus indicating a lack of excessive daytime sleepiness. We used validated questionnaires [9-13], but did not evaluate patients who had sought medical attention for OSA, which might explain the lower amount of sleeping difficulties, daytime sleepiness and depressive symptoms found compared to samples from sleep clinics [23-28]. This finding sheds light on the difficulties that nurses may have in identifying patients with OSA in primary care [29].

More studies set in primary care are needed to explore symptom profiles and clinical characteristics of patients with OSA. Research thus far has predominantly been performed in other settings [15,16,21]. Knowledge from primary care studies can facilitate nurses to identify patients with a high cost-benefit for referral to sleep clinics. Questionnaires, such as the BSAQ [9,30] and simple two channel recording devices [31] may be suitable for nurses working at hypertensive clinics in primary care to identify patients. However, they are not comparable to validated diagnostic tools, such as polygraphy or polysomnography, and need to be more thoroughly evaluated regarding sensitivity and specificity. Limitations of this study include the cross-sectional design and the relatively low participation rate. Stratifying men and women with different levels of OSA will strengthen the

Table 5. Linear regression model for perceived health in patients with hypertension (n = 394).

Variable	Beta	R^2	R^2 change	p
Block 1				
AHI $\log^{10}$	0.133			
		0.015	0.018	0.013
Block 2				
AHI $\log^{10}$	0.158			0.004
Gender (Male 1, female 2)	0.104			NS
		0.028	0.010	0.008
Block 3				
AHI $\log^{10}$	0.142			0.010
Gender	0.124			0.024
Ischemic heart disease	0.063			NS
Diabetes	0.117			0.028
Respiratory disease	0.160			0.002
		0.073	0.045	0.001
Block 4				
AHI $\log^{10}$	0.064			NS
Gender	0.118			0.027
Ischemic heart disease	0.073			NS
Diabetes	0.069			NS
Respiratory disease	0.141			0.007
Body Mass Index	0.231			0.001
		0.116	0.043	0.001
Block 5				
AHI $\log^{10}$	0.065			NS
Gender	0.112			0.017
Ischemic heart disease	0.085			0.060
Diabetes	0.074			NS
Respiratory disease	0.104			0.021
Body Mass Index	0.160			0.001
HAD score	0.270			0.001
Non-restorative sleep	0.311			0.001
		0.331	0.215	0.001

Key: ESS—Epworth sleepiness scale, HAD—Hospital anxiety and depression scale, SaO2-M—Mean saturation, SaO2-N—Nadir saturation.

treatment evidence for nursing care interventions. Still, these results suggest that snoring patients with hypertension, elevated BMI and/or diabetes should be investigated for OSA. Treating OSA may positively influence hypertension, sleep quality, depression, and GPH, although further nursing research is needed to confirm such a benefit.

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