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ORIGINAL ARTICLE

Sex-dependent GOAL screening performance in adults at risk for obstructive sleep apnea

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Abstract
Objective: To evaluate possible sex-related differences in the performance of the GOAL, a 4-item obstructive sleep apnea (OSA) screening instrument in adults.
Methods: Between July 2019 and June 2021, this cross-sectional study included consecutively recruited patients from one Brazilian sleep laboratory undergoing overnight polysomnography. Individuals with GOAL scores $\geq$ 2 of a maximum of 4 points are classified at high risk for OSA diagnosis. Actual OSA severity was based on the apnea-hypopnea index: $\geq$ 5.0/h as any OSA, $\geq$ 15.0/h as moderate-to-severe OSA, and $\geq$ 30.0/h as severe OSA. Performance of the GOAL instrument in women and men was assessed by the discriminatory ability (obtained from area under the curve [AUC]-Receiver Operating Characteristic curves) and 2×2 contingency tables.
Results: A total of 2,978 subjects (55.3% males) were evaluated. The frequency of GOAL-defined OSA high-risk was statistically higher in men when compared to women ($p < 0.001$). The GOAL predictive parameters for screening all severity OSA levels were as follows: in females, sensitivity ranging from 58.2% to 78.3% and specificity ranging from 60.0% to 77.6%, while in males, sensitivity ranging from 90.5% to 96.9% and specificity from 20.7% to 46.8%. The GOAL questionnaire had similar discriminatory properties, assessed by AUC, in women and in men: i) any OSA: 0.741 vs. 0.771 ($p = 0.204$), ii) moderate-to-severe OSA: 0.727 vs. 0.737 ($p = 0.595$), and iii) severe OSA: 0.728 vs. 0.703 ($p = 0.240$); respectively.
Conclusions: The GOAL instrument emerges as a useful tool for screening adult individuals and displays similar performance in both women and men.

Introduction

Obstructive sleep apnea (OSA) is a sleep disorder characterized by recurrent episodes of upper airway obstruction, resulting in intermittent hypoxemia, sleep fragmentation,

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as well as cardiovascular, metabolic, and neurocognitive complications.[1] The prevalence of this condition has increased considerably in recent decades,[2-4] possibly due to the aging trends in the population and the worldwide increases in obesity rates. A systematic review evaluated the prevalence of OSA in adults in the general population, which ranged from 9% to 38% for any OSA (apnea-hypopnea index [AHI] $\geq$ 5/h) and from 6% to 17% for moderate-to-severe OSA (AHI $\geq$ 15/h), being as high as 49% in aged individuals.[4] In addition, it has recently been suggested that approximately 1 billion people worldwide may suffer from OSA.[5]

Throughout the world, it is common for sleep laboratories to have a large number of individuals with suspected sleep-breathing disorders, who are waiting to be tested.[1,6] To date, the gold standard for diagnosing OSA and other sleep-breathing disorders rests on full overnight polysomnography (PSG) performed in the sleep laboratory.[1] However, this test is not widely available and requires trained technical personnel, which places a burden on health services, especially in areas with limited economic resources.[7,8] To this effect, OSA screening instruments can be useful in stratifying patients with suspected OSA, and based on such evaluation develop valid alternative approaches, such as portable or home-based diagnostic methods.[1,9-15]

The GOAL questionnaire is a concise screening instrument containing only 4 clinical parameters that are easily obtained in clinical practice, namely male gender, obesity with body mass index [BMI] $\geq$ 30.0 kg/m^2, age $\geq$ 50 years, and presence of loud snoring.[15] Each parameter is categorically answered as either 0 (negative statement) or 1 (positive statement), totaling a score of 0-4 points, whereby individuals with scores $\geq$ 2 points are classified as being at high risk for OSA.[15] The GOAL questionnaire has already been validated in several clinical contextual settings and has consistently shown a similar performance to other validated screening instruments, such as the STOP-Bang questionnaire and the NoSAS score.[16,17]

The discrepancies revolving around several clinical, demographic, anthropometric, and polysomnographic characteristics between women and men could possibly influence the performance of any screening instrument. Men with OSA usually present with more typical symptoms of the disease, such as snoring, observed apnea, and excessive sleepiness; in contrast, women with OSA often report atypical symptoms, such as insomnia, morning headaches, and fatigue.[18-22] In general, women with OSA are older at diagnosis, more obese, and may have more OSA-related comorbidities, such as hypertension and type 2 diabetes mellitus; conversely, neck circumference (NC) tends to be higher in men than in women.[18-22] Usually, OSA screening instruments include mostly if not exclusively men at the expense of women. A question that naturally arises is whether there will be a need to use different cutoff points of the GOAL questionnaire to assess the risk of OSA in men and women separately. This issue, along with a clear difference in OSA symptomatology between the sexes, means that the sex-related performance of the GOAL instrument deserves further exploration. Based on polysomnographic findings, women have a lower prevalence of OSA and greater evidence of worse sleep quality when compared to men.[18-22] Therefore, significant differences between the sexes are detectable, not only in the prevalence of OSA but also in the clinical phenotypes commonly associated with the presence of this disorder.

Despite the several sex-related differences in the clinical phenotypic presentation and polysomnographic characteristics of OSA, there are only a few studies that have assessed whether sex-related differences are present among OSA screening instruments, and the GOAL questionnaire is no exception. In light of the above, the main objective of this study was to compare between women and men the predictive performance and discriminatory ability of the GOAL.

Methods

In the period between July 2019 to June 2021, a cross-sectional study was carried out with consecutively recruited adult individuals (aged $\geq$ 18 years), who were referred for sleep assessment by their respective attending physicians. Patients with previously diagnosed OSA, a sleep-related disease diagnosis based on the use of portable home monitors, and incomplete clinical data making it impossible to complete the GOAL questionnaire were considered as exclusion criteria. If the same patient was subjected to more than one PSG, only the sleep test that achieved the longest total sleep time was retained in the analysis. Moreover, those individuals who were diagnosed with central sleep apnea were later excluded from the final analysis. The study protocol was in strict accordance with the 1964 Declaration of Helsinki and was previously approved by the Ethics Committee of the *Universidade Federal do Rio de Janeiro* (number 1.764.165). Written informed consent was obtained from all volunteers, and the anonymity of each participant was strictly preserved.

All clinical, demographic, and anthropometric characteristics, in addition to the collection of data necessary for completing the GOAL questionnaire, were systematically obtained by experienced sleep technicians immediately before the overnight PSG. Clinical data consisted of sex, age, BMI, NC, Epworth Sleepiness Scale (ESS), and self-reported comorbidities such as hypertension and type 2 diabetes mellitus. BMI was calculated by dividing weight in kilograms by the square of height in meters (kg/m^2). NC (in cm) was measured, using a measuring tape with all individuals who were asked to remain erect, with the upper edge of the measuring tape being placed just below the laryngeal prominence and applied perpendicularly along the long axis of the neck.[23] ESS is an 8-item questionnaire that assesses the subjective probability of falling asleep in various daily settings, with a final score from 0 to 24 points, being excessive daytime sleepiness characterized by a minimum score of 11 points.[24,25]

GOAL screening instrument

The GOAL questionnaire contains 4 clinical parameters: male sex, BMI $\geq$ 30 kg/m^2, age $>$ 50 years, and presence of loud snoring. Each parameter is categorically scored as 0 (negative answer) or 1 (positive answer), being that scores $\geq$ 2 (from 0 to 4) indicate individuals at high risk for OSA diagnosis.[15]

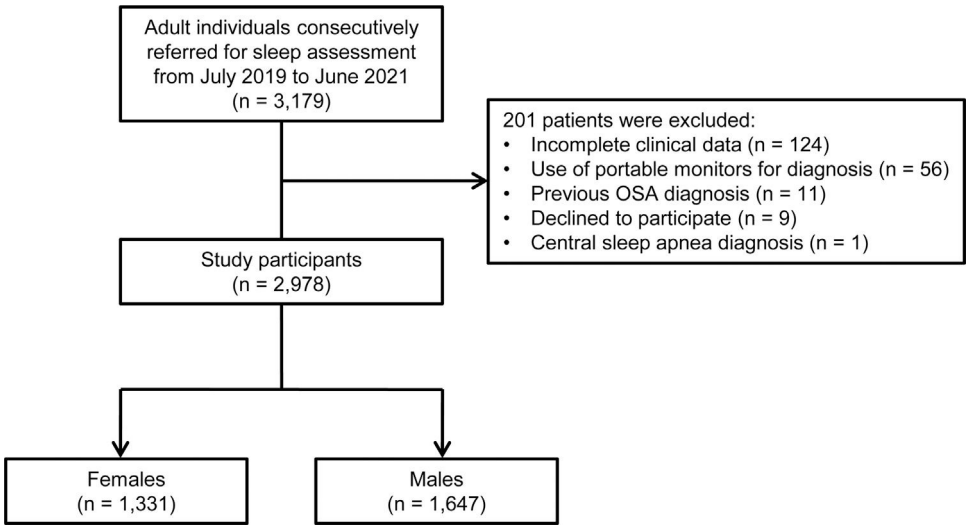

Fig. 1 Flow chart of the study. OSA: obstructive sleep apnea.

Overnight sleep studies

All polysomnographic assessments (EMBLA® S7000, Embla Systems, Inc., Broomfield, CO, USA) were conducted in a single sleep center (*SleepLab - Laboratório de Estudo dos Distúrbios do Sono*, Rio de Janeiro, Brazil). The recordings consisted of continuous monitoring of the electroencephalogram, electrooculogram, electromyogram, electrocardiogram, airflow, chest and abdominal impedance belts, pulse oximeter to measure peripheral oxygen saturation (SpO_2) and heart rate, snoring microphone, and body position sensors. The manual scoring of each sleep exam was performed by two board-certified sleep physicians, according to a previously published guideline,[26] being that both physicians were blind to the GOAL scores, which were collected prior to PSG. Obstructive apneas were classified by a drop of at least 90% in airflow for at least 10 seconds, associated with the presence of thoracoabdominal movement. Hypopneas were classified with a drop of at least 30% in airflow for at least 10 seconds associated with oxygen desaturation $\geq$ 3% or arousal.[26] The OSA diagnosis was based on the AHI: an AHI $\geq$ 5.0/h, $\geq$ 15.0/h, or $\geq$ 30.0/h was considered as any OSA, moderate-to-severe OSA, and severe OSA; respectively.

Statistical analysis

The data were tabulated and processed using the SPSS statistical software (version 21.0, Chicago, IL, USA). Results were summarized by the median with interquartile range [IQR] (numerical variables) and number with percentage (categorical variables). Categorical variables were compared using chi-square tests, while numerical variables were assessed using non-parametric Mann-Whitney tests. The predictive performance of the GOAL screening instrument was evaluated by 2×2 contingency tables and discriminatory ability, which was estimated from the area under the curve (AUC) obtained from Receiver Operating Characteristic (ROC) curves. An AUC $>$ 0.7 was considered as clinically significant discrimination.[27] Pairwise comparison among sex-related AUCs was assessed using the previously described methodology.[28] All estimates (sensitivity, specificity, positive predictive value [PPV], and negative predictive value [NPV]) were expressed with their respective 95% confidence intervals (95% CI). A two-tailed p-value $<$ 0.05 was considered to be statistically significant.

Results

This cross-sectional study enrolled 2,978 subjects who were consecutively referred to a single sleep center: 1,331 women (44.7%) and 1,647 men (55.3%); Fig. 1. As can be seen in Table 1, women were older (p = 0.001) and had a lower NC than men (p $<$ 0.001). In addition, women had a higher frequency of type 2 diabetes mellitus (14.5% versus 12.0%; p = 0.049). As expected, men had a higher severity of OSA compared to women, as can be seen from the higher AHI, higher ODI, and lower values of SpO_2 (all with p $<$ 0.001); Table 1. The frequency of high-risk individuals, assessed by the GOAL questionnaire, was statistically higher in men than in women: 88.0% versus 49.7% (p $<$ 0.001; Table 1). The OSA prevalence was always statistically higher in men than in women: (p $<$ 0.001 for all OSA severity levels); Table 1. The median AHI measurements increased linearly according to increasing GOAL questionnaire scores: i) in females from 1.5 events/h (IQR: 0.3-4.6) to 25.6 events/h (IQR: 13.0-46.6); p $<$ 0.001 and ii) in males from 7.3 events/h (IQR: 2.5-16.3) to 49.5 events/h (IQR: 27.9-70.5); p $<$ 0.001.

Predictive performance

Table 2 shows the sex-related performance of the GOAL instrument. In females, sensitivity ranged from 58.2% to 78.3% and specificity from 60.0% to 77.6%. In males, sensitivity ranged from 90.5% to 96.9% and specificity from 20.7% to 46.8%. For all levels of OSA severity, men always had higher sensitivity at the expense of lower specificity than women. In addition, as OSA severity increased, there was an increase in sensitivity and reduction in specificity in both females and males.

Table 1 Baseline characteristics of the cohort (n = 2,978).

Parameter	Females (n = 1,331)	Males (n = 1,647)	p-value
Clinical data			
Age, years	47.0 (35.0-60.0)	44.0 (35.0-56.0)	0.001
BMI, kg/m^2	29.2 (25.6-34.8)	29.4 (26.4-33.1)	0.296
NC, cm	37.0 (34.0-39.0)	42.0 (40.0-45.0)	< 0.001
EDS	519 (39.0)	686 (41.7)	0.143
Hypertension	436 (32.8)	566 (34.4)	0.370
Type 2 diabetes mellitus	193 (14.5)	198 (12.0)	0.049
High risk for OSA, %			
GOAL	662 (49.7)	1,450 (88.0)	< 0.001
Polysomnographic data			
Sleep efficiency, %	80.2 (68.9-87.9)	80.5 (69.2-89.3)	0.670
AHI, events/h	14.5 (5.4-30.1)	29.4 (14.8-51.8)	< 0.001
Average SpO_2, %	94.2 (92.7-95.5)	93.5 (92.0-94.7)	< 0.001
Lowest SpO_2, %	85.0 (79.0-90.0)	83.0 (77.0-87.0)	< 0.001
ODI at 3%, events/h	7.0 (2.1-17.7)	16.3 (6.1-37.2)	< 0.001
OSA frequency, %			
Any OSA	1,018 (76.5)	1,538 (93.4)	< 0.001
Moderate-to-severe OSA	651 (48.9)	1,231 (74.7)	< 0.001
Severe OSA	337 (25.3)	816 (49.5)	< 0.001

Numeric and categorical variables are reported as median (interquartile range) and n (%), respectively. BMI: body mass index; NC: neck circumference; EDS: excessive daytime sleepiness (Epworth Sleepiness Scale ≥ 11 points); OSA: obstructive sleep apnea; AHI: apnea/hypopnea index; SpO_2: oxygen saturation; ODI: oxygen desaturation index. Individuals were classified as high risk for OSA diagnosis through the following cutoff point: GOAL questionnaire ≥ 2 (from 0 to 4 points). OSA was assessed by an apnea/hypopnea index ≥ 5.0/h as any OSA, ≥ 15.0/h as moderate-to-severe OSA, and ≥ 30.0/h as severe OSA.

Pairwise comparison of ROC curves

Fig. 2 illustrates the discriminatory power of the GOAL questionnaire. The 4-item GOAL instrument proved to be a useful tool for OSA screening, at all severity levels, both in males and in females (all AUCs were higher than 0.7). Moreover, comparisons between men and women revealed that the GOAL exhibited similar discrimination for predicting any OSA (p = 0.204), moderate-to-severe OSA (p = 0.595), and severe OSA (p = 0.240).

Table 2 Predictive parameters of the GOAL questionnaire in identifying OSA (n = 2,978).

	Females (n = 1,331)	Males (n = 1,647)
Any OSA		
Sensitivity, %	58.2 (56.8-59.4)	90.5 (89.9-91.1)
Specificity, %	77.6 (73.1-81.7)	46.8 (38.0-55.7)
PPV, %	89.4 (87.3-91.4)	96.0 (95.3-96.7)
NPV, %	36.3 (34.2-38.2)	25.9 (21.0-30.8)
Moderate-to-severe OSA		
Sensitivity, %	68.2 (65.5-70.8)	94.9 (93.8-95.8)
Specificity, %	67.9 (65.4-70.4)	32.2 (29.2-35.0)
PPV, %	67.1 (64.4-69.6)	80.6 (79.7-81.4)
NPV, %	69.1 (66.4-71.6)	68.0 (61.6-73.9)
Severe OSA		
Sensitivity, %	78.3 (74.0-82.2)	96.9 (95.6-97.9)
Specificity, %	60.0 (58.5-61.3)	20.7 (19.4-21.7)
PPV, %	39.9 (37.7-41.8)	54.6 (53.8-55.1)
NPV, %	89.1 (86.9-91.0)	87.3 (81.9-91.4)

Data are presented as estimates (95% confidence intervals). PPV: positive predictive value; NPV: negative predictive value. OSA was assessed by an apnea/hypopnea index ≥ 5.0/h as any OSA, ≥ 15.0/h as moderate-to-severe OSA, and ≥ 30.0/h as severe OSA. Individuals were classified as high risk for obstructive sleep apnea (OSA) diagnosis through the following cutoff point: GOAL questionnaire ≥ 2 (from 0 to 4 points).

Discussion

The present study, which includes a large sample of individuals clinically referred for full in-lab PSG, revealed that the GOAL screening instrument is a useful tool for the identification of OSA at all severity levels, and it functions equally well among males and females. Our findings clearly emphasize the role of GOAL as a practical and concise screening tool for identifying OSA.

The performance of each screening instrument can vary widely according to the type of sleep test used to diagnose OSA, the study population, and the AHI cutoff point employed to diagnose OSA.[1,9-11] Besides, in general, the sensitivity of a screening instrument increases at the expense of a reduction in specificity and *vice versa*. In the case of a highly prevalent disease such as OSA, it is possibly more important that a screening test is equipped with high sensitivity instead of having high specificity, particularly in a population with a high pre-test probability.[1,9-11] Those desirable characteristics are clearly part of the attributes of the GOAL instrument. In contrast, high sensitivity associated with low specificity, as observed in the GOAL questionnaire, increases referral for costly sleep studies due to a high false-positive rate. Moreover, for the prediction of any OSA, the GOAL questionnaire had, in both sexes, a high PPV, which made it therefore much more useful to rule in than to rule out a

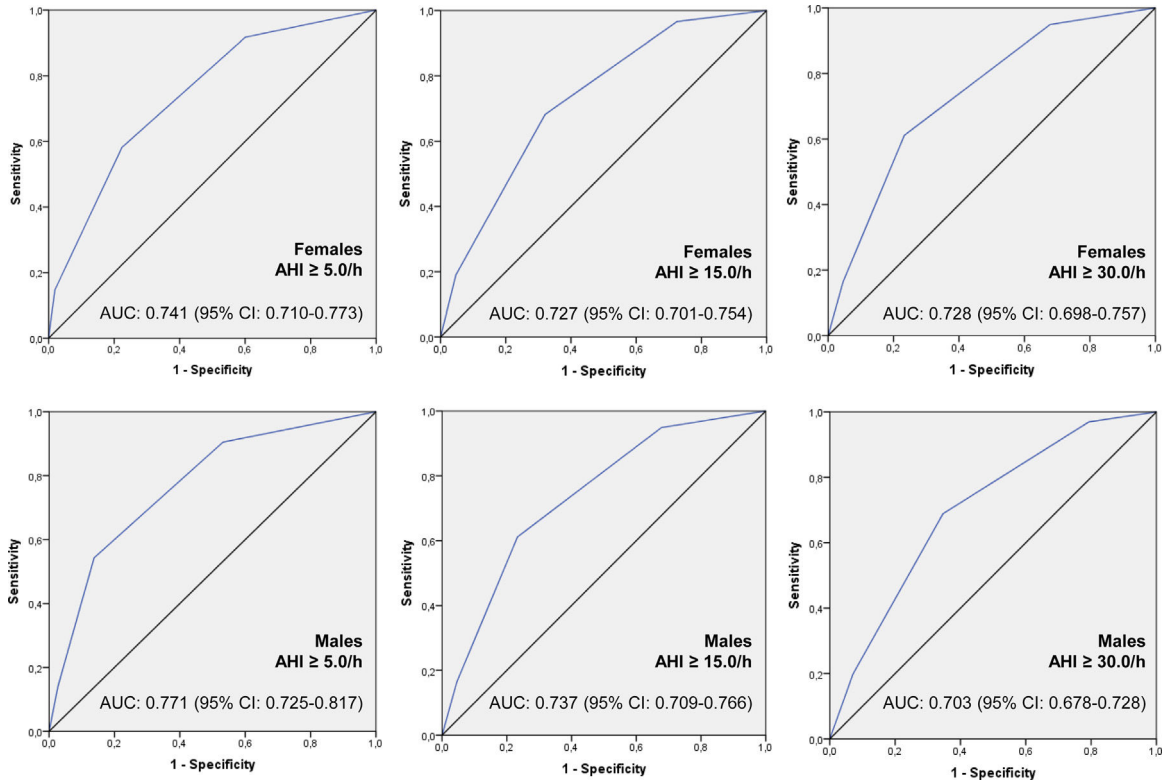

Fig. 2 Discriminatory performance, reported as the area under the curve (AUC) and 95% confidence interval (CI), of the GOAL questionnaire in females (n = 1,331) and in males (n = 1,647) for screening of any obstructive sleep apnea (OSA), moderate-to-severe OSA, and severe OSA. OSA severity was assessed by an apnea/hypopnea index (AHI) $\geq$ 5.0/h as any OSA, $\geq$ 15.0/h as moderate-to-severe OSA, and $\geq$ 30.0/h as severe OSA. Pairwise comparison of AUC showed similar sex-related GOAL discrimination for any OSA (p = 0.204), moderate-to-severe OSA (p = 0.595), and severe OSA (p = 0.240).

possible diagnosis of OSA. On the other hand, in predicting severe OSA, the high NPV obtained by GOAL, in men and women, makes it more useful to rule out rather than confirm a diagnosis of severe OSA.

In light of the multiple clinical, demographic, anthropometric, and polysomnographic differences that are readily detectable among men and women, there are surprisingly few studies that have compared the performance of screening instruments between sexes, and such studies have yielded conflicting findings.[29-35] A retrospective analysis of 1,119 adults reported that the discriminatory ability of the NoSAS score at all AHI cutoffs was significantly lower in men than in women (all with $p < 0.01$).[30] Similarly, predicting moderate-to-severe OSA among 251 bariatric surgery patients, the STOP-Bang and NoSAS, but not ESS, performed better in women than in men.[31] Conversely, in a large sample of adults, No-Apnea, STOP, STOP-Bang, and NoSAS exhibited discriminatory abilities for predicting any, moderate-to-severe, and severe OSA that were similar between sexes, except for the ESS, which performed better in men than in women at all OSA severity levels.[15] However, it should be emphasized that ESS, despite being widely used in clinical practice, is a scale that measures the degree of excessive daytime sleepiness and should therefore not be considered as a screening tool for OSA. Furthermore, similar to our findings, the predictive performance of the various screening instruments generally tends to be more sensitive and less specific in men than in women.[33-35]

The original GOAL study was developed in a large cohort of patients undergoing full overnight PSG in the sleep laboratory.[15] In the derivation cohort, screening any OSA, moderate-to-severe OSA, and severe OSA, the GOAL achieved sensitivities ranging from 83.3% to 94.0% and specificities ranging from 62.4% to 38.5%. In the validation cohort, the GOAL corroborated such initial findings as illustrated by sensitivities ranging from 83.7% to 94.2% and specificities ranging from 63.4% to 37.7% (in the three OSA severity AHI-based cutoff values).[15] Thus, the current findings further reinforce the robust GOAL diagnostic accuracy as a screening tool and illustrate its relative homogeneity among men and women. Nonetheless, we should also be cognizant that the most frequently mentioned OSA screening tool is the STOP-Bang questionnaire. This 8-item instrument was originally developed and later validated in surgical patients,[13] and was subsequently more widely validated in several settings, with consistent reports of high sensitivity and low-to-moderate specificity for predicting OSA.[36-40] The GOAL instrument, similar to the STOP-Bang questionnaire, has also consistently presented high sensitivity with low-to-moderate specificity in predicting OSA.[15-17] Interestingly, the current study shows that GOAL exhibits greater sensitivity and lower specificity in men compared to women. However, the overall diagnostic accuracy of the GOAL tool when applied to all-comers was similar for men and women.

The present study has several limitations that obviously deserve to be highlighted. The cohort sample was recruited

from patients being referred to a single Brazilian sleep center, thereby limiting the generalization of our findings to other populations. Also, the study group was predominantly composed of individuals with a high pre-test probability, rather than reflecting a more generalized primary care population. Therefore, and as would be expected, we found a high prevalence of OSA, which could also influence the performance of GOAL as a screening instrument. Our study did not preferentially include individuals of other racial/ethnic groups, such as Asians or Africans, who may have different anthropometric characteristics, and much more skewed approaches will require verification in future studies. All study participants underwent one night PSG, and as such, we cannot completely exclude the possibility of night-night variability or first night effect in the sleep laboratory. Notwithstanding, we should also point out several strengths of the present study. Our sample consisted of almost 3,000 outpatient subjects who underwent an overnight PSG in the sleep laboratory, which was scored by experienced physicians using the same criteria and approaches proposed in 2012 by the American Academy of Sleep Medicine,[26] and such internal consistency probably increased the robustness of our findings. To date, this is the first study that was effectively designed and developed to assess sex-related differences if any in GOAL performance.

Conclusions

Our study indicates that the GOAL questionnaire is a useful tool for predicting OSA in a reasonably large sample of adult individuals referred to a sleep laboratory. In addition, the sex-related GOAL discrimination was similar in predicting all severities of OSA such that there is no need for different cut-off values to be applied among men and women.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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