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Beyond Apnea-Hypopnea Index: how clinical and comorbidity are important in obstructive sleep apnea

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Abstract

Introduction: The classification of the severity of obstructive sleep apnea (OSA) based on the Apnea/Hypopnea Index (AHI) does not reflect the heterogeneity and prognosis of the disease. The Baveno classification proposes a new assessment system that includes symptoms and comorbidities. The aim of our study was to evaluate the application of the Baveno classification in clinical practice and to explore its association with sleep indices, adherence to therapy and symptoms over a 6-months period.

Material and methods: Prospective study including patients diagnosed with OSA between January and July 2021 was conducted. Patients were divided into 4 groups (A–D) according to the Baveno classification. The adherence to PAP treatment and Epworth Sleepiness Scale (ESS) values were obtained 6 months after initiation of therapy.

Results: A total of 91 patients (84% male, 58 ± 13 years) were included in the study. The median ESS score was 10 (6–15), mean AHI was 28.4 ± 22.2 events/hour and the time with SpO_2 < 90% (T90) was 9.7 ± 14.9%. At diagnosis, patients were classified into Baveno groups: A: 30%; B: 35%; C: 17%, D: 19%. There were no statistical differences in AHI between the different groups. On the other hand, T90 had higher values in patients with comorbidities (C, D). Regarding the treatment, the prescription of PAP was higher in patients with comorbidities (C, D), and adherence to this treatment at 6 months was higher in group D. Among patients under PAP therapy, there was a statistically significant decrease in daytime sleepiness at 6 months in groups B and D.

Conclusions: The Baveno classification distributes patients with OSA evenly across the different phenotypes, regardless of the AHI value. The treatment decision was linked to the comorbidities (C, D) were the ones who had the greatest adherence to treatment at 6 months were in group D. ESS improved with greater emphasis in the most symptomatic (B, D), while the AHI is essential for the diagnosis of OSA, the Baveno classification may guide physicians better in their treatment decision.

Key words: obstructive sleep apnea, Apnea-Hypopnea Index, Baveno classification

Introduction

Obstructive Sleep Apnea (OSA) is a high prevalent disorder [1], characterized by repetitive collapse of the upper airway during sleep, leading to nocturnal hypoxemia and sleep fragmentation [2, 3]. It is a heterogeneous and complex disease associated with several adverse clinical conditions, including excessive daytime sleepiness (EDS), impaired cognition performance, reduced quality of life, metabolic dysfunction and cardiovascular morbidity and mortality [4–6]. OSA diagnosis is mainly based on sleep and respiratory indices captured by polysomnography or respiratory polygraphy and its severity is traditionally expressed by the apnea-hypopnea index (AHI), defined as the number of apneas and hypopneas per hour of sleep [7]. Similarly, the therapy with positive airway pressure (PAP) is implemented essentially based on AHI and daytime sleepiness.

However, AHI fails to reflect the heterogeneity of OSA and its complex underlying pathophysiology [8–10]. Several studies have shown no significant correlations between AHI and sleepiness [11, 12], and furthermore, the AHI has not been shown to be predictive of outcomes, such as cardiovascular comorbidities or mortality [13, 14]. In addition, there has been also limited correlation of treatment success with baseline AHI [15].

Considering these challenges, different approaches have been proposed to identify different clinical phenotypes of OSA across the community. Recently, a Sleep Disordered Breathing Group of the European Respiratory Society and the European Sleep Research Society developed the Baveno classification. This classification is a novel multicomponent grading system for OSA severity that integrate symptoms, comorbidities and the presence of end organ damage to classify patients in four groups [16]. In this study, we aim to evaluate the application of the Baveno classification in clinical practice and to explore the association between this multicomponent grading system and sleep indices, adherence to therapy and symptoms over a 6-months period.

Material and methods

Protocol and study population

The present study was a prospective monocentric cohort study with patients newly diagnosed with OSA in the Medicine Sleep Center at the Centro Hospitalar e Universitário de Coimbra. The follow-up visits of the patients within a time window of 6 months after baseline were considered for the longitudinal analysis. The study was conducted between January and August 2021.

Patients included were aged ≥ 18 years old and had a total AHI ≥ 5/h in the sleep study. The criteria for exclusion were: total AHI < 5/h; absence of any typical OSA symptom; mandibular advancement device; or initiation of PAP therapy before diagnosis.

Sleep study results, demographic data, anthropometric measurements, information on daytime symptoms and cardiometabolic comorbidities were obtained from medical records. Corresponding follow-up data and PAP therapy adherence were collected 6 months later when patients return as part of routine medical follow-up consultation.

At the time of inclusion in the study, patients were divided into four groups (group A to D), according to the Baveno classification, considering their symptoms and the presence of comorbidities [16]. Symptoms were classified according to their absence or presence and comprised the following: daytime sleepiness as defined by an Epworth Sleepiness Scale (ESS) score ≥ 11; hypersomnia defined by subjective sleep length ≥ 11 hours; and diagnosis of insomnia. If at least one of these conditions were met, the patient was classified as having severe symptoms and thus allocated to the Baveno group B or D. Comorbidities associated with OSA which were taken in account are atrial fibrillation, difficult-to-control arterial hypertension, heart failure, stroke, and diabetes mellitus. Difficult-to-control hypertension was considered if blood pressure control is not obtained despite optimal therapy with at least three anti-hypertension drugs. If at least one of these comorbidities was present, end-organ impact was deemed major calling for an allocation to Baveno group C or D.

Sleep studies were performed using type 3 portable monitors (portable home sleep apnea test (HSAT) devices). The HSAT results including AHI, oxygen desaturation index (ODI), mean peripheral oxygen saturation (SpO_2) and sleep time with oxygen saturation below 90% (T90) during sleep were reviewed according to the AASM Manual for the Scoring of Sleep and Associated Events [7].

Adherence to PAP therapy in the 6 months follow-up consultation was objectively measured by reading the device's built-in time counters. A threshold of ≥ 4 h/nightly of PAP use on 70% of nights has been adopted to define adherence [17].

Statistical analysis

Descriptive statistics was used to describe the characteristics of all the participants. Quantitative data with a normal distribution were expressed as mean and standard deviation (SD) and those variables without normal distribution were expressed as median and interquartile range (P25–P75). Normal distribution was tested using the Shapiro-Wilk test. Differences of continuous variables with normal distribution were determined by ANOVA and those with non-normal distribution with nonparametric Kruskal-Wallis test. Differences between baseline and follow-up within the same patients were tested with the one-sample Wilcoxon signed-rank test. Categorical variables were compared using the χ^2 test. A p value less than 0.05 was considered statistically significant. Statistical analysis was performed by using the SPSS 25.0 software.

Results

Baseline characteristics of the patients

A total of 91 patients were included in the study, 83.5% male, with a mean age of 58 ± 13 years and a mean body mass index (BMI) 30 ± 4 kg/m^2. The baseline characteristics of the patients are shown in Table 1. The median ESS score was 10 [6–15] and 49.5% of patients had a ESS score ≥ 11.

Concerning HSAT result, the mean AHI was 28.4 ± 22.2 events/hour and the ODI was 26.4 ± 23.3 events/hour. The median SpO2 was 93% (92–94), the minimum SpO2 was 82% (76–86) and T90 was 9.7 ± 14.9% and 9.6 minutes (2.5–48.4).

Regarding cardiovascular comorbidities, 52% patients had difficult-to-control hypertension, 8.8% atrial fibrillation, 11% heart failure, 18.7% diabetes mellitus and 8.8% had a history of stroke.

Distribution according to the Baveno classification

Patients were distributed into the four groups of Baveno classification according to the previous defined parameters: 30% in group A, 35% in group B, 17% in group C, and 19% in group D. Analyzing the patients that composed each of the groups, it was verified that the mean age was higher in group C (70 ± 13 years) and lower in group A (52 ± 12 years) ($p < 0.001$). There were no differences regarding gender and BMI between the four groups.

Regarding the respiratory events, there were no substantial differences in AHI and ODI mean values between groups ($p = 0.093$ and $p = 0.088$, respectively). However, there was a slight increase of group A in patients with an AHI 5–14 events/h ($p = 0.023$) and an increase of group D in patients with an AHI ≥ 30 events/h ($p = 0.018$). On the other hand, there were substantial differences in the T90 across groups, with higher values found in patients of group C and D (patients with comorbidities) compared to group A and B. Groups C and D and groups A and B did not differ from each other.

Clinical outcome according to the Baveno classification

In what concerns therapy decision, 80.2% patients were proposed to PAP therapy and 19.8% were treated with non-PAP therapies (16.5% mandibular advancement device, 2.2% medical therapy and 1.1% positional therapy). The prescription of PAP contrasted among groups, being this therapy more often considered for the patients with comorbidities (groups C and D) presenting 93.3% and 100%, respectively, contrasting with 66.7 and 75% of groups A and B, respectively. $p = 0.023$).

The treatment compliance of the patients proposed to PAP therapy was evaluated in the follow-up visit at 6 months and it differ significantly according to Baveno groups. Patients with comorbidity (group C and D) exhibited higher rates of compliance than A and B groups (A: 50%, B: 61%, C: 64%, D: 100%; $p = 0.08$). AHI has not a predictor of PAP adherence.

This study also investigated the change of sleepiness between baseline and follow-up in the different Baveno groups and the ESS score showed a statistically significant decrease compared to baseline in the groups B and D ($Z = -3.703$, $p < 0.001$; $Z = -3.190$, $p = 0.01$, respectively).

Discussion

In our study, the Baveno classification separates our OSA population into equivalent groups, without considerable over or underrepresentation of any groups. These findings support that reported by Randerath et al. that the separation of the OSA patients based on symptoms and comorbidities represents an epidemiologically reasonable and clinically practicable compromise [16]. Moreover, our results reinforce that this system stratifies the population independent of the baseline AHI. In fact, in our study, the AHI did not differ substantially between the distribution of patients to the Baveno groups. This underlines the previous findings that the addition of the severity of breathing disturbances to the classification of OSA did not predict symptoms or comorbidities [11–14]. Although the absent of relationship between AHI and comorbidities, we found a relatively higher value of group D in the AHI ≥ 30 events/h group, possibly translating previous observations from other prospective studies that the association with mortality was observed in only those participants with an AHI ≥ 30 events/h [18, 19]. Interestingly, in the other hand, the hypoxic burden, as reflected by T90, showed the highest values in group C and D (patients with comorbidities) compared to groups A and B. This is in line with the results of recent studies emphasizing the hypoxic burden as a major determinant and predictor of long-term cardiometabolic outcomes [20, 21].

In what concerns therapy decision, PAP prescription was driven more strongly by comorbidities than for symptoms as shown by the different proportions of treated and untreated patients. Groups C and D (patients with high impact of comorbidities) showed at least 18% higher prescription rates compared to group A and B. Although the AHI is essential for the diagnosis of OSA, in our population it did not play the most important role in PAP prescription as the treatment was purposed independently of AHI. In fact, the recent published MERGE trial has also found, even in mild OSA, PAP treatment significantly improves quality of life [22].

Adherence to PAP was significantly higher among patients with severe symptoms and comorbidity (group D). Although evidence in literature suggests that greater daytime sleepiness predicts PAP adherence [23], improvement in patient functional status also predicts continued use [24–26]. Nevertheless, we found notable that rates of PAP adherence in the all groups were greater than 50% at 6-months follow-up. AHI was not a predictor of PAP adherence, being in line with previous studies [15].

The median ESS score improved significantly with high clinical relevance in groups B and D. This shows that the parameters applied in Baveno classification clearly discriminated between symptomatic and asymptomatic patients and confirms that PAP has a huge effect in symptomatic patients.

These results of our study support the idea of indicating treatment based on the groups. Groups B and D improved in symptoms and benefit with PAP treatment. Although group C fails to show improvement of ESS, the prevalence of comorbidities and higher hypoxic burden strongly recommends the treatment. In contrast, group A differs in low prevalence in comorbidities, shows no benefit in sleepiness and demonstrated low compliance to PAP treatment. Assuming a low impact of major comorbidities and a low hypoxic burden, may PAP treatment for these patients does not seem to be indicated. However, a recent prospective study exploring the Baveno groups changes over 5 years of patients non-eligible for PAP therapy found that one fifth of patients classified from group A in baseline were reclassified into group C and D over 5 years period [27]. Further research is needed to evaluate these results in long periods of observation and in large cohort prospective studies.

Despite the relevant findings obtained in our study, it had some limitations. Firstly, this was a prospective study with a short follow-up period to evaluated adherence to PAP therapy. Despite that, results from previous studies show that early PAP use predicts long-term adherence [23, 28]. Secondly, the study population belonged to a single hospital and the sample size was limited. Thirdly, it is possible than an information bias occurred due to obtaining the variables from the patients' medical records.

Conclusions

The heterogeneity of OSA, a multi-organ chronic disease, advocates against a simple approach focusing mainly on AHI. The Baveno classification integrate a multifactorial approach and separates the OSA population into equivalent groups with respect to clinical symptoms and comorbidities. The difference between groups in hypoxic load, known to be correlated with poor cardiovascular and metabolic outcomes, may indicate the prognostic relevance of this grading system. In routine clinical practice, allocating patients to one of these clusters might help in implementing personalized medicine in OSA. This may facilitate an individualized and critical use of positive airway pressure and emerging new therapies.

Conflict of interest

None to declared.

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Table 1. Baseline characteristics of patients included in this study

	All patients (n = 91)	**Group A (n = 27)**	**Group B (n = 32)**	**Group C (n = 15)**	**Group D (n = 17)**
Age [years], mean ± SD	58 ± 13	52.2 ± 12.1*#	53.7 ± 11.5*#	70.2 ± 12.7§ +	65.2 ± 8.2§ +
Male sex, n (%)	74 (83.5)	23 (85.2)	25 (78.1)	12 (80)	16 (94.1)
BMI [kg/m^2], mean ± SD	30 ± 4	28.4 ± 4.2	30 ± 4.3	29.7 ± 3.5	30.3 ± 3.2
ESS, median (IQR)	10 (6–15)	6 (2.5–9)	15 (13–17)	7 (4–9)	14 (12–15)
Total AHI, mean ± SD	28.4 ± 22.2	24.2 ± 16.6	24.8 ± 20	31.6 ± 33.4	39.4 ± 19.1
ODI, mean	26.4 ± 23.3	21.2 ± 16.8	22.6 ± 20	31 ± 34.5	37.4 ± 22

± SD					
SpO2, median (IQR)	93 (92–94)	93 (92–95)	93.5 (92–94)	92 (90–94)	93 (91.5–94.5)
SpO2, minimum (IQR)	82 (76–86)	84 (76–87)	84 (80.8–86.3)	80 (75–87)	76 (71–82.5)
T90, mean ± SD	9.7 ± 14.9	6.2 ± 7.3*#	4.1 ± 5.8*#	17.9 ± 19.5§ +	18.5 ± 23.7§ +

Data are presented as frequency (n) and percentage (%), mean and standard deviation (SD) or median and interquartile range (IQR)

AHI — apnoea–hypopnoea index; BMI — body mass index; BP — blood pressure; ESS — Epworth Sleepiness Scale; ODI — oxygen desaturation index; SpO2 — peripheral oxygen saturation; T90 — percentage of sleep time with SpO2 < 90%

p-values < 0.05 were considered statistically significant and these values were highlighted in bold.

*: p < 0.05 vs C; #: p < 0.05 vs D; §: p < 0.05 vs A; + p < 0.05 vs B