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Hypertension control in patients with moderate-severe obstructive sleep apnea

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Abstract

Introduction: The ongoing obesity pandemic is partly responsible for the rising prevalence of obstructive sleep apnea (OSA). The condition induces nocturnal apneic and hypopneic episodes, which in turn activate the sympathetic nervous system and the renin-angiotensin-aldosterone axis, leading to increased cardiovascular risk. Hypertension is highly prevalent among patients with OSA, and it usually embraces a non-dipping circadian profile. Methods: We analysed anthropometric and ambulatory blood pressure monitoring (ABPM) results in 44 patients with moderate-severe OSA prior to the initiation of continuous positive airway pressure therapy. Results: Mean apnea-hypopnea index was 40,49 events/h. 4,4% of our patients were females. 81,81% of our subjects had a body mass index > 30, but all of our patients fulfilled the criteria for abdominal obesity. Only 2 of our patients were normotensive. Renin-angiotensin-aldosterone inhibitors and beta-blockers were frequently prescribed to our subjects. Conclusions: Hypertension and obesity were highly prevalent in our moderate-severe OSA patients. Age is negatively correlated with body mass index and average diastolic blood pressure. We found a borderline statistically significant correlation between apnea-hypopnea index and resting heart rate, but not with any of the analysed ABPM variables. However, mean nocturnal O2 saturation was correlated with both abdominal circumference and body mass index.

Keywords: hypertension, obstructive sleep apnea, metabolic syndrome, ambulatory blood pressure monitoring, obesity

Introduction

Obstructive sleep apnea (OSA) is a form of sleep disordered breathing that induces upper airway collapse during rest, causing hypopneas and apneas and consequent hypoxemia and hypercapnia [1]. Most apneic episodes induce microawakenings and thus sleep fragmentation, leading to daytime sleepiness, decreased concentration and impaired quality of life [1]. Although overnight polysomnography is the gold standard diagnostic test for OSA, cardio-respiratory polygraphy is still considered acceptable. OSA severity is quantified according to the apnea-hypopnea index

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(AHI): 5-15, 15-30 and >30 for mild, moderate and severe OSA, respectively [2]. Due to the ongoing obesity-pandemic, the prevalence of OSA has substantially increased, the latest studies estimating that 14% of males and 5% of females in the United States have AHI >=5 along with daytime sleepiness [3].

Obesity, male sex and aging are well-known OSA risk factors [1]. The association between obesity and OSA can be explained by reduced lung volumes, elevated breathing effort and local fat deposition which causes increased upper airway collapsibility [4]. 40% of patients with hypertension (HBP), 30% of subjects with coronary artery disease, atrial fibrillation and chronic heart failure suffer from OSA, making it a frequent comorbidity in cardiovascular patients [2]. On the other hand, HBP and OSA have several common risk factors (age, gender, obesity, alcohol use, systemic inflammation, oxidative stress, endothelial dysfunction) [1,5] and longitudinal studies have yielded controversial results regarding the relationship between OSA and hypertension. While the Vitoria Sleep Cohort Study did not find a significant association between the two after adjusting its results for age and body mass index [6], the Wisconsin Sleep Cohort study suggested that OSA elevates HBP susceptibility [1,3]. A recent meta-analysis found that patients with high AHI present a significantly increased risk of developing HBP (OR=1.77, p=0,001, CI=1,3-2,41) compared to those with lower AHI. According to the same study, every increase in AHI with 10 events/hour increases the risk of developing HBP by 17% (p=0,001) [7]. Furthermore, the fact that continuous positive airway pressure (CPAP) therapy is effective in reducing both systolic and diastolic blood pressure values (with 2,6 and 2 mmHg, respectively) proves that OSA is involved in the etiopathogenesis of HBP [8]. In analysing this apparent insignificant effect, one should keep in mind that a reduction of BP values by 2-3 mmHg is associated with a reduction of cardio-vascular event risk by up to 10% [9].

The negative cardiovascular effects of OSA can be explained by intermittent hypoxia, intrathoracic pressure changes, nocturnal microawakenings which lead to hyperactivation of the sympathetic nervous system and of the renin-angiotensin-aldosterone system (RAAS), oxidative stress and endothelial dysfunction [5]. Physiologically, BP values are 10-20% lower during the night than during day-time, a process known as BP-dipping. Several studies have associated a non-dipping or a riser profile with cardiovascular event risk and hypertension-related organ damage [5]. Even in the absence of HBP, OSA circadian BP values have a similar pattern to that of hypertensive non-dippers [5]. This report aims to investigate BP control in CPAP-naïve patients with moderate-severe OSA.

Material and Methods

Our study included 44 CPAP-naïve patients referred to our Cardiovascular Rehabilitation Hospital after being diagnosed with moderate-severe OSA in the local Pulmonogy Clinic. All patients underwent clinical examination, anthropometric evaluation (weight, height, abdominal circumference (AC), body mass index (BMI), resting heart rate (HR), SBP and DBP) and ABPM (24-h ambulatory blood pressure monitoring). Our subjects also completed the Epworth and the EQ-5D-5L (Euro Quality of Life) [10] questionnaires. Statistical analysis was performed in Microsoft Excel and SPSS.

Results

Our study included 20 patients with moderate OSA and 24 subjects with severe OSA. Mean AHI and mean desaturation index were 40,49 and 38,68, respectively. Study group characteristics are listed in Table 1. Although average nocturnal O_2 saturation did not differ between the 2 subgroups, significant differences were found regarding desaturation index and minimum nocturnal O_2 saturation.

Our group included 34 males and 10 females (5 with moderate apnea and 5 with severe apnea), 13, 16 and 7 subjects with grade 1, 2 and 3 obesity, respectively. Although 8 patients were overweight according to BMI (25-29,9), all 44 OSA subjects fulfilled the latest criteria for abdominal obesity (AC >80 cm in females and > 94 cm in males) (Tables 2,3).

Patients in the severe OSA subgroup seem to have poorer 24h, daytime and nocturnal systolic BP control, although the results did not reach statistical significance. 24 h diastolic BP values were relatively similar in the 2 groups (with a tendency to be more elevated in patients with moderate OSA). Mean 24 h, diurnal

Table 1. Main characteristics of our study group.

	Moderate OSA	Severe OSA	p
AHI	23.1	53.47	
Desaturation index	23.32	50.21	0.000
Average nocturnal O_2 saturation	92.27	90.73	0.188
Minimum nocturnal O_2 saturation	79.77	70.25	0.001
Age	56.83	57.5	0.810
BMI	35.03	35.56	0.749
AC	116.56	117.25	0.850
HR	68.28	73.58	0.08

AHI – apnea hypopnea index; CPAP – continuous positive airway pressure; BMI – body mass index; AC – abdominal circumference.

Table 2. Weight status in patients with moderate and severe OSA, respectively.

	Moderate OSA	Severe OSA
Overweight	4 (20%)	4 (16.66%)
Grade 1 obesity	7 (35%)	6 (25%)
Grade 2 obesity	5 (25%)	11 (45.83%)
Grade 3 obesity	4 (20%)	3 (12.5%)
Abdominal obesity	20 (100%)	24 (100%)

Table 3. Relationship between abdominal circumference and weight status according to BMI.

	Overweight	Grade 1 obesity	Grade 2 obesity	Grade 3 obesity
Abdominal obesity (no)	8	13	16	7
AC	106.62	108.87	121.5	131.28
AC males	108.5	109.5	124.16	135
AC females	101	102	113.5	126.33

BMI – body mass index; No – number; AC – abdominal circumference.

Table 4. Blood pressure profile in patients with moderate and severe OSA.

	Moderate OSA	Severe OSA	p
Normotensive	2	0	
Grade 1 HBP	0	2	
Grade 2 HBP	1	8	
Grade 3 HBP	17	14	
SBP	135.89	136.54	0.913
DBP	84.72	85.13	0.907
Average number of antihypertensive drugs	2.4	2.29	
Max SBP	163.8	162.95	0.727
Max DBP	104.25	101	0.542
Min SBP	102.65	100.45	0.386
Min DBP	54.45	52.16	0.466
Mean SBP 24 h	130.61	130.58	0.995
Mean DBP 24 h	75.33	74.58	0.739
Mean SBP daytime	133.72	132.54	0.788
Mean DBP daytime	78	75.46	0.316
Mean SBP night	123.89	124.42	0.912
Mean DBP night	69.94	69.08	0.755
Dipping index	6.83	5.8	0.660
Non-dipper	7 (35%)	15 (62.5%)	
Riser	4 (20%)	4 (16.66%)	
Extreme dipper	0	1 (4.16%)	
Dipper	9 (45%)	4 (16.66%)	
Systolic abnormal ratio 24 h	32.10	35.56	0.662
Diastolic abnormal ratio 24 h	15.23	13.4	0.965
Systolic abnormal ratio daytime	27.54	30.68	0.704
Diastolic abnormal ratio daytime	14.41	16.63	0.728
Systolic abnormal ratio night	43.03	59.36	0.128
Diastolic abnormal ratio night	17.95	18.24	0.965
Epworth score	8.39	7.83	0.75
Quality of life	64	70	0.349

HBP – high blood pressure; HR – heart rate; SBP – systolic blood pressure; DBP – diastolic blood pressure. Max – maximum; Min – minimum.

Table 5. Profile of moderate-severe OSA patients depending upon grade of hypertension.

	Normotensive	Grade 1 HBP	Grade 2 HBP	Grade 3 HBP
No. of patients	2	2	9	31
Age	52.5	46.5	56.11	59.06
Moderate OSA	2 (100%)	0	1 (11.11%)	17 (54.83%)
Severe OSA	0	2 (100%)	8 (88.88%)	14 (45.16%)
AHI	19.15	54.7	53.65	36.89
BMI	30.16	34.66	34.67	35.97
AC	105	113.5	117.33	117.65
Beta blocker	0	2 (100%)	5 (55.55%)	20 (64.51%)
Diuretic	0	0	3 (33.33%)	16 (51.61%)
RAAS inhibitors	0	1 (50%)	8 (88.88%)	29 (93.54%)
Calcium channel blockers	0	0	0	16 (51.61%)
Central antihypertensive drugs	0	0	0	3 (9.67%)
Average number of antihypertensive drugs	0	1.5	1.77	2.7
Quality of life	85%	87.5%	78.33%	60.73%

OSA – obstructive sleep apnea; AHI – apne hypopnea index; BMI – body mass index; AC – abdominal circumference; HBP – high blood pressure; HR – heart rate.

and nocturnal BP values were also comparable between the two subgroups (Table 4). However, patients with severe OSA more frequently presented a non-dipper profile.

AHI was significantly correlated with desaturation index (r=0.87, p=0.000), average and minimum nocturnal O_2 saturation (r=-0.488, p=0.001 and r=-0.558, p=0.000, respectively), but not with age (p=0.937), BMI (p=0.273) or abdominal circumference (p=0.314). The correlation between AHI and resting HR reached borderline statistical significance (r=0.3, p=0.05). AHI was not significantly correlated to any of the analysed ABPM parameters, Epworth score results or perceived daily quality of life, according to the EQ-5D-5L visual analog scale.

Average nocturnal O_2 saturation was negatively correlated with BMI (r=-0.453, p=0.003) and abdominal circumference (r=-0.458, p=0.003). Surprisingly, age was negatively correlated to BMI and AC (r=-0.315, p=0.037; r=-0.364, p=0.016, respectively), but also with mean 24 h (r=-0.442, 0.003) and mean daytime DBP (r=-0.407, p=0.006). We found significant correlations between BMI and nocturnal systolic abnormal ratio (r=0.325, p=0.032) but also between resting HR and mean nocturnal (r=0.4, p=0.007) and 24 h SBP (r=0.297, p=0.05).

AHI is significantly higher in the hypertensive OSA patients than in the normotensive ones. BMI and AC seem to increase along with hypertension grade. Patients with more severe hypertension receive on average a higher number of hypotensive drugs, especially RAAS inhibitors (Table 5).

Therapeutical choices in OSA subjects are reviewed in figures 1–4. Most patients in our study group

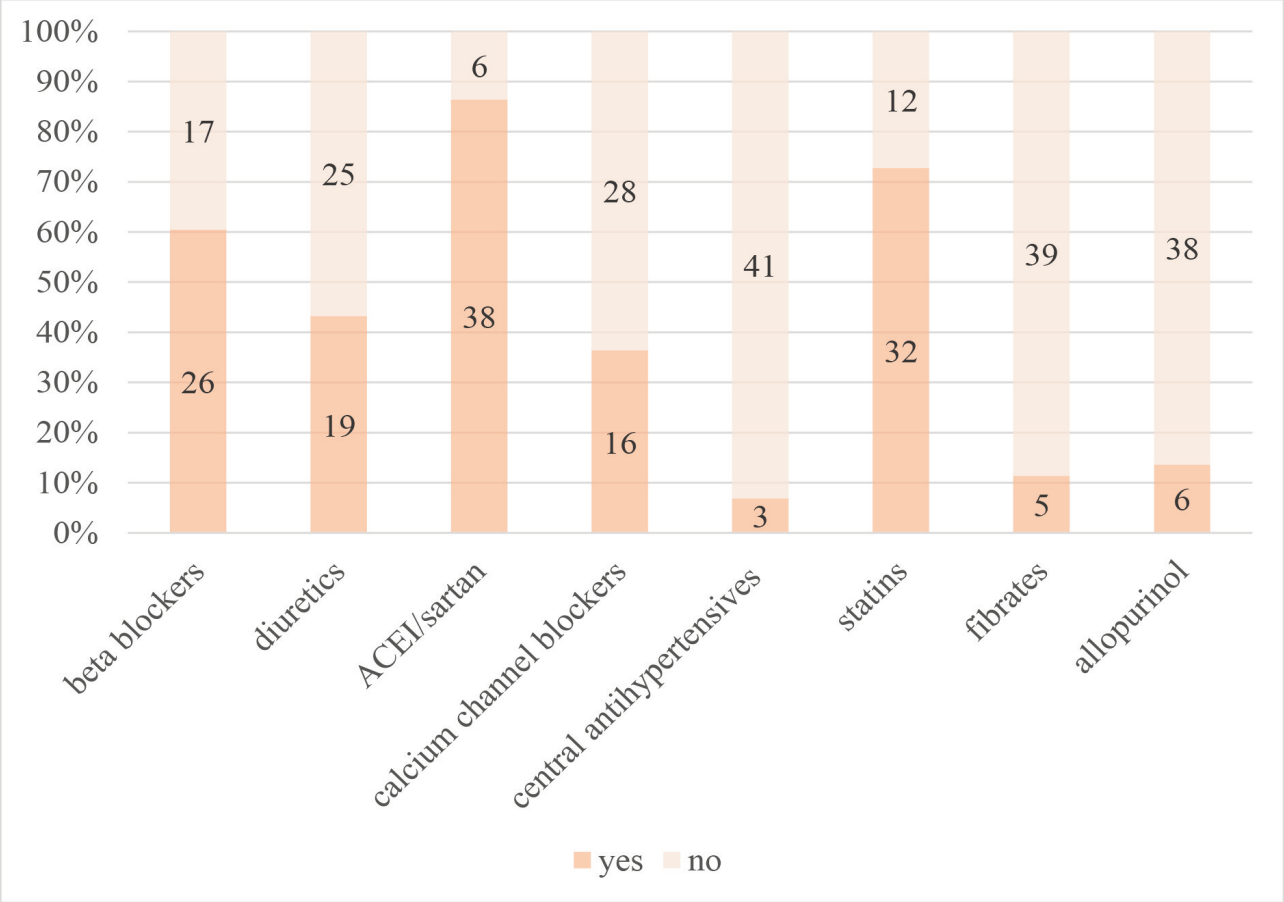

Figure 1. Therapeutic regimen in OSA patients.

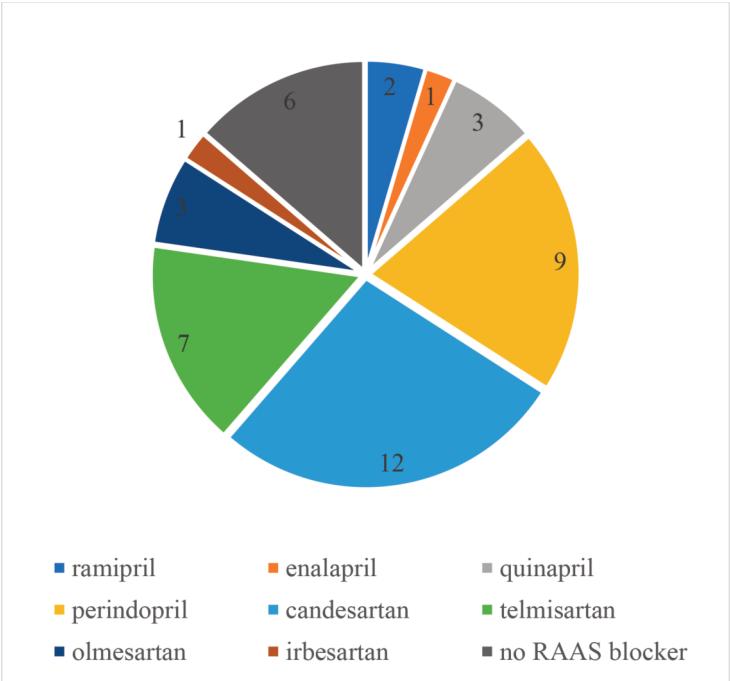

Figure 2. RAAS blockers in OSA patients.

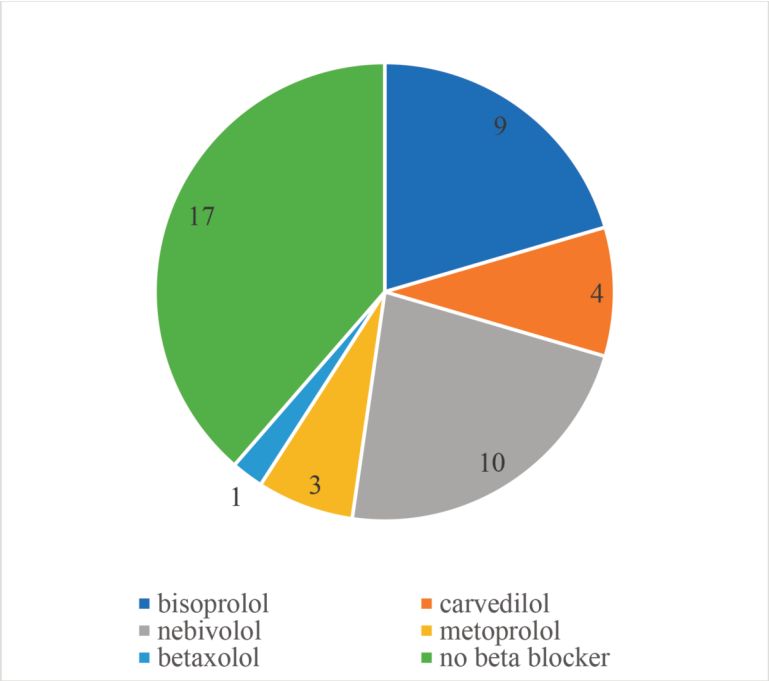

Figure 3. Beta blockers in OSA patients.

(86.36%) received treatment with a RAAS blocker. Beta-blockers were also a common drug choice (59% of cases), but calcium channel blockers (mainly amlodipine), diuretics and central antihypertensives were less frequently prescribed (36.36%, 43.18% and 6.81%, respectively).

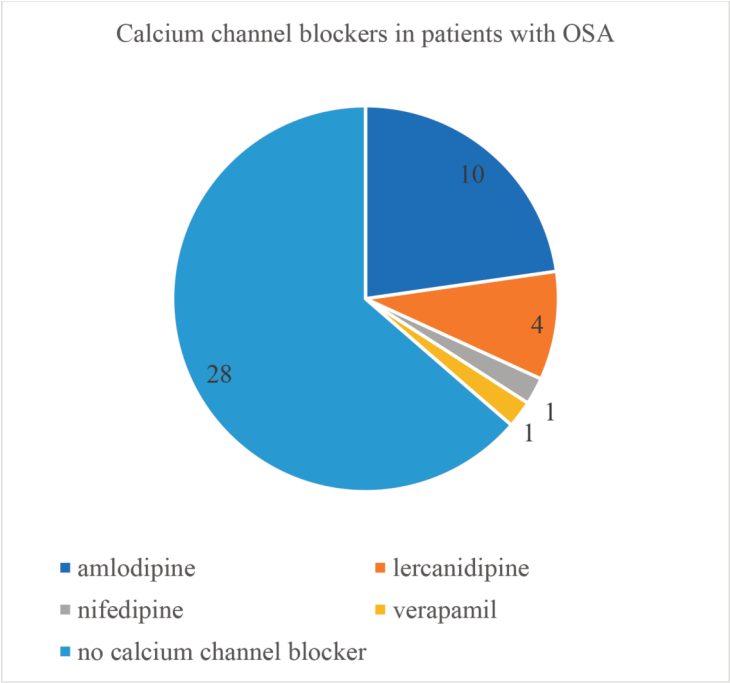

Figure 4. Calcium channel blockers in OSA patients.

Discussion

As reported by previous articles, the prevalence of OSA was much higher among males than in our study group female patients (77.27% and 22.72%, respectively). OSA prevalence increases with age, explaining the relatively high mean age of our subjects (57.59 years old) [1]. Several reports show that the strength of association between HBP and OSA seems to diminish with age, with a probable cut off value of 60 years old [1,12]. This could explain why we did not find significant correlations between AHI and ABPM variables.

Although Baguet et al. found that 42% of apneic patients had office HBP, 58% daytime HBP and 76% night-time HBP, the prevalence of hypertension in our study was much higher (95.45%) [13]. Castro-Grattoni et al. also found a surprisingly low prevalence of HBP among patients with severe OSA (only 28.4%) [14]. On the other hand, all of Delsart's OSA subjects were hypertensive [15].

Mean HR in our study group is slightly lower than in other reports (71.61 versus 79.5) [16]. Resting HR was higher in our severe OSA subgroup, possibly due to sympathetic nervous system activity triggered by OSA severity. The lack of statistical significance can be explained by the small number of subjects included in our study.

Our average sleep SBP and DBP, as well as daytime SBP are similar to that reported by other authors (123.97 versus 120.7 mmHg; 69.52 versus 72.7 mmHg and 132.43 versus 134.4 mmHg, respectively) [16]. However, patients in our study group had lower daytime DBP than other studied OSA groups (76.72 versus 85.9 mmHg) [16]. Our 24h DBP was similar to that reported by Correa et al., although we found 24h SBP to be 10 mmHg higher than the other authors (132.43 mmHg versus 122.3 mmHg) [17]. Furthermore, our patients appeared to have a better control of diurnal and nocturnal diastolic values (assessed through BP abnormal ratios) and a worse management of both diurnal and nocturnal systolic values, than the patients studied by Correa et al [17]. However, we should note that our subjects were on average 17 years older and had a more severe form of OSA (AHI was greater by 16 events/h).

A previous study that included patients somewhat younger and with a lower BMI than our group (mean age 45 years old, mean BMI 29.6) but with similar OSA severity (mean AHI 38.1 compared to 40.49), reported significant correlations between AHI, BMI and BP values [16]. In our group, BMI was indeed correlated with average 24 h and nocturnal SBP.

Previous literature reports found a prevalence as high as 84% of non-dippers among CPAP-naive moderate-severe OSA patients [18]. Another study reported a correlation between AHI, nocturnal mean BP and dipping status [19] and a previous article proved not only that BP is influenced by OSA severity but also that the physiologic nocturnal dipping profile decreases with apnea severity [20]. Although we found no significant association between AHI and dipping index, non-dipper profile was highly prevalent among our OSA subjects (50%) and 18,18% of patients had a reverse-dipper (riser) profile. AHI was not significantly correlated to any of the analysed ABPM parameters, or with the Epworth score results in our OSA patients. Surprisingly, age was negatively correlated with BMI, AC and mean DBP values.

Patients with moderate OSA appear to take a higher number of antihypertensive drugs than those with severe OSA (Table 4). This intriguing result could be explained by submaximal dosing of each drug, patient comorbidities, or the fact that OSA severity impact on BP values diminishes in elderly individuals [12]. Surprisingly, subjective quality of life, assessed through the EQ-5D-5L Visual Analog Scale was higher in patients with severe OSA than in those with AHI 15-30 (Table 4). However, grade of hypertension seems to have an impact on perceived quality of life. Epworth score results were slightly higher in the moderate OSA subgroup, proving once again that the Epworth Score is not a useful tool in stratifying OSA severity.

Conclusions

Hypertension and obesity are highly prevalent among subjects with moderate-severe OSA. Younger OSA patients are more obese and have higher average 24 h and daytime DBP. Average nocturnal O2 saturation, but not AHI, was significantly correlated with BMI and AC. The correlation between AHI and resting HR reached borderline statistical significance (r=0.3, p=0.05) but we found no significant correlations between AHI and any of the analysed ABPM parameters. Furthermore, OSA severity did not impact perceived quality of life in our group, according to the EQ-5D-5L Visual Analog Scale.

Conflict of interests

The authors report no conflict of interests concerning this publication.

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