Milan Sova[1], Samuel Genzor[1], Marketa Sovova[2], Eliska Sovova[2], Katarina Moravcova[2], Shayan Nadjarpour[3], Jana Zapletalova[4]

[1]Department of Respiratory Medicine, Faculty of Medicine and Dentistry, Palacky University and University Hospital Olomouc, Olomouc, Czech Republic
[2]Department of Sports Medicine and Cardiovascular Rehabilitation, University Hospital and Faculty of Medicine and Dentistry, Palacky University Olomouc, Olomouc, Czech Republic
[3]Faculty of Medicine and Dentistry, Palacky University Olomouc, Olomouc, Czech Republic
[4]Department of Medical Biophysics, Faculty of Medicine and Dentistry, Palacky University, Olomouc, Czech Republic

High incidence of masked hypertension in patients with obstructive sleep apnoea despite normal automated office blood pressure measurement results

Abstract

Introduction: Obstructive sleep apnoea (OSA) is a well-known risk factor for masked hypertension (MH) and masked uncontrolled hypertension (MUCH). Automated ambulatory office blood pressure measurement (AOBP) might better correlate with the results of ambulatory blood pressure measurements (ABPM) compared to routine office blood pressure measurement (OBPM). The aim of this study was to compare the diagnostic rate of MH/MUCH when using OBPM and AOBP in combination with ABPM.

Material and methods: 65 OSA patients, of which 58 were males, (AHI > 5, mean 44.4; range 5–103) of average age 48.8 ± 10.7 years were involved in this study. Following MH/MUCH criteria were used; Criteria I: OBPM < 140/90 mm Hg and daytime ABPM > 135/85 mm Hg; Criteria II: AOBP < 140/90 mm Hg and daytime ABPM > 135/85 mm Hg; Criteria III: AOBP < 135/85 mm Hg and daytime ABPM > 135/85 mm Hg.

Results: MH/MUCH criteria I was met in 16 patients (24.6%) with criteria II being met in 37 patients (56.9%), and criteria III in 33 (51.0%), p < 0.0001. Both systolic and diastolic OBPM were significantly higher than AOBP; Systolic (mm Hg): 135.3 ± 12.3 *vs* 122.1 ± 10.1 (p < 0.0001); Diastolic (mm Hg): 87.4 ± 8.9 *vs* 77.1 ± 9.3 (p < 0.0001). AOBP was significantly lower than daytime ABPM; Systolic (mm Hg): 122.1 ± 10.1 *vs* 138.9 ± 10.5 (p < 0.0001); Diastolic (mm Hg): 77.1 ± 9.3 *vs* 81.6 ± 8.1 (p < 0.0001). Non-dipping phenomenon was present in 38 patients (58.4%). Nocturnal hypertension was present in 55 patients (84.6%).

Conclusions: In patients with OSA there is a much higher prevalence of MH/MUCH despite normal AOBP, therefore it is necessary to perform a 24-hour ABPM even if OBPM and AOBP are normal.

Key words: masked hypertension, masked uncontrolled hypertension, automated office blood pressure measurement, obstructive sleep apnoea

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Introduction

Arterial hypertension remains a major cause of cardiovascular morbidity and mortality. Over the last few decades, with the introduction of ambulatory blood pressure measurement (ABPM), new types of hypertension were established: sustained normotension, sustained hypertension, white coat hypertension, masked hypertension (MH) and masked uncontrolled hypertension (MUCH) [1]. MH can be found in approximately 15% of patients with a normal office blood pressure (OBPM). The prevalence of MH is higher in young males, and with respect to lifestyle is higher with smoking,

alcohol consumption, those with higher levels of physical activity, anxiety and an increased job stress [2]. The prevalence with respect to comorbidities increases in those with diabetes, obesity, chronic kidney disease, family history of hypertension and high-normal OBPM [3].

MH and MUCH impair the prognosis and present an important risk factor for cardiovascular disorders. According to meta-analysis Thakkar *et al.* [4] patients with MH/MUCH were 2.09 times more likely to suffer adverse cardiovascular and/or cerebrovascular events compared to patients with sustained normotension.

Obstructive sleep apnoea (OSA) is a well-known risk factor for cardiovascular disease. In patients with OSA, cardiovascular diseases have an increased incidence and are associated with worse functional outcomes and increased mortality [5].

OSA is considered to be an important risk factor of arterial hypertension [6], with the prevalence of MH/MUCH estimated to be 30–60% [7, 8].

Automated office blood pressure measurement (AOBP) is now widely available in high income countries and, according to some authors, should replace routine OBPM [9]. Presently, the relationship between blood pressure readings obtained with conventional OBPM and AOBP remains unclear, but available evidence suggests that conventional OBPM readings may be at least 5–15 mm Hg higher than systolic blood pressure levels obtained by AOBP [10].

There is also very limited evidence on the prognostic value of AOBP, i.e. whether they guarantee at least the same ability to predict outcomes as conventional OBPM [11].

In the general population, AOBP is similar to the awake ABPM, with both AOBP and awake ABPM being around 15/8 mm Hg lower than routine OBPM taken in clinical practice [9]. Possible advantages of AOBP over OBPM are recognized by several guidelines like the European Society of Hypertension and the European Society of Cardiology [3], U.S. Preventive Services Task Force [12] and the 2017 United States American College of Cardiology/American Heart Association Recommendations [13]. Accordingly, the Canadian Hypertension Education Program guidelines in 2016 recommended AOBP as the preferred method of in-office blood pressure measurement [14]. In general population-based studies, AOBP correlates better with daytime ABPM than routine OBPM [15–17].

However, contrary to this, in a recently published study conducted with a high cardiovascular risk cohort, there was a large discrepancy found between systolic AOBP and systolic daytime ABPM [18]. Moreover, higher cardiovascular risk was independently associated with a larger discrepancy between AOBP and ABPM. In OSA patients similar risk factors are present like in the previously stated study population and in the available literature, there is no data regarding AOBP in patients with OSA. There is an apparent need to establish the possible difference in MH/MUCH diagnostic rate when using routine office blood pressure measurement and AOBP.

The aim of this study was to compare the efficiency of combined use of AOBP with ABPM compared to OBPM with ABPM in the diagnostic rate of MH/MUCH in OSA patients.

Material and methods

Sixty five patients were involved in this study, of which, 58 were male and the average age of the group was 48.8 ± 10.7 years. All patients were initially referred to the sleep laboratory because of suspected OSA. Patients were randomly selected and the whole group represents the standard population diagnosed and subsequently treated with obstructive sleep apnoea. First, anthropometric data of the patients were obtained, and patients completed an Epworth Sleepiness Scale (ESS) questionnaire.

Pre-existing arterial hypertension was present in 55.4% of the patients.

During hospitalization, the sleep study was performed in a sleep laboratory using a Porti 8 device (F+G, Germany). The results of the sleep study were manually re-scored using the International classification of sleep disorders (ICD-3), 3rd diagnostic and coding manual [19]. Parameters measured were blood oxygen saturation and heart rate (pulse oximetry); flow of exhaled air to detect apnoea/hypopnea; thoracic and abdominal movements, and patients position during sleep.

Patients with an apnoea-hypopnea index (AHI) ≥ 5 were then enrolled in this study. OBPM: blood pressure was measured in the following way. The patients were seated comfortably in a quiet environment for 5 minutes prior to taking blood pressure measurements. The blood pressure was measured using validated manual sphygmomanometer three times at 5-minute intervals by experienced staff involved with the study, an average of the last two measurements was used in the later analysis. AOBP: blood pressure was measured using SunTech CT40-SunTech Medical, USA. Standard protocol was used, patient was seated for 5 minutes in quite room
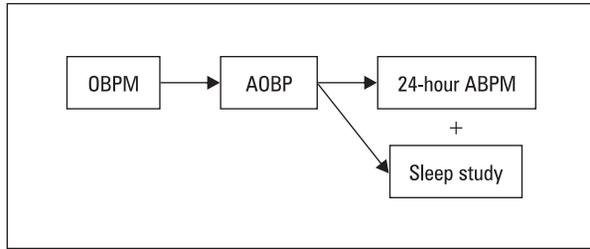
Figure 1. The sequence of blood pressure measurements. ABPM — ambulatory blood pressure measurement; AOBP — automated office blood pressure measurement; OBPM — office blood pressure measurement

Table 1. Basic clinical parameters and Epworth sleepiness scale. SD — standard deviation

Parameter	Mean ± SD	Median (min–max)
Age [years]	48.8 ± 10.7	48.0 (26.0–69.0)
Height [cm]	176.6 ± 7.8	176.0 (158.0–194.0)
Weight [cm]	107.2 ± 18.8	103.0 (64.0–153.0)
Neck circumference [cm]	43.0 ± 4.0	43.0 (36.0–64.0)
Waist circumference [cm]	114.6 ± 12.1	115.0 (77.0–150.0)
Hip circumference [cm]	112.7 ± 9.5	112.0 (92.0–139.0)
Epworth sleepiness scale	9.1 ± 4.6	8.0 (0.0–21.0)

Table 2. List of comorbidities

Comorbidity	Arterial hypertension	Atrial fibrillation	Ischemic heart disease	Diabetes mellitus
N [%]	36 (55.4)	3 (4.6)	2 (3.1)	10 (15.4)

and subsequently 5 measurements at 2-minute intervals were performed. The average of these 5 measurements was taken to be the result used.

24-hour ABPM: BTL ABPM device, Czech Republic was used. Measurements were performed at the following intervals: 15 minutes during daytime and 30 minutes during night. 70% of valid measurements were needed to fulfil reproducibility criteria.

The sequence of different blood pressure measurements is presented in Figure 1.

The primary aim of this study was to compare the difference of prevalence of MH/MUCH when using OBPM or AOBP. Three criteria of MH/MUCH were used:
— MH/MUCH criteria I: OBPM < 140/90 mm Hg and daytime ABPM > 135/85 mm Hg;
— MH/MUCH criteria II: AOBP < 140/90 mm Hg and ABPM > 135/85 mm Hg;
— MH/MUCH criteria III: AOBP < 135/85 mm Hg and ABPM > 135/85 mm Hg.

Nocturnal hypertension was defined as blood pressure > 120/70 mm Hg during the night. Ethical approval: All procedures performed in studies that involved human participants were in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by local Ethics Committee. Informed consent: Informed consent was obtained from all individual participants included in the study.

Statistical analysis

SPSS software version 15.0 (SPSS Inc., Chicago, USA) was used for the statistical analysis. The normality of distribution was checked by the Shapiro-Wilk test with P < 0.05 being considered statistically significant. This study is registered in ClinicalTrials.gov as NCT03869125.

Results

Basic clinical parameters and ESS are presented in Table 1. Comorbidities are listed in Table 2, note that 55.4% of patients had a known history of arterial hypertension - pharmacologically treated. Sleep study parameters are presented in Table 3. Results of OBPM, AOBP and ABPM are presented in Table 4.

Most of the patients involved in the study had severe OSA (86.2%), with 4.6% having moderate OSA and 9.2% with mild.

The mean difference between OBPM and AOBP was -13.2 ± 10.4 mm Hg for systolic and -10.3 ± 8.6 mm Hg for diastolic blood pressure.

Both systolic and diastolic OBPM were significantly higher than AOBP; systolic (mm Hg): 135.3 ± 12.3 *vs* 122.1 ± 10.1 (p < 0.0001); diastolic (mm Hg): 87.4 ± 8.9 *vs* 77.1 ± 9.3, (p < 0.0001) (Figure 2).

AOBP was significantly lower than daytime ABPM; systolic (mm Hg): 122.1 ± 10.1 *vs* 138.9 ± 10.5 (p < 0.0001); diastolic (mm Hg): 77.1 ± 9.3 *vs* 81.6 ± 8.1 (p < 0.0001) (Figure 3).

The mean difference between daytime ABPM and AOBP was -16.75 ± 8.0 mmHg for systolic and -4.54 ± 7.6 mm Hg for diastolic blood pressure.

There was no statistically significant correlation between OBPM/AOBP difference, and nocturnal hypertension (p = 0.820), and nocturnal non-dipping phenomenon (p = 0.0823).

Table 3. Result of sleep breathing study. SD — standard deviation

Parameter	Mean ± SD	Median (min–max)
Apnoea hypopnoea index	44.4 ± 28.4	45.0 (5.0–103.0)
Oxygen desaturation index	50.5 ± 28.1	46.0 (3.3–114.0)
Time $SpO_2 < 90\%$	17.4 ± 21.5	7.5 (0.0–77.0)
Average oxygen saturation [%]	91.3 ± 5.9	93.0 (53.0–96.0)

Table 4. Results of blood pressure measurements; ABPM — ambulatory blood pressure measurement; AOBP — automated office blood pressure measurement; OBPM — office blood pressure measurement; SD — standard deviation

Parameter (mm Hg)	Mean ± SD	Median (min–max)
OBPM		
Systolic	135.3 ± 12.4	133.3 (106.7–173.3)
Diastolic	87.4 ± 8.9	86.7 (66.7–118.3)
AOBP		
Systolic	122.1 ± 10.1	122.0 (99.0–147.0)
Diastolic	77.1 ± 9.3	77.0 (55.0–98.0)
ABPM		
24 hr systolic	135.2 ± 10.6	135.0 (111.0–167.0)
24 hr diastolic	78.8 ± 8.1	79.0 (55.0–103.0)
Daytime systolic	138.9 ± 10.5	138.0 (115.0–165.0)
Daytime diastolic	81.6 ± 8.1	83.0 (60.0–104.0)
Nocturnal systolic	129.1 ± 12.8	128.0 (103.0–169.0)
Nocturnal diastolic	73.8 ± 9.0	73.0 (48.0–101.0)

MH/MUCH criteria I was met by 16 patients (24.6%), MH/MUCH criteria II was met in 37 patients (56.9%) and MH/MUCH criteria III in 33 (51.0%). The difference was statistically significant (p < 0.0001; McNemar test) (Figure 4).

Discussion

This is the first study of the use of AOBP in the context of MH/MUCH diagnosis in patients with OSA. The aim of this study was to compare the diagnostic rate of MH/MUCH when using OBPM and AOBP in combination with ABPM.

The main finding of this study was a large discrepancy between daytime systolic ABPM and systolic AOBP (-16.75 ± 8.0 mm Hg). This was much higher than in previous reports by Myers (-1.8 mm Hg) [20] and Godwin (1.8 mm Hg) [21].

Results were much closer to those published by Seo *et al.* (-7.3 mm Hg) [18]. The difference in diastolic blood pressure was in concordance with the previous studies stated (-4.54 mm Hg). An explanation for this could be possible different characteristics of arterial hypertension in OSA patients, especially higher overall sympathetic activity. However, more robust studies are needed to confirm this discrepancy, and to shed more light onto possible pathophysiology. In comparison with the Seo et al study, ischemic heart disease was diagnosed in only 3.1% of patients, but the estimated overall cardiovascular risk will be possibly higher in comparison with the general population.

The diagnostic rate of MH/MUCH criteria I and II (24.6% and 56.9% respectively) in patients with OSA was in concordance with previously published studies [7, 8].

When we used AOBP threshold < 135/85 mm Hg (criteria III), which is recommended according to several studies [22], we have found similar prevalence of MH/MUCH (51.0%). Also, when we consider nocturnal hypertension (84.6%) the diagnostic rate of MH/MUCH would be much higher than previously reported. According to current guidelines, any out of office value of blood pressure should be used, on the other side these guidelines are not primarily focused on OSA patients where nocturnal hypertension is highly prevalent.

The important finding of this study is the much higher diagnostic rate of MH/MUCH when AOBP is used, which could increase the risk of general cardiovascular disease. Some studies reported that patients with MH/MUCH have a similar risk to patients with sustained hypertension [23, 24]. For example, in previous studies a significant association between MH/MUCH and left ventricular hypertrophy, increased carotid intima-media thickness, albuminuria, aortic stiffness and early hypertensive retinal changes were shown [25–27].

Also, the prevalence of nocturnal hypertension was high in this sample (84.6%) and the non-dipping phenomenon was present in 38 patients (58.4%). These two entities are common in OSA patients as was previously found in different studies [8].

Elevated nocturnal blood pressure adds to the poor outcome of OSA patients [28]. Findings from the MAPEC (Monitorizacion Ambulatoria para Prediccion de Eventos Cardiovasculares) study suggest that normalizing of nocturnal blood pressure significantly reduces cardiovascular disease risk [29].
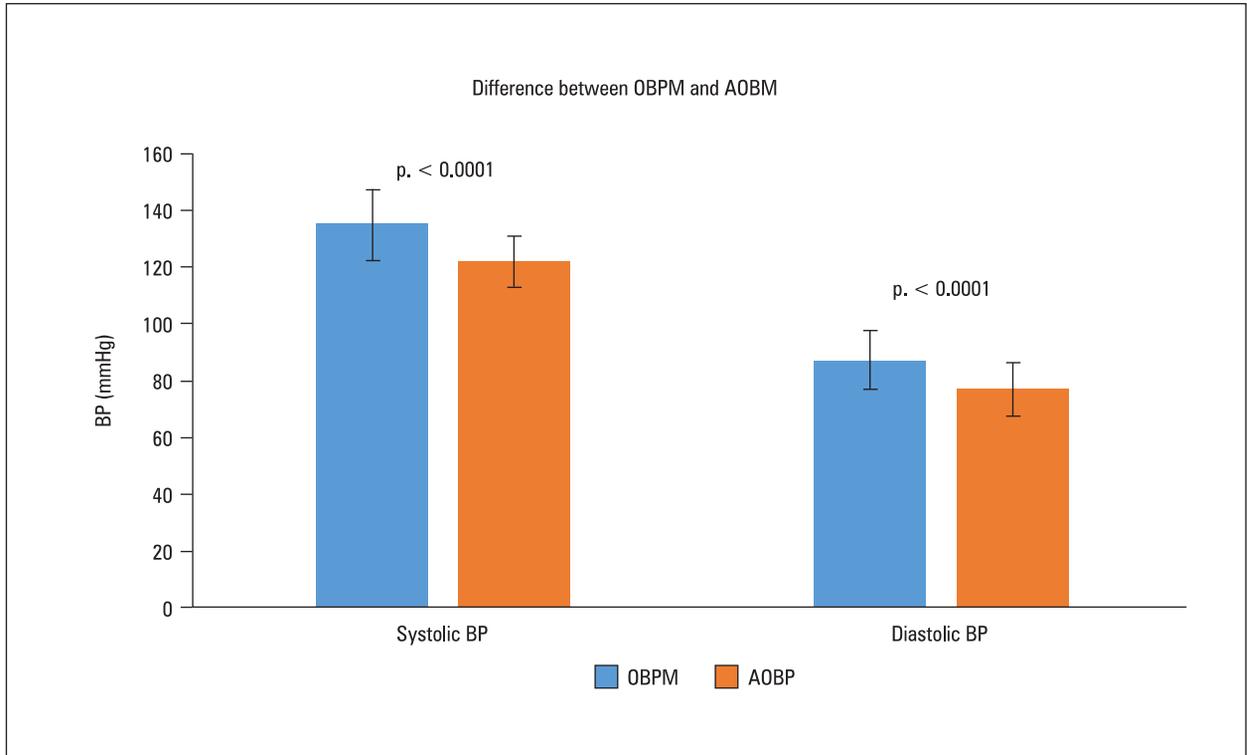
Figure 2. The difference between office and automated blood pressure monitoring (Student´s t-test). AOBP — automated office blood pressure measurement; OBPM — office blood pressure measurement
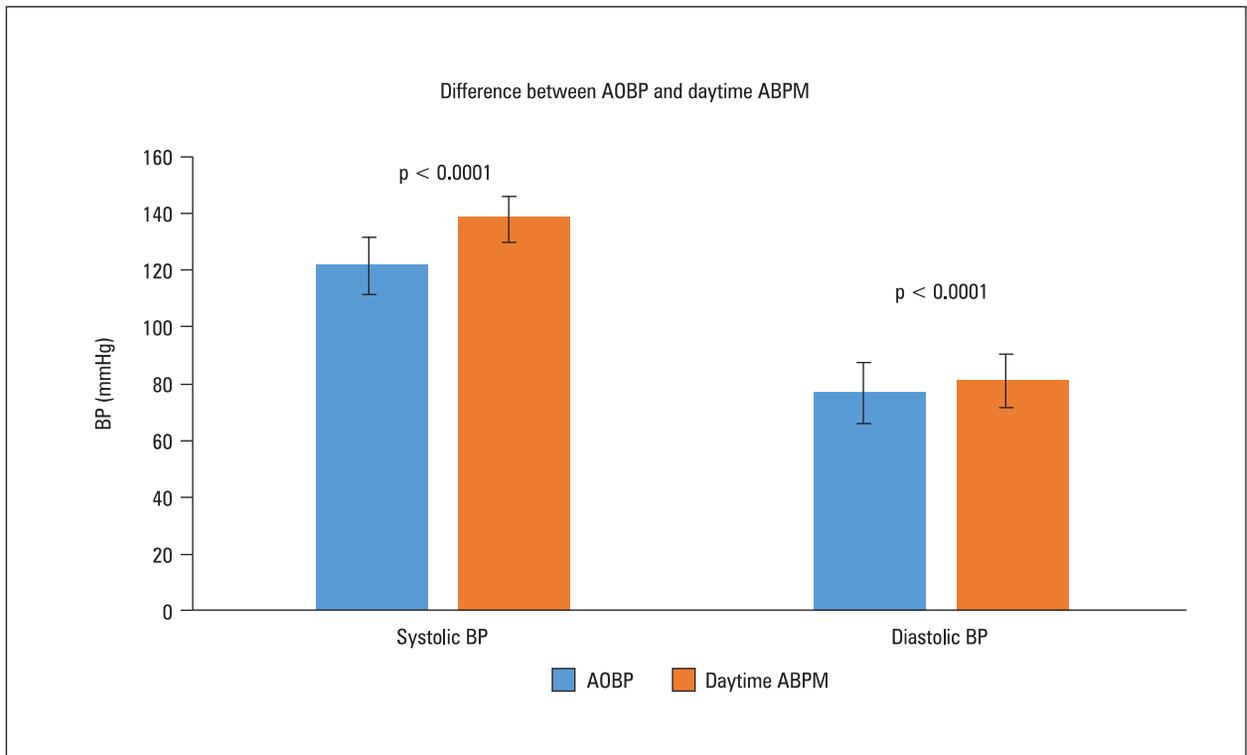

Figure 3. The difference between automated office blood pressure monitoring and daytime ambulatory blood pressure monitoring (Student´s t-test); ABPM — ambulatory blood pressure measurement; AOBP — automated office blood pressure measurement; BP — blood pressure
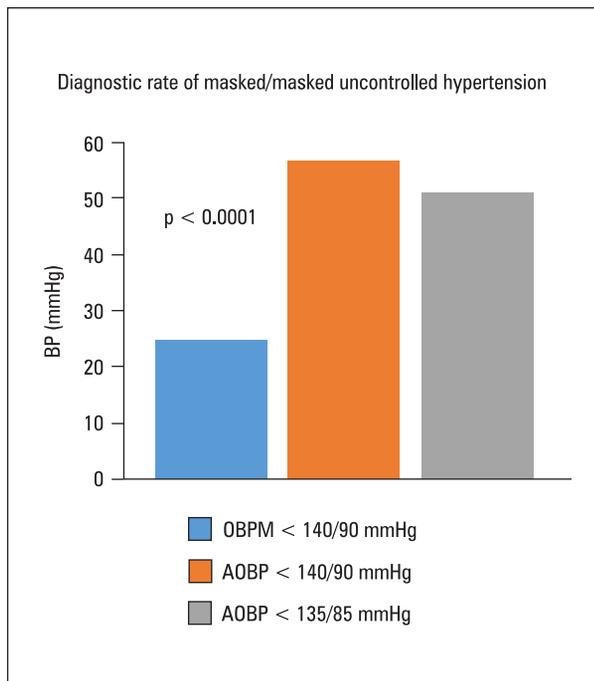
Figure 4. Diagnostic rate of masked/masked uncontrolled hypertension according to different criteria (McNemar test). Non-dipping phenomenon was present in 38 patients (58.4%). Nocturnal hypertension was present in 55 patients (84.6%). ABPM — ambulatory blood pressure measurement; AOBP — automated office blood pressure measurement; OBPM — office blood pressure measurement

This study has several limitations. The first, being the relatively small study sample size. The second is the limited sleep study performed; namely, the use of overnight respiratory polygraphy instead of polysomnography, therefore without the use of an electroencephalography it is unclear whether patients were asleep throughout the whole duration of the sleep study which could contribute to a possible bias in the overestimation or underestimation of OSA severity in some patients. On the other hand, this method is widely used, and is considered a suitable diagnostic method for OSA, and the possible correlations with OSA severity are not the objective of this study. However, only a small part of the study group had mild OSA (9.2%). Finally, the additional stress the patient has during the study in the sleep laboratory could contribute to a skew in the results.

Conclusion

In OSA patients there is a much higher prevalence of MH/MUCH despite normal AOBP, therefore it is necessary to perform a 24-hour ABPM even if OBPM and AOBP are normal.

Conflict of interest

None declared.

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