SLEEP



# Predicting Obstructive Sleep Apnea in Patients with Insomnia: A Comparative Study with Four Screening Instruments

Ricardo L. M. Duarte<sup>1,2</sup> · Flavio J. Magalhães-da-Silveira<sup>1</sup> · Tiago S. Oliveira-e-Sá<sup>3,4</sup> · Marcelo F. Rabahi<sup>5</sup> · Fernanda C. Q. Mello<sup>2</sup> · David Gozal<sup>6</sup>

Received: 12 February 2019 / Accepted: 27 April 2019 © Springer Science+Business Media, LLC, part of Springer Nature 2019

#### Abstract

**Purpose** Obstructive sleep apnea (OSA) and insomnia are very prevalent disorders, especially in sleep-lab setting, and insomnia may be the presenting complaint of OSA. Here, we aimed to validate No-Apnea as screening tool for OSA in patients with self-reported insomnia complaints and to compare its performance with other models.

**Methods** This cross-sectional study involved evaluation of No-Apnea as well as STOP-Bang, NoSAS and Epworth Sleepiness Scale (ESS) in subjects with insomnia being evaluated with full in-lab polysomnography. Discrimination was assessed by area under the curve (AUC), while predictive parameters were calculated by contingency tables. OSA severity was classified based on the apnea/hypopnea index:  $\geq$  5.0/h as any OSA (OSA $_{\geq 5}$ ),  $\geq$  15.0/h as moderate/severe OSA (OSA $_{\geq 15}$ ), and  $\geq$  30.0/h as severe OSA (OSA $_{\geq 30}$ ).

**Results** Overall, 2591 patients with a clinical diagnosis of insomnia were included. Diagnosis of  $OSA_{\geq 5}$ ,  $OSA_{\geq 15}$ , and  $OSA_{\geq 30}$  was of 76.3%, 53.1%, and 32.6%, respectively. At all levels of OSA severity, No-Apnea had sensitivity ranging from 84.5 to 94.1% and specificity ranging from 58.2 to 35.1%. For screening of  $OSA_{\geq 5}$ ,  $OSA_{\geq 15}$ , and  $OSA_{\geq 30}$ , discriminatory ability (AUC) of No-Apnea was: 0.790 [95% confidence interval (CI) 0.770–0.810], 0.758 (95% CI 0.740–0.777), and 0.753 (95% CI 0.734–0.772), respectively. Based on AUCs, No-Apnea, STOP-Bang, and NoSAS performed similar at all levels of OSA severity. The ESS did not present satisfactory discrimination as OSA screening model.

**Conclusions** In a large sample of patients with insomnia, No-Apnea, STOP-Bang, and NoSAS, but not ESS, enable satisfactory and similar discrimination at all levels of OSA severity.

Keywords Obstructive sleep apnea · Polysomnography · Screening · Insomnia · Diagnosis

Ricardo L. M. Duarte rlmduarte@gmail.com

- <sup>1</sup> Centro Médico BarraShopping, Sleep Laboratório de Estudo Dos Distúrbios Do Sono, Avenida das Américas 4666, sala 309, Barra da Tijuca, Rio de Janeiro 22649-900, Brazil
- <sup>2</sup> Instituto de Doenças Do Tórax Universidade Federal Do Rio de Janeiro, Rio de Janeiro, Brazil
- <sup>3</sup> Centro Hospitalar Lisboa Central, Hospital de Santa Marta, Lisbon, Portugal
- <sup>4</sup> NOVA Medical School, Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Lisbon, Portugal
- <sup>5</sup> Faculdade de Medicina, Universidade Federal de Goiás, Goiânia, GO, Brazil
- <sup>6</sup> Department of Child Health, University of Missouri School of Medicine, Columbia, MO, USA

# Introduction

Obstructive sleep apnea (OSA) is a very prevalent disease [1, 2], especially in subjects referred to a sleep laboratory, or in specific populations such as individuals undergoing preoperative assessments for bariatric surgery [3] and those with resistant hypertension [4] or stroke [5]. Currently, the prevalence of OSA has been revisited and appears to be in the rise, possibly due to the obesity epidemic and the aging of the population, with estimated prevalence of moderate to severe OSA of 13% among men and of 6% among women [1], and of 49.7% in men and 23.4% in women [2]. OSA is characterized by recurrent upper airway obstructive episodes, resulting in intermittent hypoxemia, sleep fragmentation, cardiovascular and metabolic consequences, and increased overall mortality [6].

Another highly prevalent sleep disorder is insomnia, and according to the definition used insomnia rates will vary ranging from 6 to 48% [7]. In general, the clinical diagnosis of insomnia is reached by evaluating specific sets of symptoms and their duration, namely difficulty in starting sleep, difficulty in maintaining sleep, and early morning awakenings [8, 9]. Consistent risk factors for insomnia include aging, female gender, underlying psychiatric disorder, shift work, unemployment, and lower socioeconomic status [8–10]. Therefore, appropriate screening for potential co-morbid OSA in insomnia patients may be imperative, particularly since the presence of co-morbid insomnia may also affect OSA treatment outcomes [11].

Specifically in limited-resource areas with a high prevalence of OSA, the use of screening instruments to identify high-risk patients for this disorder can be extremely helpful. The No-Apnea model [12] is a recently developed and validated practical instrument that includes only two objective parameters: neck circumference (NC) and age, with a total score ranging from 0 to 9 points. The cutoff point chosen for this tool was  $\geq$  3 to classify patients at high-risk of having OSA at all levels of severity. In the derivation cohort, the discrimination, assessed by area under the curve (AUC), for screening of any OSA (OSA>5), moderate/severe (OSA>15), and severe OSA (OSA<sub>>30</sub>) was as follows: 0.784, 0.758, and 0.754, respectively. Subsequently, the model was validated confirming its reproducibility. Importantly, No-Apnea discriminatory ability, in a high pre-test probability of OSA population, was similar to those of STOP-Bang questionnaire or NoSAS score [12].

Despite the high frequency of insomnia symptoms in patients referred for polysomnography (PSG), the use of instruments for OSA screening in this population is scarce. In addition, insomnia cohorts exhibit higher prevalence of women in relation to the general population, and the symptoms of OSA among women differ from those in men [13]. Based on aforementioned considerations, it remains unclear whether questionnaires frequently applied to patients with suspected OSA could also be successfully implemented in insomniac patients. Accordingly, the aims of the present study were: (i) to validate the No-Apnea tool in a sample of consecutive adult patients with self-reported insomnia complaints and (ii) to compare its performance with those obtained from three other frequently used screening instruments, namely STOP-Bang questionnaire, NoSAS score, and Epworth Sleepiness Scale (ESS).

## **Methods**

#### **Study Design and Patient Selection**

This cross-sectional study prospectively enrolled consecutive subjects with self-reported insomnia, from January 2017 to December 2018. All patients were referred for sleep test evaluation by their respective attending physicians. Inclusion criteria were subjects of both genders, aged > 18 years, with least one symptom compatible with the clinical diagnosis of insomnia. Patients were excluded for any of the following reasons: previously diagnosed OSA, use of portable studies for OSA diagnosis, incomplete clinical data, and technically inadequate PSG. Patient characteristics included gender, age, body-mass index (BMI), NC, and self-reported comorbidities (hypertension, diabetes mellitus, and smoking). The BMI was calculated by dividing the weight in kilograms by the square of the height in meters (kg/m<sup>2</sup>), while NC (in cm) was systematically measured using a tape measure. On the evening of the PSG, all demographic, anthropometric, and clinical data were collected by qualified sleep technicians, in addition to completing the instruments: No-Apnea, STOP-Bang, NoSAS, and ESS.

## **Ethical Considerations**

The study protocol complied with the Declaration of Helsinki and was approved by Ethics Committee of the Federal University of Rio de Janeiro (#1.764.165). All participants provided written informed consent before study enrollment.

## **Insomnia Definition**

Insomnia was defined as present if a patient indicated one or more of the following complaints, which were investigated through a semi-structured interview: (i) difficulty initiating sleep, (ii) difficulty maintaining sleep, and/or (iii) waking up earlier than desired, representing initial insomnia, middle insomnia, and late insomnia, respectively. Furthermore, this sleep disorder has to occur at least three nights a week for a period of  $\geq 3$  months and to be related to the presence of daytime impairments [14].

#### **Screening Instruments**

No-Apnea [12] is a 2-item instrument (NC and age): NC is scored as follows: 37.0-39.9 cm (1 point), 40.0-42.9 cm (3 points), and  $\geq 43.0 \text{ cm} (6 \text{ points})$ , while age is scored as follows: 35-44 years (1 point), 45-54 years (2 points),  $\geq$  55 years (3 points), totaling a score of 0–9 points. A score  $\geq$  3 points was considered as high risk of presence of OSA.

STOP-Bang [15] is a tool containing eight yes-or-no questions (1 point for each positive answer): loud snoring, tiredness, observed apnea, hypertension, BMI > 35 kg/m<sup>2</sup>, age > 50 years, NC > 40 cm, and male gender, totaling a score of 0–8 points. A score  $\geq$  3 points was considered as high risk of presence of OSA.

NoSAS [16] is an instrument containing five parameters: NC > 40 cm (4 points), BMI 25.0–29.9 kg/m<sup>2</sup> (3 points), BMI  $\ge$  30.0 kg/m<sup>2</sup> (5 points), snoring (2 points), age > 55 years (4 points), male gender (2 points); totaling a score of 0–17 points. A score  $\ge$  8 points was considered as high risk of presence of OSA.

ESS [17] is a widely and extensively used 8-item questionnaire that assesses the subjective likelihood of falling asleep in various settings. Each item is scored from zero (would never doze) to three (high chance of dozing), totaling a score of 0–24 points. A score  $\geq 11$  points was considered indicative of excessive daytime sleepiness.

#### Sleep Test

All PSG were conducted at a single Brazilian sleep center: Sleep Laboratory - Centro Medico BarraShopping, Rio de Janeiro. All patients underwent an attended, full PSG (EMBLA® S7000, Embla Systems, Inc., Broomfield, CO, USA), consisting of continuous monitoring of electroencephalography, electrooculography, electromyography (chin and legs), electrocardiography, airflow, thoracic and abdominal impedance belts for respiratory effort, oxygen saturation (SpO<sub>2</sub>), snoring microphone, and body position sensors. Data from PSG were manually scored by two boardcertified sleep physicians in accordance with previous guidelines [18], and both physicians were blinded for No-Apnea, STOP-Bang, NoSAS, and ESS results. Apneas were classified with a drop  $\geq$  90% of baseline in airflow lasting at least 10 s, while hypopneas were defined as a drop  $\geq$  30% of preevent during  $\geq 10$  s and were associated with more than 3% oxygen desaturation or an arousal [18]. Diagnosis of OSA was based on an apnea/hypopnea index (AHI)  $\geq$  5.0/h, being its severity classified according to AHI thresholds:  $\geq$  5.0/h  $(OSA_{\geq 5}), \geq 15.0/h (OSA_{\geq 15}), and \geq 30.0/h (OSA_{\geq 30}).$ 

#### **Statistical Analysis**

Data analysis was performed using SPSS (version 21.0; Chicago, IL, USA). Results were reported as mean  $\pm$  standard deviation for quantitative variables and as number and percentage for qualitative variables. Comparisons between groups were performed using the Chi-square test for dichotomous variables, Student's *t* test and univariate analysis of variance (ANOVA) for continuous variables. Discrimination, the ability of a model to distinguish between patients with and without different outcomes, was estimated from the AUC obtained by receiver operator characteristic (ROC) curves, which may range from 0.5 (no discrimination) to 1.0 (perfect discrimination) [19]. An AUC > 0.7 was considered as clinically significant, being that the AUCs obtained were compared using prior algorithm [20]. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy (rate of correctly classified patients) were calculated using contingency tables, being all estimates reported with their respective 95% confidence interval (CI). All two-tailed tests were performed at a 5% significance level.

## Results

#### **Study Population**

A flowchart illustrating the study approach is summarized in Fig. 1, being the study population composed by 2591 subjects, with subtypes of insomnia divided as follows: 1160 subjects (44.8%) had sleep-onset insomnia, 1164 subjects (44.9%) had middle of the night insomnia, and 1682 subjects (64.9%) had early morning insomnia. Characteristics of the patients with insomnia are listed in Table 1, being that 56.3% were females. Overall, 74.4%, 79.1%, 64.3%, and 42.8% of the patients were classified as high risk of OSA patients according to No-Apnea, STOP-Bang, NoSAS, and ESS, respectively. As would be anticipated from the study design and the high pre-test risk inherent to a sleep-lab referral cohort, we found a high prevalence of OSA<sub>>5</sub> (76.3%),  $OSA_{\geq 15}$  (53.1%), and  $OSA_{\geq 30}$  (32.6%). The prevalence of OSA<sub>>5</sub>, OSA<sub>>15</sub>, and OSA<sub>>30</sub> was statistically higher in males than in females: 88.2% versus 67.1% (p < 0.001), 69.1% versus 40.6% (p < 0.001), and 48.8% versus 20.0% (p < 0.001), respectively. The probability of having OSA<sub>>5</sub>, OSA<sub>>15</sub>, and OSA<sub>>30</sub> was higher in men than in women: odds ratio (OR) 3.656 (95% CI 2.961-4.513), OR 3.276 (95% CI 2.781-3.859), and OR 3.813 (95% CI 3.207-4.535), respectively.

#### Predicting OSA

Table 2 shows the predictive performance of the four screening tools evaluated. For screening of different levels of OSA severity, No-Apnea tool had sensitivity ranging from 84.5 to 94.1% and specificity ranging from 58.2 to 35.1%. Among all instruments, STOP-Bang showed a highest sensitivity for screening of OSA<sub> $\geq 5$ </sub> (88.2%), OSA<sub> $\geq 15$ </sub> (92.5%), and OSA<sub> $\geq 30$ </sub> (96.7%). For screening of OSA<sub> $\geq 5$ </sub>, NoSAS showed a higher specificity (69.3%), while for screening of OSA<sub> $\geq 15$ </sub> and



Fig. 1 Flowchart of the study. Diagnosis of obstructive sleep apnea (OSA) obtained by polysomnography (PSG) was based on an apnea/hypopnea index  $\geq$  5.0/h as any OSA,  $\geq$  15.0/h as moderate/severe OSA, and  $\geq$  30.0/h as severe OSA

 $OSA_{\geq 30}$ , the highest specificity was obtained by ESS: 63.8% and 62.2%, respectively. As can be seen in Fig. 2, ESS did not show adequate discrimination for screening of  $OSA_{\geq 5}$ ,  $OSA_{\geq 15}$ , and  $OSA_{\geq 30}$ . Conversely, No-Apnea, STOP-Bang, and NoSAS emerged as adequate screening tools for OSA in patients with insomnia (all AUCs > 0.7 at all levels of OSA severity). In addition, at all levels of OSA severity, there were no statistically significant differences when comparing the discriminatory power obtained by No-Apnea, STOP-Bang, and NoSAS (all comparisons with *p* value > 0.05).

## Discussion

The present study, with a large sample of prospectively recruited patients with insomnia and who were referred to a sleep laboratory, showed that the screening instruments No-Apnea, NoSAS, and STOP-Bang, but not the ESS, were useful to detect patients at-risk of OSA. Furthermore, despite its obvious simplicity and objectivity, the discrimination obtained by No-Apnea was similar to those exhibited by the STOP-Bang and NoSAS models. The discriminatory ability of a model to distinguish between patients with and without a specific condition was estimated from the AUC, which plots the true positive rate against false positive rate for consecutive cut-points for the probability of a defined condition being present or absent [19]. In addition, it is possible to compare the AUCs obtained by different screening approaches using previously described algorithms [20]. Similar to the No-Apnea derivation and validation study [12], the cutoff point  $\geq$  3 was associated with high sensitivity and moderate specificity. Of particular importance is the fact that No-Apnea is a 2-item tool, while the STOP-Bang is an 8-item instrument and the NoSAS is a 5-item instrument: this simplified approach clearly enables much greater facility and ease of screening of OSA, particularly among high pre-test probability populations [12, 21]. Identical findings evidencing similar discriminatory capacity between No-Apnea, STOP-Bang, and NoSAS were also observed in the No-Apnea derivation and validation study [12] as well as in the study involving morbidly obese patients [22].

Accordingly, high-risk patients can be properly designated for portable diagnostic methods and thus reduce long waiting lists in sleep centers across many countries. Furthermore, since the No-Apnea does not contain subjective variables, it can be used in patients in whom sleep-related information from the bed partner is not always available. These findings are particularly relevant, since some studies have shown a high prevalence of insomnia symptoms among patients referred for PSG [23–25].

Both OSA and insomnia are considered as risk factors for cardiovascular disease [26, 27], end organ damage [28, 29], and are associated with an increase in direct and indirect healthcare and overall economic costs [30, 31]. Although OSA and insomnia are very prevalent disorders, especially in sleep-lab individuals, some differences should be emphasized: (i) the diagnosis of OSA is based on objective sleep study, while the diagnosis of insomnia

<b>Table 1</b> Summary of patient characteristics ( $n = 259$	1 Summary of patient characteristics (n =	2591 -	)
---	---	--------	---

Parameter	Values
Clinical data	
Female gender (%)	1460 (56.3)
Age (years)	$47.1 \pm 14.0$
BMI (kg/m <sup>2</sup> )	$33.5 \pm 8.0$
NC (cm)	$40.1 \pm 5.1$
Current smokers (%)	270 (10.4)
Hypertension (%)	1131 (43.7)
Diabetes mellitus (%)	362 (14.0)
Screening tools	
No-Apnea (points)	$4.3 \pm 2.5$
STOP-Bang (points)	$4.0 \pm 1.8$
NoSAS (points)	$8.9 \pm 4.0$
ESS (points)	$9.7 \pm 5.3$
No-Apnea $\geq$ 3 points	1927 (74.4)
STOP-Bang $\geq$ 3 points	2049 (79.1)
$NoSAS \ge 8$ points	1665 (64.3)
$ESS \ge 11$ points	1109 (42.8)
Polysomnographic data	
Total sleep time (min)	$333.3 \pm 72.7$
Sleep efficiency (%)	$77.1 \pm 15.5$
Awakenings (n)	$9.5 \pm 6.3$
WASO (min)	$59.8 \pm 52.2$
Sleep latency (min)	$38.8 \pm 43.0$
REM latency (min)	$149.4 \pm 81.0$
Stage N1 (%)	$5.0 \pm 5.7$
Stage N2 (%)	$67.3 \pm 12.5$
Stage N3 (%)	$11.6 \pm 9.3$
Stage R (%)	$15.6 \pm 7.9$
Arousal index ( <i>n</i> /h)	$28.1 \pm 24.2$
AHI (n/h)	$25.8 \pm 26.4$
AI ( <i>n</i> /h)	$13.1 \pm 22.1$
HI ( <i>n</i> /h)	$12.6 \pm 12.7$
Awake SpO <sub>2</sub> (%)	$95.3 \pm 2.1$
Mean SpO <sub>2</sub> (%)	$93.5 \pm 3.3$
Nadir SpO <sub>2</sub> (%)	$82.3 \pm 9.0$

Numeric and categorical variables were reported as mean  $\pm$  SD and *n* (%), respectively

*BMI* body-mass index, *NC* neck circumference, *ESS* Epworth sleepiness scale, *WASO* wake after sleep onset, *REM* rapid eye movement, *AHI* apnea/hypopnea index, *AI* apnea index, *HI* hypopnea index, *SpO*<sub>2</sub> oxygen saturation

relies on clinical history [32] and (ii) OSA is a disease that most commonly affects men, while insomnia is typically more common among women [33, 34]. Our findings also showed a preponderance of women over men in individuals with insomnia; however, the male gender was associated with a higher prevalence of OSA than female gender at all levels of OSA severity. Sleep laboratories around the world have large numbers of patients with suspected OSA waiting to be tested. The gold standard for diagnosis of OSA is overnight in-lab PSG; however, the prevalence of OSA is far higher than the volume of patients that can be handled by the available sleep laboratories around the world. To better address the utilization of scarce resources and detect those patients more likely to benefit from such onerous diagnostic test, several instruments have been developed and published in the literature. Moreover, we should also emphasize that the performance of an OSA screening tool may exhibit considerable variability, which is usually related to the patient population and AHI thresholds employed [35].

The STOP-Bang is a nowadays widely used mnemonic screening approach that was initially developed for screening surgical patients showing the following reported characteristics: sensitivity: 83.6%, specificity: 56.4%, PPV: 81.0%, and NPV: 60.8% [15]. The yield of the STOP-Bang in screening sleep clinic patients for OSA was previously evaluated [36]: to detect OSA $_{\geq 5}$ , OSA $_{\geq 15}$ , and OSA $_{\geq 30}$ , sensitivity ranged from 90 to 96% and specificity ranged from 49 to 25%, respectively. In addition, the AUC was consistently > 0.72 for all OSA severities [36].

In the HypnoLaus cohort, NoSAS identified individuals at high-risk of having clinically OSA (defined as an AHI  $\geq$  20.0 events/h) with an AUC of 0.74, while in the EPISONO cohort, it performed with an AUC of 0.81 [16]. Afterwards, this instrument was validated in different settings, always reporting adequate performance as screening model for OSA: in a multiethnic Asian cohort [37], in a hospital-based sample [38, 39], and in subjects suffering from depressive disorder [40].

Similar to our findings, ESS was deemed insufficiently accurate as a screening tool for OSA, possibly because it is based on the level of excessive daytime sleepiness, which is not always present in OSA [41–44]. Although ESS was not specifically developed for OSA screening but rather for excessive daytime sleepiness, this tool has been widely used in several OSA-related studies.

## **Limitations and Strengths**

Our study has some obvious limitations based on its design, since it examined the screening instruments in referred patients with a high pre-test probability, which may limit its external validity. In addition, it was performed at a single institution, and its implications for the general population or other sleep centers may also vary. Another possible limitation is that the diagnosis of insomnia was merely subjective through selfreported data, being that patients suffering from insomnia may underestimate their sleep times and overestimate their waking times. Conversely, the present study has several important

Lung

**Table 2** Predictive parameters of all models (n = 2591)

	Screening instruments					
	No-Apnea	STOP-Bang	NoSAS	ESS		
$AHI \ge 5.0/h$						
Sensitivity	84.5 (83.5-85.5)	88.2 (87.2-89.1)	74.7 (73.7–75.7)	45.4 (44.4–46.5)		
Specificity	58.2 (55.0-61.3)	50.1 (47.0-53.1)	69.3 (66.0–72.4)	65.7 (62.2–69.0)		
PPV	86.7 (85.6-87.7)	85.0 (84.1-85.9)	88.6 (87.4–89.8)	81.0 (79.1-82.8)		
NPV	53.9 (50.9–56.8)	56.8 (53.3-60.3)	46.0 (43.8-48.1)	27.3 (25.8–28.6)		
Accuracy	78.3 (76.7–79.8)	79.1 (77.6-80.6)	73.4 (71.8–74.9)	50.3 (48.6-51.8)		
$AHI \ge 15.0/h$						
Sensitivity	90.8 (89.4–92.0)	92.5 (91.2–93.7)	82.5 (80.8-84.0)	48.7 (46.8–50.5)		
Specificity	44.2 (42.6–45.6)	36.1 (34.6–37.4)	56.3 (54.5-58.1)	63.8 (61.8–65.8)		
PPV	64.8 (63.8–65.7)	62.1 (61.2–62.9)	68.1 (66.8–69.4)	60.3 (58.1-62.6)		
NPV	80.9 (78.0-83.5)	81.0 (77.7-84.0)	74.0 (71.6–76.3)	52.4 (50.7-54.0)		
Accuracy	68.9 (67.4–70.2)	66.0 (64.7–67.3)	70.2 (68.5–71.9)	55.8 (53.8–57.7)		
$AHI \ge 30.0/h$						
Sensitivity	94.1 (92.3–95.5)	96.7 (95.3–97.7)	87.3 (85.1–89.3)	53.2 (50.4–56.0)		
Specificity	35.1 (34.3–35.8)	29.4 (28.7–29.9)	46.9 (45.8–47.8)	62.2 (60.9–63.6)		
PPV	41.2 (40.4–41.8)	39.8 (39.2-40.3)	44.3 (43.1–45.3)	40.5 (38.4-42.6)		
NPV	92.5 (90.3–94.3)	94.8 (92.6–96.5)	88.4 (86.4–90.2)	73.3 (71.7–74.9)		
Accuracy	54.3 (53.2–55.3)	51.3 (50.4–52.0)	60.1 (58.6–61.3)	59.3 (57.5–61.1)		

Data were presented as estimates (95% confidence intervals)

No-Apnea is a 2-item model: neck circumference (NC) is scored as follows: 37.0-39.9 cm (1 point), 40.0-42.9 cm (3 points), and  $\geq 43.0 \text{ cm}$  (6 points); while age is scored as follows: 35-44 years (1 point), 45-54 years (2 points),  $\geq 55$  years (3 points); totaling a score of 0–9 points [score  $\geq 3$  was considered as high-risk for presence of any obstructive sleep apnea (OSA), moderate/severe OSA, and severe OSA]. STOP-Bang is an 8-item model (1 point for each positive answer): loud snoring, tiredness, observed apnea, hypertension, body-mass index (BMI)  $> 35 \text{ kg/m}^2$ , age > 50 years, NC > 40 cm, and male gender; totaling a score of 0–8 points [score  $\geq 3$  was considered as high-risk for presence of any OSA, moderate/severe OSA, and severe OSA]. NoSAS is a 5-item model: NC > 40 cm (4 points), BMI 25.0–29.9 kg/m<sup>2</sup> (3 points), BMI  $\geq 30.0 \text{ kg/m}^2$  (5 points), snoring (2 points), age > 55 years (4 points), male gender (2 points); totaling a score of 0–17 points [score  $\geq 8$  was considered as high-risk for presence of any OSA, moderate/severe OSA, and severe OSA]. Epworth Sleepiness Scale (ESS) is an 8-item model that assesses the subjective likelihood of falling asleep in various settings. Each item is scored from zero (would never doze) to three (high chance of dozing), totaling a score from 0–24 points [a score  $\geq 11$  points was considered indicative of excessive daytime sleepiness]

OSA severity was classified based on the AHI thresholds:  $\geq$  5.0/h as any OSA,  $\geq$  15.0/h as moderate/severe OSA, and  $\geq$  30.0/h as severe OSA

AHI apnea/hypopnea index, PPV positive predictive value, NPV negative predictive value

strengths: a large sample of patients consecutively and prospectively recruited, all of them evaluated with full PSG and scored according to the current guidelines proposed in 2012 by the American Academy of Sleep Medicine [18]. Furthermore, this is the first study that was effectively designed to assess differences in No-Apnea, STOP-Bang, NoSAS, and ESS performance among subjects with insomnia and referred for PSG.

## Conclusions

The No-Apnea, a 2-item instrument, showed adequate discrimination and predictive performance for diagnosis of  $OSA_{\geq 5}$ ,  $OSA_{\geq 15}$ , and  $OSA_{\geq 30}$  with a cutoff point  $\geq 3$ . Its performance was comparable to those of STOP-Bang and NoSAS, besides being superior to ESS. Further studies evaluating the applicability of No-Apnea as a referral tool for OSA diagnosis in the context of primary care setting among patients with a primary complaint of insomnia should be forthcoming.



**Fig. 2** Discriminatory ability–reported as area under the curve (95% confidence interval)–obtained by No-Apnea, STOP-Bang, NoSAS, and Epworth Sleepiness Scale (ESS) for screening of obstructive sleep apnea (OSA). OSA severity was classified based on the apnea/ hypopnea index:  $\geq$  5.0/h as any OSA (OSA<sub> $\geq$ 5</sub>),  $\geq$  15.0/h as moderate/ severe OSA (OSA<sub> $\geq$ 15</sub>), and  $\geq$  30.0/h as severe OSA (OSA<sub> $\geq$ 30</sub>). In predicting OSA<sub> $\geq$ 5</sub>, OSA<sub> $\geq$ 15</sub>, and OSA<sub> $\geq$ 30</sub>, No-Apnea performed similar

#### **Compliance with Ethical Standards**

**Conflict of interest** The authors declare that they have no competing interests.

## References

- Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM (2013) Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 177:1006–1014
- Heinzer R, Vat S, Marques-Vidal P, Marti-Soler H, Andries D, Tobback N et al (2015) Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. Lancet Respir Med 3:310–318
- Duarte RL, Magalhães-da-Silveira FJ (2015) Factors predictive of obstructive sleep apnea in patients undergoing pre-operative evaluation for bariatric surgery and referred to a sleep laboratory for polysomnography. J Bras Pneumol 41:440–448
- Muxfeldt ES, Margallo VS, Guimarães GM, Salles GF (2014) Prevalence and associated factors of obstructive sleep apnea in patients with resistant hypertension. Am J Hypertens 27:1069–1078
- Johnson KG, Johnson DC (2010) Frequency of sleep apnea in stroke and TIA patients: a meta-analysis. J Clin Sleep Med 6:131–137
- 6. Muraja-Murro A, Kulkas A, Hiltunen M, Kupari S, Hukkanen T, Tiihonen P et al (2013) The severity of individual obstruction events is related to increased mortality rate in severe obstructive sleep apnea. J Sleep Res 22:663–669
- 7. Ohayon MM (2002) Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med Rev 6:97–111
- Chung KF (2005) Insomnia subtypes and their relationships to daytime sleepiness in patients with obstructive sleep apnea. Respiration 72:460–465
- 9. Krell SB, Kapur VK (2005) Insomnia complaints in patients evaluated for obstructive sleep apnea. Sleep Breath 9:104–110

when compared with STOP-Bang or NoSAS: p=0.532 and p=0.592; p=0.444 and p=0.705; p=0.182 and p=0.743, respectively. In predicting OSA<sub> $\geq 5$ </sub>, OSA<sub> $\geq 15$ </sub>, and OSA<sub> $\geq 30$ </sub>, STOP-Bang performed similar when compared with NoSAS: p=0.246; p=0.253; and p=0.096, respectively. No-Apnea, STOP-Bang, and NoSAS presented higher discrimination than that presented by ESS at all levels of OSA severity (all *p*-values < 0.001)

- Taylor D, Mallory LJ, Lichstein KL, Durrence HH, Riedel BW, Bush AJ (2007) Comorbidity of chronic insomnia with medical problems. Sleep 30:213–218
- Wallace DM, Sawyer AM, Shafazand S (2018) Comorbid insomnia symptoms predict lower 6-month adherence to CPAP in US veterans with obstructive sleep apnea. Sleep Breath 22:5–15
- Duarte RLM, Rabahi MF, Magalhães-da-Silveira FJ, de Oliveirae-Sá TS, Mello FCQ, Gozal D (2018) Simplifying the screening of obstructive sleep apnea with a 2-item model, No-Apnea: a crosssectional study. J Clin Sleep Med 14:1097–1107
- Nigro CA, Dibur E, Borsini E, Malnis S, Ernst G, Bledel I et al (2018) The influence of gender on symptoms associated with obstructive sleep apnea. Sleep Breath 22:683–693
- American Association of Sleep Medicine (2014) ICSD-3 International Classification of Sleep ICSD-3 Disorders. American Association of Sleep Medicine, Dartmouth
- Chung F, Yegneswaran B, Liao P, Chung SA, Vairavanathan S, Islam S et al (2008) STOP questionnaire: a tool to screen patients for obstructive sleep apnea. Anesthesiology 108:812–821
- Marti-Soler H, Hirotsu C, Marques-Vidal P, Vollenweider P, Waeber G, Preisig M et al (2016) The NoSAS score for screening of sleep-disordered breathing: a derivation and validation study. Lancet Respir Med 4:742–748
- 17. Johns MW (1991) A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 14:540–545
- Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK et al (2012) Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. J Clin Sleep Med 8:597–619
- Steyerberg EW, Vickers AJ, Cook NR, Gerds T, Gonen M, Obuchowski N et al (2010) Assessing the performance of prediction models: a framework for some traditional and novel measures. Epidemiology 21:128–138
- Hanley JA, McNeil BJ (1983) A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology 148:839–843

- Duarte RLM, Fonseca LBM, Magalhães-da-Silveira FJ, Silveira EAD, Rabahi MF (2017) Validation of the STOP-Bang questionnaire as a means of screening for obstructive sleep apnea in adults in Brazil. J Bras Pneumol 43:456–463
- Duarte RLM, Mello FCQ, Magalhães-da-Silveira FJ, Oliveirae-Sá TS, Rabahi MF, Gozal D (2019) Comparative performance of screening instruments for obstructive sleep apnea in morbidly obese patients referred to a sleep laboratory: a prospective crosssectional study. Sleep Breath. https://doi.org/10.1007/s11325-019-01791-w
- Hagen C, Patel A, McCall WV (2009) Prevalence of insomnia symptoms in sleep laboratory patients with and without sleep apnea. Psychiatry Res 170:276–277
- 24. Mysliwiec V, Gill J, Lee H, Baxter T, Pierce R, Barr TL et al (2013) Sleep disorders in US military personnel. A high rate of comorbid insomnia and obstructive sleep apnea. Chest 144:549–557
- Smith S, Sullivan K, Hopkins W, Douglas J (2004) Frequency of insomnia report in patients with obstructive sleep apnoea hypopnea syndrome (OSAHS). Sleep Med 5:449–456
- Li M, Zhang XW, Hou WS, Tang ZY (2014) Insomnia and risk of cardiovascular disease: a meta-analysis of cohort studies. Int J Cardiol 176:1044–1047
- Sofi F, Cesari F, Casini A, Macchi C, Abbate R, Gensini GF (2014) Insomnia and risk of cardiovascular disease: a meta-analysis. Eur J Prev Cardiol 21:57–64
- Lu JL, Freire AX, Molnar MZ, Kalantar-Zadeh K, Kovesdy CP (2018) Association of chronic insomnia with mortality and adverse renal outcomes. Mayo Clin Proc 93:1563–1570
- Molnar MZ, Mucsi I, Novak M, Szabo Z, Freire AX, Huch KM et al (2015) Association of incident obstructive sleep apnoea with outcomes in a large cohort of US veterans. Thorax 70:888–895
- Daley M, Morin CM, LeBlanc M, Grégoire JP, Savard J (2009) The economic burden of insomnia: direct and indirect costs for individuals with insomnia syndrome, insomnia symptoms, and good sleepers. Sleep 32:55–64
- Léger D, Bayon V (2010) Societal costs of insomnia. Sleep Med Rev 14:379–389
- 32. Subramanian S, Guntupalli B, Murugan T, Bopparaju S, Chanamolu S, Casturi L et al (2011) Gender and ethnic differences in prevalence of self-reported insomnia among patients with obstructive sleep apnea. Sleep Breath 15:711–715
- Lichstein KL, Thomas SJ, Woosley JA, Geyer JD (2013) Cooccurring insomnia and obstructive sleep apnea. Sleep Med 14:824–829
- Krakow B, Melendrez D, Ferreira E, Clark J, Warner TD, Sisley B et al (2001) Prevalence of insomnia symptoms in patients with sleep-disordered breathing. Chest 120:1923–1929

- Abrishami A, Khajehdehi A, Chung F (2010) A systematic review of screening questionnaires for obstructive sleep apnea. Can J Anesth 57:423–438
- 36. Nagappa M, Liao P, Wong J, Auckley D, Ramachandran SK, Memtsoudis S et al (2015) Validation of the STOP-Bang questionnaire as a screening tool for obstructive sleep apnea among different populations: a systematic review and meta-analysis. PLoS ONE 10:e0143697. https://doi.org/10.1371/journal.pone.01436 97.eCollection2015
- Tan A, Hong Y, Tan LWL, van Dam RM, Cheung YY, Lee CH (2017) Validation of NoSAS score for screening of sleep-disordered breathing in a multiethnic Asian population. Sleep Breath 21:1033–1038
- Hong C, Chen R, Qing S, Kuang A, Yang H, Su X et al (2018) Validation of the NoSAS score for the screening of sleep-disordered breathing: a hospital-based retrospective study in China. J Clin Sleep Med 14:191–197
- Peng M, Chen R, Cheng J, Li J, Liu W, Hong C (2018) Application value of the NoSAS score for screening sleep-disordered breathing. J Thorac Dis 10:4774–4781
- 40. Guichard K, Marti-Soler H, Micoulaud-Franchi JA, Philip P, Marques-Vidal P, Vollenweider P et al (2018) The NoSAS score: a new and simple screening tool for obstructive sleep apnea syndrome in depressive disorder. J Affect Disord 227:136–140
- Vana KD, Silva GE, Goldberg R (2013) Predictive abilities of the STOP-Bang and Epworth Sleepiness Scale in identifying sleep clinic patients at high risk for obstructive sleep apnea. Res Nurs Health 36:84–94
- 42. Panchasara B, Poots AJ, Davies G (2017) Are the Epworth Sleepiness Scale and Stop-Bang model effective at predicting the severity of obstructive sleep apnoea (OSA); in particular OSA requiring treatment? Eur Arch Otorhinolaryngol 274:4233–4239
- 43. Duarte RLM, Rabahi MF, Oliveira-e-Sá TS, Magalhães-da-Silveira FJ, Mello FCQ, Gozal D (2019) Fractional exhaled nitric oxide measurements and screening of obstructive sleep apnea in a sleep-laboratory setting: a cross-sectional study. Lung 197:131–137
- 44. Mediano O, Barceló A, de la Peña M, Gozal D, Agustí A, Barbé F (2007) Daytime sleepiness and polysomnographic variables in sleep apnoea patients. Eur Respir J 30:110–113

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.