Sleep Breath (2011) 15:665–672
DOI 10.1007/s11325-010-0417-5

ORIGINAL ARTICLE

APAP impact on metabolic syndrome in obstructive sleep apnea patients

Patrícia Caetano Mota · Marta Drummond · João Carlos Winck · Ana Cristina Santos · João Almeida · José Agostinho Marques

Received: 5 April 2010 / Revised: 20 July 2010 / Accepted: 6 September 2010 / Published online: 24 September 2010

Abstract
Purpose Prevalence of metabolic syndrome (MS) in obstructive sleep apnea (OSA) patients is high. The effect of autoadjusting positive airway pressure (APAP) on MS remains unclear. This study aimed to determine the prevalence of MS in OSA patients before and 6 months after APAP, and to identify potential determinants of metabolic status change.
Methods Seventy-four male patients with moderate to severe OSA were enrolled. MS diagnosis was established according to the National Cholesterol Education Program/ Adult Treatment Panel III. APAP was prescribed to all patients.
Results In the studied population, mean age was 55.9 years (SD 10.7 years), median body mass index (BMI), Epworth sleepiness scale (ESS), and respiratory disturbance index (RDI) were 33.4 kg/m^2 (interquartile range (IQR) 8.4 kg/m^2), 12.0 (IQR 8.0), and 46.9/h (IQR 33.6/h), respectively. Prevalence of MS before and 6 months after APAP was 63.5% and 47.3%, respectively, and this difference was statistically significant (p=0.004). In the subgroup of patients with MS at baseline (n=47), 14 did not present MS after APAP. In these patients, a significant negative association with RDI (p=0.016) and a positive association with percent of total days of usage (p=0.014) were found. Blood pressure (p=0.018) and serum triglycerides (p=0.001) had a statistically significant reduction during this period. In patients that still had MS, 22.2% presented a reduction of the number of MS criteria.
Conclusions After 6 months, APAP reduced the prevalence of MS, mainly in patients with less severe OSA and with a better therapeutic compliance. Blood pressure and serum triglycerides reduction contributed to this metabolic status change.

Keywords Autoadjusting positive airway pressure · Metabolic syndrome · Obstructive sleep apnea · Prevalence

P. C. Mota (✉) · M. Drummond · J. C. Winck · J. Almeida · J. A. Marques
Department of Pulmonology, Hospital de São João, Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal
e-mail: patmota@net.sapo.pt

M. Drummond · J. C. Winck · J. A. Marques
Faculdade de Medicina da Universidade do Porto, Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal

A. C. Santos
Department of Hygiene and Epidemiology, Faculdade de Medicina da Universidade do Porto, Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal

Introduction

Obstructive sleep apnea (OSA) is a common disorder with a prevalence of 2% to 4% in adult middle-aged population [1]. It is characterized by repeated episodes of upper airway obstruction during sleep, associated with increasing respiratory efforts, intermittent arterial oxygen desaturation, systemic and pulmonary arterial blood pressure surges, and sleep disruption [2]. Current knowledge on the natural history of the disease is still limited, but the long-term consequences of OSA appear relevant. Patients with OSA have a higher incidence of cardiovascular morbidity and mortality [2, 3]. Recent data suggest that OSA may be associated with a number of cardiovascular risk factors, independently of obesity, such as hypertension, insulin resistance, impaired glucose tolerance, and dyslipidemia,

which together comprise the metabolic syndrome (MS) [2, 4]. This syndrome affects millions of people worldwide and since its first description in the 1920s, the definition of MS has undergone several modifications. They all share similar definitional criteria, although they differ somewhat regarding etiology of the MS and degree of importance assigned to each of its components [4, 5]. According to MS definition used, its prevalence in USA varies between 22% and 39% [6, 7], affecting 26.8% of men and 16.6% of women [8]. The overall prevalence of the MS in nondiabetic adult Europeans is 15% (15.7% in men and 14.2% in women) [9].

A growing recognition of the presence of various metabolic abnormalities in subjects with OSA has been observed during the past two decades, and the association of OSA and MS was highlighted as "syndrome Z" in the late 1990s [10]. Prevalence of MS in OSA patients is high, varying between 60% and 90% [4, 11–13]. Despite the rather prolific data that suggest a contributing role of OSA towards the various components of MS and the entity itself, the exact relationship between OSA and MS remains controversial [4, 11–18].

There are multiple potential mechanistic pathways involved in the interaction between OSA and MS [19]. Chronic intermittent hypoxia and sleep fragmentation with sleep loss present in OSA can lead to generation of reactive oxygen species and neurohumoral changes, respectively. These key triggers likely initiate or contribute to the inflammation, a prominent phenomenon of this interaction [2, 4, 17, 19].

Continuous positive airway pressure (CPAP) is the primary treatment for OSA since it eliminates upper airway collapse during sleep, and improves sleep fragmentation, daytime symptoms, and quality of life [20]. Accumulative evidence supports that CPAP also reduces cardiovascular morbidity, through alterations in each of the components of MS [4, 12, 17, 21–26]. However, these results are not consistent, and some studies only reveal a positive effect of CPAP in highly compliant patients and in different treatment time courses [17, 21–24].

Autoadjusting positive airway pressure (APAP), an alternative treatment to CPAP, has been showing similar effectiveness in eliminating respiratory events and improving subjective sleepiness [27], while in some studies presenting superiority against CPAP in terms of patients' satisfaction and preference [28]. However, one study suggested that CPAP and APAP, despite significant effects on OSA indexes and symptoms, do not improve cardiovascular risk factors into the same extent [29].

Data on the impact of OSA treatment, mainly with APAP, on MS entity are scanty.

Thus, this study aimed to evaluate the prevalence of MS in OSA patients before and 6 months after APAP. This study had also the purpose of identifying the potential determinants of metabolic status change.

Methods

This is a prospective observational study. All patients gave written informed consent to participate in the study. The study protocol was approved by the Hospital Ethics Committee and the study was performed in accordance to the guidelines of the Declaration of Helsinki and its current revision.

Subjects

Seventy-four male patients, referred to our Sleep-Disordered Breathing Clinic, with newly diagnosed moderate/severe OSA (respiratory disturbance index—RDI >20/h), confirmed by domiciliary sleep study, were included in the study.

Exclusion criteria were established previously: neoplastic diseases, systemic inflammatory chronic diseases, active infectious diseases, systemic long-term corticotherapy, female gender, a weight loss greater than 10%, changes in current medication regimens (antihypertensive, antidiabetic and antidyslipidemic drugs), and major changes in smoking habits.

Study procedures

An overnight sleep study was performed using a five-channel recording device (AlphaScreen®, Vyasis). This device produces a computerized recording of variations in oronasal airflow (measured by nasal cannula), body position, wrist actimetry, pulse rate, and arterial oxygen saturation (measured by finger pulse oximetry). The device estimates the total sleep time from the wrist actimetry registry, eliminating those periods with high activity. It automatically calculates the number of apneas plus hypopneas per hour of estimated sleep time (automatic RDI) and it also provides information of desaturations >4% per hour of estimated sleep time and the cumulative percentages of sleep time under 90% oxygen saturation. In all cases, sleep technicians carried out a manual analysis of the recordings, by counting apnea (events of airflow cessation lasting for at least 10 s) and hypopnea episodes (events of airflow reduction to 20% to 50% of the previously observed lasting for at least 10 s, joined with a 4% dip in oxygen saturation), dividing the total number of these episodes by the sleep time in hours, thus obtaining the manual RDI [30].

APAP (REMstar™ Auto, Respironics Inc., Murrysville, PA, USA) therapy was prescribed to all patients with a

mean minimum pressure of 4 cmH_2O and a mean maximum pressure of 17 cmH_2O. Concerning therapy effectiveness, a periodic follow-up was conducted (1 week, 1 month, 3 months, and 6 months post-treatment initiation) with evaluation of the clinical symptoms (by Epworth sleepiness scale (ESS)) and APAP compliance variables, such as: number of hours per night; pressure on 90% nighttime (P_{90}); percentage of total days of APAP usage; and residual RDI.

At baseline, 24-h ambulatory blood pressure (Spacelab, Inc 90207 Neural) was performed in all but two patients who refused the examination as they considered the arm discomfort intolerable. Hypertension was considered according to established criteria [5].

Fasting morning venous blood samples were collected between 8 and 10 a.m. before treatment and 6 months after the treatment initiation. Blood samples were immediately sent to the laboratory for estimation of glucose and lipids.

The clinical identification of MS was performed according to the National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATPIII) criteria, which were updated in 2005 in a statement from the American Heart Association/National Heart, Lung, and Blood Institute [5]. Patients were classified as having MS when three or more of the following constituent components were present: abdominal obesity, defined as a waist circumference ≥102 cm; serum triglycerides ≥150 mg/dL or drug treatment for elevated triglycerides; serum high-density lipoprotein cholesterol (HDL-C) <40 mg/dL or drug treatment for low HDL-C; fasting blood glucose ≥100 mg/dL or drug treatment for elevated blood glucose; elevated blood pressure defined as a systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or antihypertensive drug treatment.

Statistical analysis

Statistical analysis was performed using the SPSS version 17.0 software (SPSS Inc., Chicago, Illinois, USA). All probabilities were two-tailed and p values <0.05 were regarded as significant.

Data were described as mean and standard deviation (SD) or as median and interquartile range (IQR) for quantitative variables and as counts and proportions. For comparison of quantitative variables the Student's t test and the Mann–Whitney test were used. The Chi-square test or the Fisher exact test were used to compare categorical variables whenever was appropriate.

In comparison with the study baseline and after 6 months of APAP, the Wilcoxon test and the McNemar test were used for quantitative variables and for categorical variables, respectively.

Results

Overall studied population characteristics at baseline are presented in Table 1 and according to its initial metabolic status in Table 2. Patients with MS at baseline (n=47) were significantly younger (54.0 years (SD 10.7 years) versus 59.2 years (SD 10.1 years); p=0.041), presented higher body mass index (BMI) (35.4 kg/m^2 (IQR 6.0 kg/m^2) versus 28.0 kg/m^2 (IQR 5.0 kg/m^2); p<0.001) and waist circumference (114.0 cm (IQR 13.0 cm) versus 100.0 cm (IQR 19.0 cm); p<0.001) and a more severe sleep-disordered breathing [(RDI: 56.6/h (IQR 36.8/h) versus 33.2/h (IQR 20.3/h); p<0.001), (desaturation index: 55.3/h (IQR 35.7/h) versus 28.1/h (IQR 22.3/h); p<0.001), (lowest arterial oxygen saturation: 67.0% (IQR 17.5%) versus 77.0% (IQR 8.0%); p<0.001)], compared to those without MS (n=27; Table 2). The severity of daytime sleepiness (evaluated by ESS), smoking habits, and presence of comorbidities did not significantly differ between both groups.

During the 6 months of APAP treatment, patients did not lose significant weight (median baseline weight: 92.0 kg (IQR 22.3 kg) versus median final weight: 93.3 kg (IQR 22.8 kg); p=0.992) nor changed their fat distribution evaluated by waist-hip ratio (WHR; median baseline and final WHR=1.00 (IQR 0.1); p=0.110), and no change in their current medication was performed.

The prevalence of MS at baseline and after 6 months of APAP was 63.5% and 47.3%, respectively, and this difference was statistically significant (p=0.004). Regarding the participants that were defined as having MS at study

Table 1 Sample characteristics at baseline

Variable[a]	n=74
Age (years), mean (SD)	55.9 (10.7)
BMI (kg/m^2), median (IQR)	33.4 (8.4)
Waist circumference (cm), median (IQR)	112 (16.3)
ESS, median (IQR)	12.0 (8.0)
RDI (events/h), median (IQR)	46.9 (33.6)
Smoking habits, n (%)	
Non-smokers	29 (39.2)
Former smokers	31 (41.9)
Current smokers	14 (18.9)
Congestive heart failure, n (%)	7 (9.5)
Stroke, n (%)	10 (13.5)
Acute myocardial infarction, n (%)	5 (6.8)
Angina, n (%)	3 (4.1)

BMI body mass index, *ESS* Epworth sleepiness scale, *RDI* respiratory disturbance index

[a] Quantitative variables are expressed as mean and standard deviation (SD) or as median and interquartile range (IQR)

Table 2 Sample characteristics according to baseline metabolic status

Variable[a]	With MS at baseline (n=47)	Without MS at baseline (n=27)	p value
Age (years), mean (SD)	54.0 (10.7)	59.2 (10.1)	0.041
BMI (kg/m^2), median (IQR)	35.4 (6.0)	28.0 (5.0)	<0.001
Waist circumference, median (IQR)	114.0 (13.0)	100.0 (19.0)	<0.001
ESS, median (IQR)	14.0 (9.0)	11.0 (5.5)	0.059
RDI (events/h), median (IQR)	56.6 (36.8)	33.2 (20.3)	<0.001
Desaturation index (events/h), median (IQR)	55.3 (35.7)	28.1 (22.3)	<0.001
Lowest O_2 saturation (%), median (IQR)	67.0 (17.5)	77.0 (8.0)	<0.001
Smoking habits, n (%)			
Non-smokers	18 (38.3)	11 (40.7)	0.408
Former smokers	18 (38.3)	13 (48.1)	
Current smokers	11 (23.4)	3 (11.1)	
Congestive heart failure, n (%)	6 (12.8)	1 (3.7)	0.411
Stroke, n (%)	9 (19.1)	1 (3.7)	0.082
Acute myocardial infarction, n (%)	3 (6.4)	2 (7.4)	1.000
Angina, n (%)	1 (2.1)	2 (7.4)	0.550

MS metabolic syndrome, *BMI* body mass index, *ESS* Epworth sleepiness scale, *RDI* respiratory disturbance index

[a] Quantitative variables are expressed as mean and standard deviation (SD) or as median and interquartile range (IQR)

entry (n=47), the subgroup of patients that ameliorated its metabolic profile (n=14) presented a significant lower median RDI, comparing to the subgroup of patients that maintained MS at 6 months (n=33; 50.2/h (IQR 35.9/h) versus 62.1/h (IQR 37.4/h); p=0.016). No significant differences were found between both subgroups regarding age, BMI, ESS, desaturation index, and lowest arterial oxygen saturation. Also, participants that ended without MS had significantly higher percentage (%) of total days of usage of APAP (98.1% (IQR 7.3%) versus 88.2% (IQR 17.7%); p=0.014; Table 3). Residual RDI did not differ between both subgroups, and its value was under five events per hour for both (data not shown).

The MS components that significantly improved, taking into account the cut-offs of MS criteria, during the 6 months of treatment and among those that were defined as having MS at baseline, were high blood pressure (p=0.018) and high serum triglycerides (p=0.001; Table 4).

Evaluating the components of MS individually, 6 months of APAP therapy reduced significantly median systolic (p< 0.001) and diastolic blood pressure (p<0.001) and median serum triglycerides levels (p=0.010; Table 5).

A reduction of the number of criteria accounted for MS diagnosis was observed among six patients (22.2%) who maintained MS after treatment. Most of them changed from a total of four to three criteria (n=5). An improvement in HDL-C (n=3) and fasting blood glucose (n=2) contributed to that change (data not shown).

Table 3 Characteristics of participants with MS at baseline concerning their metabolic status after 6 months of APAP

Variable[a]	With MS after 6 months of APAP (n=33)	Without MS after 6 months of APAP (n=14)	p value
Age (years)	53.0 (12.0)	56.5 (14.0)	0.073
BMI (kg/m^2)	35.3 (4.2)	36.9 (10.3)	0.843
ESS	15.0 (9.0)	11.5 (7.3)	0.382
RDI (events/h)	62.1 (37.4)	50.2 (35.9)	0.016
Desaturation index (events/h)	54.9 (44.5)	55.6 (33.1)	0.410
Lowest O_2 saturation (%)	67.5 (13.8)	63.0 (21.3)	0.327
APAP compliance variables			
P_{90} (cmH_2O)	10.6 (2.5)	10.6 (2.6)	0.635
% total days of usage	88.2 (17.7)	98.1 (7.3)	0.014
Hours per night	5.3 (2.0)	6.4 (1.8)	0.075

MS metabolic syndrome, *APAP* autoadjusting positive airway pressure, *BMI* body mass index, *ESS* Epworth sleepiness scale, *RDI* respiratory disturbance index, P_{90} pressure on 90% nighttime

[a] Variables are expressed as median and interquartile range (IQR)

Two patients with no MS at baseline developed it after treatment, determining a cumulative incidence of MS at 6 months of 7.5%. Comparing with patients that maintained or resolved MS, these two patients presented a significant worse APAP compliance in what concerns median values

Table 4 MS components status in patients with and without MS after 6 months of APAP

MS components	With MS after 6 months of APAP (n=33)	Without MS after 6 months of APAP (n=14)	p value
High waist circumference (n=45)			
Yes, n (%)	31 (96.9)	11 (84.6)	
No, n (%)	1 (3.1)	2 (15.4)	0.196
High blood pressure (n=38)			
Yes, n (%)	19 (76.0)	4 (30.8)	
No, n (%)	6 (24.0)	9 (69.2)	0.018
Low HDL-C (n=12)			
Yes, n (%)	4 (44.4)	2 (66.7)	
No, n (%)	5 (55.6)	1 (33.3)	1.000
High triglycerides (n=33)			
Yes, n (%)	22 (95.7)	4 (40.0)	
No, n (%)	1 (4.3)	6 (60.0)	0.001
High fasting glucose (n=31)			
Yes, n (%)	19 (82.6)	5 (62.5)	
No, n (%)	4 (17.4)	3 (37.5)	0.335

MS metabolic syndrome, *APAP* autoadjusting positive airway pressure, *HDL-C* high-density lipoprotein cholesterol

Table 5 Effect of APAP on the MS components in patients with MS at baseline

Variable[a]	Baseline	6 months after APAP	*p* value
Waist circumference (cm)	114.0 (13.0)	114.0 (13.0)	0.151
Blood pressure (mmHg)			
Systolic	137.0 (16.0)	130.0 (13.0)	<0.001
Diastolic	84.0 (8.0)	77.0 (11.0)	<0.001
HDL-C (mg/dL)	46.0 (16.0)	45.0 (13.0)	0.045
Triglycerides (mg/dL)	199.0 (134.0)	163.0 (77.0)	0.010
Fasting glucose (mg/dL)	110.5 (56.0)	106.0 (48.0)	0.152

APAP autoadjusting positive airway pressure, *MS* metabolic syndrome, *HDL-C* high-density lipoprotein cholesterol

[a] Variables are expressed as median and interquartile range (IQR)

of percent of total days of usage of APAP (52.0%; p=0.022) and number of hours per night (2.3 h; p=0.017; data not shown).

Discussion

MS is a constellation of cardiovascular risk factors consisting of abdominal or central obesity, hypertension, dyslipidemia, and hyperglycemia [5]. Patients with OSA have been found to have abnormalities of each of the components of MS [2, 4]. Obesity, particularly visceral obesity, is an important factor in the assessment of the adverse metabolic outcome in OSA. A growing body evidence supports an association between OSA, MS, and cardiovascular morbidity [4, 10–14, 17, 31–33]. According to literature, the direction of this causality relationship remains to be elucidated. It is not clear whether OSA is observed as part of the basic pathophysiology of the MS or whether the OSA through repetitive night hypoxemia and other mechanisms induces the appearance of MS characteristics [4, 11–17, 19, 34].

As it was expected, the studied patients presented a high prevalence of MS (63.5%). Those with MS presented a more severe OSA, confirming the positive association between the severity of OSA and the presence of MS, which has been shown in previous studies [11, 31, 33, 35].

Our study addressed the long-term effect of APAP on MS, as a complete entity, in a group of patients with moderate to severe OSA. Prevalence of MS decreased significantly, from 63.5% to 47.3%, after 6 months of APAP treatment. Compared to patients that maintained MS (n=33), the 14 patients that improved their metabolic status presented less severe sleep-disordered breathing, as it was shown by their lower median RDI, and were more compliant to APAP, presenting a significant greater percent of total days of usage. Despite absence of statistically significance, these patients also presented a greater number of hours of APAP usage per night. The found results cannot be due to weight loss or changes in current medication regimens, as they were not observed.

To date, some studies have investigated the relative time courses of the response to CPAP treatment and their impact on the number of individuals classified as having MS, and some results are contradictory. Dorkova et al. demonstrated in an observational study, which enrolled 32 patients, that 8 weeks of CPAP therapy reduced the global cardiovascular risk in patients with severe OSA and concurrent MS. Reductions in cardiovascular risk were linked to reductions in blood pressure and in serum total cholesterol levels. In addition, patients effectively treated with CPAP had reductions in insulin resistance, tumor necrosis factor-α, and oxidative stress markers. Nevertheless, these beneficial effects of therapy were confined to the group of patients who used CPAP for more than 4 h/night [25]. On the other hand, Coughlin et al. showed that 6 weeks of CPAP therapy reduced only blood pressure, without changing glucose, insulin resistance, lipids, and the proportion of patients accounted with MS [22]. Other studies showed a reduction in insulin resistance after 3 months of CPAP therapy in patients with a BMI >30 kg/m^2 [24], and a significant improvement in HDL-C after 6 months of therapy (most evident in those with abnormal initial values) [23]. Oktay et al. investigated prospectively, in 38 OSA patients, the effect of 1-year CPAP treatment on MS and components. After the follow-up period, MS prevalence decreased by 45%, and significant differences were only observed in waist circumference and HDL-C [36]. These discordant results can probably be attributed to differences in the studied populations.

In our population, considering MS definition and its criteria cut-offs [5] along with final metabolic status, APAP conducted to an improvement in metabolic profile through changes in blood pressure and lipid profile (serum triglycerides), which comes against one study that suggested CPAP superiority through APAP on this issue [29]. We must note that the small sample size of that study (n= 31) could affect the results found. In fact, our study showed significant reductions of median systolic and diastolic blood pressure and also of median serum triglycerides levels with long-term APAP treatment (Table 5).

If the effect of CPAP and APAP on blood pressure and its physiologic mechanisms has already been described [22, 25, 26, 37–39], the effects on lipid metabolism, mainly in serum triglycerides, are less well understood. To date there is only one study that showed a positive influence of 6 months of CPAP treatment on serum triglycerides [40]. The exact mechanisms of this relationship have not been clearly underlined, however experimental studies have shown that intermittent hypoxia, a key clinical manifesta-

tion of OSA, led to increases in fasting serum levels of total cholesterol, HDL-C, and triglycerides in lean mice, but not in obese mice, through mechanisms that implicate the up-regulation of enzymes of lipid biosynthesis, such as sterol element binding protein [21, 40–42]. In addition, intermittent re-oxygenation, another integral feature of OSA, resembles reperfusion injury and may result in the activation of several inflammatory pathways [21]. OSA treatment can abolish these mechanisms and potentially result in the amelioration of the lipid profile.

Despite that we found a slight reduction in HDL-C in patients with MS at baseline (Table 5), this cannot be overemphasized as a negative impact of APAP, as those patients presented high median initial and final values of HDL-C above the cut-off considered in MS definition. This finding can be in accordance with a previous study in which the authors found that the magnitude of HDL-C serum levels change was most evident in patients with abnormal initial HDL-C levels [23].

We detected that two patients aggravated their metabolic status after 6 months, but this could be explained by their poor compliance to APAP, showed by lower median values of percent of total days of usage and number of hours per night, and not as a negative treatment effect. In this context, we can speculate about the potential benefits of APAP on cardiovascular morbidity and mortality and underline the importance of compliance with APAP treatment.

We do not consider the selection criteria by gender, a limitation of this study as risk factors for MS differ concerning this characteristic. In males, age, BMI, and OSA were significantly associated with MS; whereas in females, BMI was the only risk factor [43, 44]. Additionally, MS criteria and their cut-offs, namely waist circumference and HDL-C, differ according to gender [5].

This study could have benefit from an experimental study design. However, for ethical reasons, it would be inadequate to leave patients with confirmed OSA untreated.

Also, we do not consider the OSA diagnosis based on a domiciliary sleep study, a limitation of the present study as this tool has already been compared to polysomnography (PSG), showing to be a viable, accurate, satisfactory, useful, and cost effective way of diagnosing OSA [45, 46]. In fact, our Sleep-Disordered Breathing Clinic, located at a tertiary and university Portuguese hospital, serves an enormous catchment area (>3,700,000 people) and receives patients mainly from general practitioners with a high suspicion of OSA (concerning their characteristics, namely: snoring, daytime sleepiness, and obesity). Besides, the patients enrolled in our study were considered as high pretest likelihood moderate to severe OSA patients, and showed no relevant comorbidities. Consequently, we think that our simplified OSA diagnosis approach is in accordance with scientific evidence [30] and some other centers' practices [47, 48].

Undoubtedly, full-night attended PSG or split-night studies performed in the laboratory are the preferred methods for titration of the optimal positive airway pressure level [30], however this approach to a highly prevalent condition results in inevitable discrepancies between the demands for services and the current capacity of sleep laboratories. In this context, various strategies have been proposed to expedite not only diagnosis but also OSA treatment [47–49]. Furthermore, it is already stated that certain APAP devices may be initiated and used in the self-adjusting mode for unattended treatment of patients with moderate to severe OSA without significant comorbidities [30]. This is our strategy in appropriate and selected patients without significant comorbidities, such as the population enrolled in the present study. Furthermore, as these procedures lead to considerable savings in cost and to significant reductions in the waiting list, we aimed to evaluate the efficacy of these clinical pathways (OSA diagnosis through portable monitors and its treatment with APAP) on MS in a "real world" study. In our opinion, this therapeutic strategy (using long-term APAP) is also validated by the positive results of our study (for example, significant improvement in blood pressure), that would not be seen if we had used subtherapeutic pressures as shown by Jenkinson et al. [50]. We would like also to add that in our approach, a standard attended CPAP titration is offered if symptoms do not resolve or otherwise the APAP treatment appears to lack efficacy. Of course this did not happen in any of the patients selected for our study.

Concerning the reliability of residual RDI obtained from the APAP device, a strong correlation have been found against residual RDI obtained by PSG [51]. Furthermore, we used a third-generation flow-based APAP (REMstar™ Auto, Respironics Inc., Murrysville, PA, USA), with a better performance than second-generation devices [52], and a high accuracy for estimating the residual RDI, as shown by Desai et al. [53].

In summary, in this sample of Portuguese moderate/severe OSA patients, 63.5% of them presented MS. After 6 months, APAP reduced the prevalence of MS in the studied population, mainly in patients with less severe OSA and with a better therapeutic compliance. The reduction in blood pressure and serum triglycerides levels seemed to be the most important contributors to that metabolic status change.

Acknowledgements The authors would like to sincerely thank nurses Emília Araújo and Paula Martins for their collaboration on blood sample collections, technician Delfim Souteiro for the 24-h ambulatory blood pressure measurements, as well as to all sleep technicians who manually reviewed all sleep studies.

Conflict of interest Dr. Patrícia Caetano Mota has no conflict of interest that could inappropriately influence this study.

Prof. Marta Drummond has participated in speaking activities related to industry sources, receiving honoraria from AstraZeneca, MerckSharpDohme, and GlaxoSmithKline.

Prof. João Carlos Winck was sponsored by Respironics to attend a Sleep conference in Canada 2006 and has received honoraria from GlaxoSmithKline and Boehringer Ingelheim related to speaking activities about COPD and from Respironics about NIV.

Prof. Ana Cristina Santos has no conflict of interest that could inappropriately influence this study.

Dr. João Almeida has participated in speaking activities related to industry sources, receiving honoraria from Boeheringer Ingelheim, AstraZeneca, MerckSharpDohme, and GlaxoSmithKline.

Prof. José Agostinho Marques has no conflict of interest that could inappropriately influence this study.

References

1. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S (1993) The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 328:1230–1235. doi:10.1056/NEJM199304293281704
2. McNicholas WT, Bonsigore MR, Management Committee of EU COST ACTION B26 (2007) Sleep apnea as an independent risk factor for cardiovascular disease: current evidence, basic mechanisms and research priorities. Eur Respir J 29:156–178. doi:10.1183/09031936.00027406
3. Shahar E, Whitney CW, Redline S, Lee ET, Newman AB, Javier Nieto F, O'Connor GT, Boland LL, Schwartz JE, Samet JM (2001) Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the sleep heart health study. Am J Respir Crit Care Med 163:19–25
4. Jean-Louis G, Zizi F, Clark LT, Brown CD, McFarlane SI (2008) Obstructive sleep apnea and cardiovascular disease: role of the metabolic syndrome and its components. J Clin Sleep Med 4:261–272
5. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, Spertus JA, Costa F (2005) Diagnosis and management of the metabolic syndrome: an American Heart Association/National, Heart, Lung and Blood Institute Scientific Statement. Circulation 112:2735–2752. doi:10.1161/CIRCULATIONAHA.105.169404
6. Ford ES, Giles WH, Dietz WH (2002) Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 287:356–359. doi:10.1001/jama.287.3.356
7. Ford ES (2005) Prevalence of the metabolic syndrome defined by the International Diabetes Federation among adults in the US. Diab Care 28:2745–2749. doi:10.2337/diacare.28.11.2745
8. Wilson PW, D'Agostino RB, Parise H, Sullivan L, Meigs JB (2005) Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. Circulation 112:3066–3072. doi:10.1161/CIRCULATIONAHA.105.53952
9. Hu G, Qiao Q, Tuomilehto J, Balkau B, Bord-Johnsen K, Pyorala K, DECODE Study Group (2004) Prevalence of the metabolic syndrome and its relation to all-cause and cardiovascular mortality in nondiabetic European men and women. Arch Intern Med 164:1066–1076. doi:10.1001/archinte.164.10.1066
10. Wilcox I, McNamara SG, Collins FL, Grunstein RR, Sullivan CE (1998) "Syndrome Z": the interaction of sleep apnea, vascular risk factors and heart disease. Thorax 53(Suppl 3):S25–S28. doi:10.1136/thx.53.2008.S25
11. Parish JM, Adam T, Facchiano L (2007) Relationship of metabolic syndrome and obstructive sleep apnea. J Clin Sleep Med 3:467–472
12. Ambrosetti M, Lucioni AM, Conti S, Pedretti RF, Neri M (2006) Metabolic syndrome in obstructive sleep apnea and related cardiovascular risk. J Cardiovasc Med 7:826–829. doi:10.2459/01.JCM.0000250873.01649.41
13. Kostoglou-Athanassiou I, Athanassiou P (2008) Metabolic syndrome and sleep apnea. Hippokratia 12:81–86
14. Coughlin SR, Mawdsley L, Mugarza JA, Calverley PM, Wilding JP (2004) Obstructive sleep apnea is independently associated with an increased prevalence of metabolic syndrome. Eur Heart J 25:735–741. doi:10.1016/j.ehj.2004.02.021
15. Gruber A, Horwood F, Sithole J, Ali NJ, Idris I (2006) Obstructive sleep apnea is independently associated with the metabolic syndrome but not insulin resistance state. Cardiovasc Diabetol 5:22. doi:10.1186/1475-2840-5-22
16. Lam JC, Lam B, Lam CL, Fong D, Wang JK, Tse HF, Lam KS, Ip MS (2006) Obstructive sleep apnea and the metabolic syndrome in community-based Chinese adults in Hong-Kong. Respir Med 100:980–987. doi:10.1016/j.rmed.2005.10.003
17. Tasali E, Ip MS (2008) Obstructive sleep apnea and metabolic syndrome: alterations in glucose metabolism and inflammation. Proc Am Thorac Soc 5:207–217. doi:10.1513/pats.200708-139MG
18. Onat A, Hergenc G, Uyarel H, Yazici M, Tuncer M, Dogan Y, Can G, Rasche K (2007) Obstructive sleep apnea syndrome is associated with metabolic syndrome rather than insulin resistance. Sleep Breath 11:23–30. doi:10.1007/s11325-006-0077-7
19. Calvin AD, Albuquerque FN, Lopez-Jimenez F, Somers VK (2009) Obstructive sleep apnea, inflammation, and the metabolic syndrome. Metab Syndr Relat Disord 7:271–278. doi:10.1089/met.2008.0093
20. Malhotra A, Ayas NT, Epstein LJ (2000) The art and science of continuous positive airway pressure therapy in obstructive sleep apnea. Curr Opin Pulm Med 6:490–495
21. Steiropoulos P, Tsara V, Nena E, Fitili C, Kataropoulou M, Froudarakis M, Christaki P, Bouros D (2007) Effect of continuous positive airway pressure treatment on serum cardiovascular risk factors in patients with obstructive sleep apnea-hypopnea syndrome. Chest 132:843–851. doi:10.1378/chest.07-0074
22. Coughlin SR, Mawdsley L, Mugarza JA, Wilding JP, Calverley PM (2007) Cardiovascular and metabolic effects of CPAP in obese males with OSA. Eur Respir J 29:720–727. doi:10.1183/09031936.00043306
23. Börgel J, Sanner BM, Bittlinsky A, Keskin F, Bartels NK, Buechner N, Huesing A, Rump LC, Mügge A (2006) Obstructive sleep apnea and its therapy influence high-density lipoprotein cholesterol serum levels. Eur Respir J 27:121–127. doi:10.1183/09031936.06.00131304
24. Harsch IA, Schahin SP, Radespiel-Tröger M, Weintz O, Jahreiss H, Fuchs FS, Wiest GH, Hahn EG, Lohmann T, Konturek PC, Ficker JH (2004) Continuous positive airway pressure treatment rapidly improves insulin sensitivity in patients with obstructive sleep apnea syndrome. Am J Respir Crit Care Med 169:156–162. doi:10.1164/rccm.200302-206OC
25. Dorkova Z, Petrasova D, Molcanyiova A, Popovnakova M, Tkacova R (2008) Effects of continuous positive airway pressure on cardiovascular risk profile in patients with severe obstructive sleep apnea and metabolic syndrome. Chest 134:686–692. doi:10.1378/chest.08-0556
26. Bazzano LA, Khan Z, Reynolds K, He J (2007) Effect of nocturnal nasal continuous positive airway pressure on blood pressure in obstructive sleep apnea. Hypertension 50:417–423. doi:10.1161/HYPERTENSIONAHA.106.085175
27. Ayas NT, Patel SR, Malhotra A, Schulzer M, Malhotra M, Jung D, Fleetham J, White DP (2004) Auto-titrating versus standard continuous positive airway pressure for the treatment of obstructive sleep apnea: results of a meta-analysis. Sleep 27:249–253

28. Nussbaumer Y, Bloch KE, Genser T, Thurnheer R (2006) Equivalence of autoadjusted and constant continuous positive airway pressure in home treatment of sleep apnea. Chest 129:638–643. doi:10.1378/chest.129.3.638
29. Patruno V, Aiolfi S, Costantino G, Murgia R, Selmi C, Malliani A, Montano N (2007) Fixed and autoadjusting continuous positive airway pressure treatments are not similar in reducing cardiovascular risk factors in patients with obstructive sleep apnea. Chest 131:1393–1399. doi:10.1378/chest.06-2192
30. Epstein LJ, Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD, Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine (2009) Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med 5:263–276
31. Peled N, Kassirer M, Shitrit D, Kogan Y, Shlomi D, Berliner AS, Kramer MR (2007) The association of OSA with insulin resistance, inflammation and metabolic syndrome. Respir Med 101:1696–1701. doi:10.1016/j.rmed.2007.02.025
32. Vgontzas AN, Bixler EO, Chrousos GP (2005) Sleep apnea is a manifestation of the metabolic syndrome. Sleep Med Rev 9:211–224. doi:10.1016/j.smrv.2005.01.006
33. Chin K, Oga T, Takahashi K, Takegami M, Nakayama-Ashida Y, Wakamura T, Sumi K, Nakamura T, Horita S, Oka Y, Minami I, Fukuhara S, Kadotani H (2010) Associations between obstructive sleep apnea, metabolic syndrome, and sleep duration, as measured with an actigraph, in an urban male working population in Japan. Sleep 33:89–95
34. Lam JC, Ip MS (2007) An update on obstructive sleep apnea and the metabolic syndrome. Curr Opin Pulm Med 13:484–489. doi:10.1097/MCP.0b013e3282efae9c
35. Bento J, Drummond M, Almeida J, Winck JC (2007) Obstructive sleep apnea and metabolic syndrome. Rev Port Pneumol 13(Suppl 3):S48–S49
36. Oktay B, Akbal E, Firat H, Ardiç S, Kizilgun M (2009) CPAP treatment in the coexistence of obstructive sleep apnea syndrome and metabolic syndrome, results of one year follow up. Acta Clin Belg 64:329–334
37. Haentjens P, Van Meerhaeghe A, Moscariello A, De Weerdt S, Poppe K, Dupont A, Velkeniers B (2007) The impact of continuous positive airway pressure on blood pressure in patients with obstructive sleep apnea syndrome: evidence from a meta-analysis of placebo-controlled randomized trials. Arch Intern Med 167:757–764. doi:10.1001/archinte.167.8.757
38. Dursunoğlu N, Dursunoğlu D, Cuhadaroğlu C, Kiliçaslan Z (2005) Acute effects of automated continuous positive airway pressure on blood pressure in patients with sleep apnea and hypertension. Respiration 72:150–155. doi:10.1159/000084045
39. Drummond M, Winck JC, Santos AC, Almeida J, Marques JA (2008) Long term effect of APAP on blood pressure in obstructive sleep apnea. Am J Respir Crit Care Med 177: A805
40. Ip MS, Lam KS, Ho C, Tsang KW, Lam W (2000) Serum leptin and vascular risk factors in obstructive sleep apnea. Chest 118:580–586. doi:10.1378/chest.118.3.580
41. Li J, Thorne LN, Punjabi NM, Sun CK, Schwartz AR, Smith PL, Marino RL, Rodriguez A, Hubbard WC, O'Donnell CP, Polotsky VY (2005) Intermitent hypoxia induces hyperlipidemia in lean mice. Circ Res 97:698–706. doi:10.1161/01.RES.0000183879.60089.a9
42. Li J, Grigoryev DN, Ye SQ, Thorne L, Schwartz AR, Smith PL, O'Donnell CP, Polotsky VY (2005) Chronic intermittent hypoxia upregulates genes of lipid byosynthesis in obese mice. J Appl Physiol 99:1643–1648. doi:10.1152/japplphysiol.00522.2005
43. Teramoto S, Kume H, Yamaguchi Y, Yamamoto H, Hanaoka Y, Ishii M, Ishii T, Ouchi Y (2007) Improvement of endothelial function with allopurinol may occur in selected patients with OSA: effect of age and sex. Eur Respir J 29:216–217. doi:10.1183/09031936.00104806
44. Sasanabe R, Banno K, Otake K, Hasegawa R, Usui K, Morita M, Shiomi T (2006) Metabolic syndrome in Japanese patients with obstructive sleep apnea syndrome. Hypertens Res 29:315–322. doi:10.1291/hypres.29.315
45. Golpe R, Jiménez A, Carpizo R (2002) Home sleep studies in the assessment of sleep apnea/hypopnea syndrome. Chest 122:1156–1161. doi:10.1378/chest.122.4.1156
46. Dingli K, Coleman EL, Vennelle M, Finch SP, Wraith PK, Mackay TW, Douglas NJ (2003) Evaluation of a portable device for diagnosing the sleep apnea/hypopnea syndrome. Eur Respir J 21:253–259. doi:10.1183/09031936.03.00298103
47. Mulgrew AT, Fox N, Ayas NT, Ryan CF (2007) Diagnosis and initial management of obstructive sleep apnea without polysomnography: a randomized validation study. Ann Intern Med 146:157–166.
48. Berry RB, Hill G, Thompson L, McLaurin V (2008) Portable monitoring and autotitration versus polysomnography for the diagnosis and treatment of sleep apnea. Sleep 31:1423–1431
49. Masa JF, Jiménez A, Durán J, Capote F, Monasterio C, Mayos M, Terán J, Hernández L, Barbé F, Maimó A, Rubio M, Montserrat JM (2004) Alternative methods of titrating continuous positive airway pressure: a large multicenter study. Am J Respir Crit Care Med 170:1218–1224. doi:10.1164/rccm.200312-1787OC
50. Jenkinson C, Davies RJ, Mullins R, Stradling JR (1999) Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnea: a randomised prospective parallel trial. Lancet 353:2100–2105. doi:10.1016/S0140-6736(98)10532-9
51. Woodson BT, Saurejan A, Brusky LT, Han JK (2003) Non-attended home automated continuous positive airway pressure titration: comparison with polysomnography. Otolaryngol Head Neck Surg 128:353–357. doi:10.1067/mhn.2003.35
52. Shi HB, Cheng L, Nakayama M, Kakazu Y, Yin M, Miyoshi A, Komune S (2005) Effective comparison of two auto-CPAP devices for treatment of obstructive sleep apnea based on polysomnographic evaluation. Auris Nasus Larynx 32:237–241. doi:10.1016/j.anl.2005.03.007
53. Desai H, Patel A, Patel P, Grant BJ, Mador MJ (2009) Accuracy of autotitrating CPAP to estimate the residual Apnea-Hypopnea Index in patients with obstructive sleep apnea on treatment with autotitrating CPAP. Sleep Breath 13:383–390. doi:10.1007/s11325-009-0258-2