



Original Article

Obstructive sleep apnea in patients with chronic rhinosinusitis with nasal polyps: a cross-sectional study

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ARTICLE INFO

Article history:

Received 17 December 2018

Received in revised form

6 June 2019

Accepted 7 June 2019

Available online 14 June 2019

Keywords:

Obstructive sleep apnea

Nasal polyps

Rhinosinusitis

Adults

STOP-Bang

ABSTRACT

Introduction: Adults with chronic rhinosinusitis with nasal polyps (CRSwNP) often suffer from sleep disruption and sleep apnea. As the apneic profile of CRSwNP may differ from obstructive sleep apnea (OSA) classic patients without nasal polyps (NP), it may prove useful to define a new profile for OSA screening in these patients. The aim of the current study was to compare baseline characteristics and apneic profile of OSA patients with CRSwNP to OSA patients without NP.

Materials and methods: Thirty-one apneic patients with CRSwNP and 62 apneic cases without NP were included in our study. Both groups underwent nasal endoscopy, Epworth Sleepiness Scale (ESS) evaluation, and overnight polysomnography (PSG). We additionally accessed anthropometric characteristics such as snoring, tiredness, observed apnea, high blood pressure, body mass index (BMI), age, neck circumference, male gender, and OSA risk via the STOP-Bang questionnaire.

Results: Although the patients were matched according to age and gender, the median BMI and STOP-Bang score were significantly higher in patients with OSA than in those with OSA and CRSwNP. Notably, the median ESS showed low somnolence and a low median apnea-hypopnea index in patients with CRSwNP, despite the fact that the lowest median oxygen saturation was not significantly different between groups.

Conclusions: Anthropometric characteristics in individuals with apnea caused by CRSwNP were significantly different from those in individuals with typical. This finding will improve screening and treatment of apneic patients CRSwNP.

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1. Introduction

Individuals with chronic rhinosinusitis (CRS) are known to experience sleep disruption and sleep-disordered breathing (SDB) [1,2], including Obstructive Sleep Apnea (OSA). Previous research has identified several risk factors for OSA in order to improve screening for patients with SDB [3–9]. OSA was found to be typically associated with male gender, middle age [4,5,8], loud snoring, high body mass index (BMI) [5,6], and excessive diurnal somnolence [5,9].

CRS has been shown to influence sleep and quality of life due to an immune-mediated inflammatory response that reaches the central nervous system [10]. Furthermore, chronic rhinosinusitis with nasal polyps (CRSwNP), a severe inflammatory status of sinonasal mucosa [2,10–12], may have a role in SDB, but the involvement of CRS in the clinical presentation of OSA is still unclear. Uzdán et al. [11], recently found a significant improvement in rhinomanometric nasal resistance, apnea-hypopnea index (AHI), minimal oxygen saturation (SaO₂), and quality of life scores following polypectomy in 22 patients with CRSwNP by functional endoscopic sinus surgery [11]. Another study reported an improvement of sleep quality and a reduction in excessive somnolence three months after polypectomy in 42 subjects [12].

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In order to further elucidate the role of CRSwNP in SDB, the aim of the present study was to determine the profile of CRSwNP patients with OSA compared to OSA without nasal polyps (NP).

2. Materials and methods

Patients from the Otorhinolaryngology Department of the Gafree and Guinle University Hospital/Federal University of the State of Rio de Janeiro were sequentially recruited between 07/01/2015 and 07/30/2017 following approval by the Research and Ethics Committee (CAAE 42785214.1.0000.5258) on 06/25/2015. We included apneic men between the age of 18 and 65 in this study. All subjects underwent standard polysomnography (PSG) in Labsono, which was supervised by a technician and scored by physicians blinded to the endoscopy results. Everyone undergoing PSG in LabSono was furthermore subjected to nasal endoscopy, and medical evaluation: Physical exam, STOP-Bang [15–17], Epworth Sleepiness Scale (ESS) testing [18,19]. Furthermore, subjects received transcutaneous pulse oximetry, and respiratory air flow measurement using an external thermistor and nasal pressure cannula [13]. Respiratory effort was assessed using respiratory inductance plethysmography with electroencephalographically confirmed arousal [13].

2.1. Inclusion and exclusion criteria

Forty-seven male CRSwNP patients were initially recruited and underwent PSG type 1 in Labsono. NP were identified by rigid endoscopy (30°/4 mm, Karl Storz) and computer tomography scan [14]. We identified eligible OSA patients without NP from the LabSono database and matched them 1:2 with CRSwNP patients according to age (± 3 years) and gender. We applied the following exclusion criteria for both groups: uncontrolled cardiopathy or pneumopathy; central or peripheral nervous system disease; craniofacial anomalies; aspirin-exacerbated respiratory disease; cystic fibrosis; immunodeficiency, ciliary dyskinesia, systemic vasculitis, or granulomatosis; cocaine abuse, neoplasia suspicions, or central sleep apnea syndrome [13,14]. Aspirin sensitivity was determined by the patient's history of severe lower and/or upper airway symptoms after aspirin or other NSAID intake [14]. Pulmonologist diagnosis or current treatments for asthma were used for confirmation of asthma. In the CRSwNP, we excluded five cases due to uncontrolled cardiopathy, and 11 cases due to absence of apnea.

2.2. Clinical criteria

CRSwNP in adults was defined as inflammation of the nose and the paranasal sinuses, characterized by two or more of the following symptoms: nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip) for 12 weeks or longer, associated with facial pain/pressure and reduction/loss of smell; endoscopic signs of nasal polyps; mucopurulent discharge from the middle meatus; edema/mucosal obstruction; and changes in computer tomography (eg, mucosal changes within the ostio-meatal complex and/or sinuses) [14].

OSA diagnostic criteria were 15 or more predominantly obstructive respiratory events (apnea, hypopnea), or Respiratory Effort Related Arousal (RERA) per hour of sleep during PSG or per hour of monitoring (independently of complaints), or five or more predominantly obstructive respiratory events in the presence of one or more of the following symptoms: (a) complains of sleepiness, unrefreshing sleep, fatigue, or insomnia symptoms; (b) awaking with breath holding, gasping, or choking; (c) reports of habitual snoring or breathing interruptions (or both) during sleep; or (d) diagnosis of hypertension, a mood disorder, cognitive

dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, or type II diabetes mellitus [3].

2.3. Patient evaluation

We used the 2015 Portuguese version of STOP-BANG [15,16] to measure the risk of OSA, whereby three or more affirmative answers indicated a high risk of OSA [17], and the ESS [18] to measure diurnal somnolence. In the ESS, sleep propensity was measured in eight routine situations on a scale from 0 (indicating no chance of falling asleep) to 3 (indicating a high chance of dozing off). The final score ranged from 0 to 24 points accordingly, with excessive diurnal somnolence being defined as a score higher than 10 [19].

In the physical examination, we evaluated the following measurements: BMI; enlarged tongue, defined as teeth impressions on the tongue; and mandible retrognathism [20], as verified with the head in the Frankfort horizontal position and the pogonion (most anterior prominent chin point) being greater than 2 mm behind the vertical line, delineated as touching the inferior lip.

We furthermore graded tonsil hypertrophy: (1) tonsils inside the tonsillar fossa lateral to posterior pillars; (2) tonsils occupying 25–50% of the oropharynx; (3) tonsils occupying 51–75%; (4) tonsils occupying 76% or more, almost meeting in the midline; and zero if previous tonsillectomy occurred [21].

Modified Mallampati was graded with an open mouth and the tongue in a neutral position inside the mouth for classification: class I (allowed visualization of the entire uvula and tonsils/pillars); class II (allowed visualization of the uvula but not the tonsils); class III (allowed visualization of the soft palate but not the uvula); and class IV (allowed visualization of the hard palate only) [22].

2.4. Respiratory event criteria

Respiratory events were classified according to the 2012 American Academy of Sleep Medicine (AASM) manual [13]. We used a minimally invasive nasal cannula to monitor the nasal flow [25,26]. Upper Airway Resistance Syndrome (UARS) [23] was defined as an apnea-hypopnea index score lower than 5 per hour and an arousal index score of 10 or more per hour, associated with respiratory effort [24]. Apnea was defined as a decrease of 90% or greater from the previous baseline air flow, as measured by an oronasal thermistor for at least 10 s [13]. Hypopnea was defined as a partial obstructive event with a diminution in air flow of more than 30% from baseline for at least 10 s, as measured using a nasal pressure cannula [25,26], associated with an oxygen desaturation of 3% or greater or an arousal [13,27]. RERA was defined as a sequence of breaths lasting 10 or more seconds characterized by increasing respiratory effort or by flattening of the inspiratory portion of the nasal pressure, leading to arousal from sleep when the sequence of breaths does not meet the criteria for an apnea or hypopnea [13].

2.5. Statistical analysis

All clinical and PSG data were analyzed in SPSS v13.0. We compared absolute and relative frequencies of nominal variables in patients with and without NP. In addition, the median, minimum, and maximum of continuous variables were calculated for each group. The continuous variables were compared using the Mann–Whitney U test. Comparison between apneic patients with and without NPs was performed using Pearson's chi-square test or Fisher's exact test, as indicated. Univariate analysis was performed by logistic regression. The odds ratio (OR) was adjusted by BMI. Significance level was set to 5% to reject the null hypothesis.

Table 1
Apneic population features.

Profile	Patients with OSA and nasal polyps (N = 31) Median (minimum–maximum)	Patients with OSA and without nasal polyps (N = 62) Median (minimum–maximum)	P value
BMI (kg/m ²)	26.3 (15.0–39.2)	30.5 (21.5–55.8)	<0.001 ^a
STOP-Bang	3.0 (1.0–7.0)	5.0 (3.0–10.0)	<0.001 ^a
Age (years old)	50.0 (21.0–64.0)	49.5 (20–67)	0.893

OSA: obstructive sleep apnea; BMI: body mass index.

^a Statistically significant.

3. Results

In this study, we evaluated the characteristics of 31 men with OSA and CRSwNP 62 age- and gender-matched apneic subjects without (shown in Tables 1 and 2). Despite age- and gender-matching, apneic patients with CRSwNP had significantly lower BMI values and STOP-Bang-assessed OSA risk (Table 1).

There was a lower incidence of fatigue, somnolence, and unrefreshing sleep in apneic individuals with CRSwNP (73%, 63%, and

82% lower than men without NP, respectively). Furthermore, there were 43% fewer complaints of snoring in patients with CRSwNP despite a six times higher nasal obstruction compared to patients without NP (Table 2).

Physical examination revealed that the abdominal circumference was lower in CRSwNP patients. Additionally, BMI equal to or higher than 30 kg/m², Mallampati grades, and tonsil grades (III/3, and IV/4, respectively) were less prevalent in patients with CRSwNP (Table 2), but following BMI adjustment by logistic regression, only high Mallampati were significantly less prevalent (Table 3). Controlled asthma was five times more prevalent in subjects with CRSwNP. Conversely, there were no differences in the prevalence of systemic hypertension, type II diabetes mellitus, retrognathism, or enlarged tongue between the groups (Table 2).

There were significant differences in the following PSG indexes: AHI and percentage of time of oxygen saturation levels less than 90% (T < 90%) were lower in apneic patients with CRSwNP prior to univariate analysis, and these patients were additionally found to have a higher percentage of rapid eye movement (REM) sleep (Table 4). However, there was no association with others indexes, such as arousal index (AI), N3 percentual, oxygen desaturation index (ODI), and minimal oxygen saturation (minimal SaO₂) (Tables 4 and 5). Although AHI indices over 30 per hour and somnolence (ESS over 10) were associated with CRSwNP in univariate analysis, these factors both lost statistical significance following BMI adjustment (Table 5).

4. Discussion

Our study is the first to systematically describe OSA in apneic male individuals with CRSwNP. We decided to only include men in our study as they are 2.0–3.7 times more likely to have breathing-related sleep disorders than women [4], and gender is known to affect CRS symptomatology [28] although no studies have been conducted to assess the impact of sex hormones on CRS [29]. Previous studies reported a high prevalence of OSA and sleep disruption in patients with CRS [1,2], but OSA diagnosis is usually performed according to classic clinical presentation (loud snoring and daytime sleepiness in obese male patients) [3–9]. Conversely, in our study men with OSA and CRSwNP in our study had a lower median ESS compared to OSA patients without NP and the majority had a low BMI. Moreover, CRSwNP was associated with less snoring (45.2%) and fatigue (22.6%). The occurrence of SDB in CRSwNP patients with atypical clinical presentation (low BMI and little snoring) may be explained by the inflammatory process and different nasal flow compared to patients without NP [1,12,14].

AHI and T < 90% occurred more frequently in apneic patients without NP than with NP, indicating an increased severity of OSA. This was potentially caused by a higher BMI; previous studies showed that obesity is one of the main causes of OSA [3,6,30], and only 19.4% patients with CRSwNP were obese. Despite gender and age-matching, STOP-Bang scores were higher in individuals without NP, indicating a higher OSA risk in these patients, and consequently diagnosis and treatment are likely more frequent [9]. Although CRSwNP patients had lower AHI scores and high percentages of REM sleep compared to patients without NP, there were no differences in ODI, minimal SaO₂, or AI, which have been shown to be correlated to sleep fragmentation and intermittent hypoxia [3,31–35]. This result suggests that both groups experience these disturbances in sleep patterns to a similar degree.

Patients with CRSwNP had nasal obstruction and presented with a history of asthma due to NP pathophysiology [34]. This is in line with a population-based study in Sweden, where the prevalence of NP was more frequent in males, elderly individuals, and asthmatics, compared to the general population [14,36]. High

Table 2
Complaints and physical examination date.

Profile	Patients with OSA and nasal polyps (N = 31) N (%)	Patients with OSA and without nasal polyps (N = 62) N (%)	P value	OR (95% CI)
Snore				
Yes	14 (45.2)	58 (93.5)	<0.001 ^a	0.57 ^a
No	17 (54.8)	4 (6.5)		(0.02–0.20)
Unrefreshing sleep				
Yes	7 (22.6)	38 (61.3)	<0.001 ^a	0.18 ^a
No	24 (77.4)	24 (38.7)		(0.07–0.49)
BMI (kg/m²)				
≥30	6 (19.4)	35 (56.5)	0.001 ^a	0.19 ^a
<30	25 (80.6)	27 (43.5)		(0.07–0.52)
Nasal obstruction				
Yes	27 (87.1)	32 (51.6)	0.001 ^a	6.33 ^a
No	4 (12.9)	30 (48.4)		(1.98–20.23)
Mallampati				
III, IV	4 (12.9)	26 (48.1)	0.001 ^a	0.16 ^a
I, II	27 (87.1)	28 (51.9)		(0.05–0.52)
Fatigue				
Yes	7 (22.6)	32 (51.6)	0.007 ^a	0.27 ^a
No	24 (77.4)	30 (48.4)		(0.10–0.73)
Tonsils				
3, 4	0	9 (16.4)	0.017 ^a	Not available
0, 1, 2	31 (100)	46 (83.6)		
Somnolence (ESS)				
Yes	11 (35.5)	37 (59.7)	0.028 ^a	0.37 ^a
No	20 (64.5)	25 (40.3)		(0.15–0.91)
Controlled asthma				
Yes	5 (16.1)	2 (3.4)	0.045 ^a	5.48
No	26 (83.9)	57 (96.6)		(0.99–30.13)
Enlarged tongue				
Yes	5 (16.1)	21 (34.4)	0.065	0.37
No	26 (83.9)	40 (65.6)		(0.12–1.09)
Systemic hypertension				
Yes	11 (35.5)	34 (55.7)	0.066	0.44
No	20 (64.5)	27 (44.3)		(0.18–1.07)
Diabetes mellitus II				
Yes	2 (6.5)	9 (15.0)	0.236	0.29
No	29 (93.5)	51 (85.0)		(0.08–1.93)
Retrognathism				
Yes	5 (16.1)	12 (20.3)	0.628	0.75
No	26 (83.9)	47 (79.7)		(0.24–2.37)

OSA: obstructive sleep apnea; BMI: body mass index.

ESS: Epworth Somnolence Scale.

^a Statistically significant.

Table 3
Physical exam parameters adjusted by BMI.

Physical exam	OSA patients with nasal polyps N (%)	OSA patients without nasal polyps N (%)	OR (IC)	P value	OR adjusted by continued BMI (IC)	P value
BMI						
≥30	6 (19.4)	35 (56.5)	5.40 (0.07–0.52)	0.001^a	^b	^b
<30	25 (80.6)	27 (43.5)	1			
Mallampati						
III, IV	4 (12.9)	26 (48.1)	0.16 (0.05–0.52)	0.002^a	0.22 (0.06–0.75)	0.015 ^a
I, II	27 (87.1)	28 (51.9)	1			
Abdominal circumference						
>102 cm	10 (32.3)	31 (55.4)	0.38 (0.15–0.96)	0.041^a	1.65 (0.43–6.34)	0.466
≤102 cm	21 (67.7)	25 (44.6)	1			
Tonsils						
3, 4	0	9 (16.4)	Not available	0.023^a	Not available	
0, 1, 2	31 (100)	46 (83.6)				
Neck circumference						
≥43 cm	9 (29.0)	26 (47.3)	0.46 (0.18–1.17)	0.101	1.35 (0.41–4.49)	0.623
<43 cm	22 (71.0)	29 (52.7)	1			
Retrognathism						
Yes	5 (16.1)	12 (20.3)	0.75 (0.24–2.37)	0.628	0.75 (0.21–2.69)	0.655
No	26 (83.9)	47 (79.7)	1			

OSA: obstructive sleep apnea; BMI: body mass index.

^a Statistically significant.

^b Not Applicable.

Table 4
Polysomnography indices analyses.

Polysomnography indices	Patients with OSA and nasal polyps (N = 31) Median (minimum–maximum))	Patients with OSA and without nasal polyps (N = 62) Median (minimum–maximum)	P value
REM percentual (%)	16.37 (0.53–35.01)	12.0 (0–30.16)	0.002^a
T < 90% (%)	1.17 (0–46.28)	3.57 (0–58.19)	0.038^a
AHI (events/h)	16.38 (5.26–69.79)	24.44 (5–86.39)	0.046^a
Minimal SaO ₂ (%)	77.0 (50.0–92.0)	78.0 (50.0–92.0)	0.650
N3 percentual (%)	15.94 (0–47.15)	17.63 (0–53.40)	0.741
ODI (events/h)	12.34 (0.23–85.74)	10.39 (0–80.57)	0.800
Arousal index (events/h)	20.11 (3.27–43.20)	17.79 (8.19–116.39)	0.896

OSA: obstructive sleep apnea; REM: rapid eye movements.

ODI: oxygen desaturation index.

AHI: apnea-hypopnea index; minimal SaO₂: minimal oxygen saturation.

T < 90%: the percent of the total time with oxygen saturation level lower than 90%.

^a Statistically significant.

Table 5
Epworth somnolence scale and polysomnographic parameters adjusted by body mass index.

Sleep study parameters	Patients with OSA and nasal polyps N (%)	Patients with OSA and without nasal polyps N (%)	OR (IC)	P value	OR adjusted by continued BMI (IC)	P value
AHI						
>30/h	4 (12.9)	25 (40.3)	0.22 (0.07–0.70)	0.011^a	0.32 (0.09–1.07)	0.065
≤30/h	27 (87.1)	37 (59.7)	1			
Somnolence (ESS)						
Yes	11 (35.5)	37 (59.7)	0.37 (0.15–0.91)	0.030^a	0.52 (0.20–1.35)	0.176
No	20 (64.5)	25 (40.3)	1			
REM						
<20%	22 (71.0)	52 (83.9)	0.47 (0.17–1.32)	0.151	0.50 (0.16–1.55)	0.232
≥20%	9 (29.0)	10 (16.1)	1			
Minimal SaO₂						
≤70%	14 (45.2)	23 (37.1)	1.40 (0.58–3.35)	0.455	1.56 (0.60–4.03)	0.359
>70%	17 (54.8)	39 (62.9)	1			
Arousal index						
≥10/h	29 (93.5)	53 (86.9)	2.19 (0.44–11.0)	0.342	2.20 (0.40–12.00)	0.364
<10/h	2 (6.5)	8 (13.1)	1			
N3						
≤15%	24 (38.7)	14 (45.2)	1.30 (0.55–3.12)	0.551	1.48 (0.58–3.81)	0.416
>15%	38 (61.3)	17 (54.8)	1			

OSA: obstructive sleep apnea; BMI: body mass index; AHI: apnea-hypopnea index; ESS: epworth somnolence scale; minimal SaO₂: minimal oxygen saturation; REM: rapid eye movements.

^a Statistically significant.

Mallampati grades (III and IV) have previously been shown to occur frequently in OSA patients both with and without NP [20], and are thought to lead to OSA by higher passive critical closing pressure of the upper airway [35]. Our results indicate that Mallampati grades are significantly lower in patients with NP; further research is required to explain the discrepancy between our findings and previously reported results.

OSA phenotypes have been recently defined to optimize the effectiveness of diagnosis and treatment. Eckert et al., described four phenotypes of apneic classification according to the passive critical closing pressure of the upper airway and other respiratory responsiveness aspects of OSA [37]. Although CRSwNP is not officially defined as an OSA risk factor, it has already been observed in clinical practice [1,2,10]. In our cross-sectional study, we have demonstrated that apneic patients with CRSwNP differ from the typical clinical profile for OSA [5–7,20] by exhibiting low BMI and Mallampati indices, and have fewer reports of unrefreshing sleep and complaints of snoring, that possibly represents a limitation. However, despite exhibiting lower risk factors, these patients had the same levels of AI and ODI as individuals without NP, indicating they also experienced sleep fragmentation. Despite the limitation that the patients in our study were sampled from a clinical database of a regional sleep center, the comparison between apneic groups with and without CRSwNP has been classically described in previous studies [1,2].

5. Conclusions

The present study highlights that OSA in individuals with CRSwNP is frequent. As CRSwNP patients experience intermittent hypoxia and sleep fragmentation without classic apneic predictors, we propose that a new OSA phenotype should be described in order to improve clinical screening and avoid detrimental consequences.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments

The authors thank the patients and LabSono team for working together in this project.

Conflict of interest

There is no conflict of interest to declare.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: <https://doi.org/10.1016/j.sleep.2019.06.006>.

References

- [1] Hui J, Ong J, Herdegen J, et al. Risk of obstructive sleep apnea in African American patients with chronic rhinosinusitis. *Ann Allergy Asthma Immunol* 2017;118:685–8.
- [2] Bengtsson C, Lindberg E, Jonsson L, et al. Chronic rhinosinusitis impairs sleep quality: results of the GA2LEN study. *Sleep* 2017;40:1–6. <https://doi.org/10.1093/sleep/zsw021>.
- [3] AASM – American Academy of Sleep Medicine International Classification of Sleep Disorders. International classification of sleep disorders. 3rd ed. Darien: American Academy of Sleep Medicine; 2014.
- [4] Young T, Palta M, Dempsey J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230–5.
- [5] Durán J, Esnaola S, Rubio R, et al. Obstructive sleep apnea-hypopnea and related clinical features in a population based sample of subjects aged 30 to 70 yr. *Am J Respir Crit Care Med* 2001;163(3):685–9.
- [6] Romero-Corral A, Caples SM, Lopez-Jimenez F, et al. Interactions between obesity and obstructive sleep apnea: Implications for treatment. *Chest* 2010;137:711–71.
- [7] Viner S, Szalai JP, Hoffstein V. Are history and physical examination a good screening test for sleep apnea? *Ann Intern Med* 1991;115:356–9.
- [8] Bixler EO, Vgontzas AN, Lin HM, et al. Prevalence of sleep disordered breathing in women: effects of gender. *Am J Respir Crit Care Med* 2001;163:608–13.
- [9] Nagappa M, Liao P, Wong J, et al. 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* 2015;10(12):e0143697.
- [10] Alt Ja, Smith TI. Chronic rhinosinusitis and sleep: a contemporary review. *Int Forum Allergy Rhinol* 2013;3:941–9.
- [11] Uzdán U, Gunhan K, Yilmaz U, et al. The evaluation of pattern and quality of sleep in patients with chronic rhinosinusitis with nasal polyps. *Auris Nasus Larynx* 2017;44:708–12.
- [12] Värendh M, Johannisson A, Hrubos-Strom H, et al. Sleep quality improves with endoscopic sinus surgery in patients with chronic rhinosinusitis and nasal polyposis. *Rhinology* 2017;55:45–52. <https://www.ncbi.nlm.nih.gov/pubmed/28019643>.
- [13] AASM - American Academy of Sleep Medicine. The AASM manual for the scoring of sleep and associated events. Rules, terminology and technical specifications. *Am Acad Sleep Med* 2012. <http://www.aasmnet.org/scoringmanual/v2.0.2/html/Cover.html>.
- [14] Fokkens WJ, Lund VJ, Mullol J, et al. European position paper on rhinosinusitis and nasal polyps 2012. *Rhinol Suppl* 2012;23:1–298.
- [15] Chung F, Subramanyam R, Liao P, et al. High STOP-bang score indicates a high probability of obstructive sleep apnoea. *Br J Anaesth* 2012;108:768–75.
- [16] Reis R, Teixeira F, Martins V, et al. Validation of a Portuguese version of the STOP-bang questionnaire as a screening tool for obstructive sleep apnea: analysis in a sleep clinic. *Rev Port Pneumol* 2015;21:61–8.
- [17] Boynton G, Vahabzadeh A, Hammoud S, et al. Validation of the STOP-BANG questionnaire among patients referred for suspected obstructive sleep apnea. *J Sleep Disord Treat Care* 2013;2:4.
- [18] Johns M. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991;14:540–5.
- [19] Bertolazi NA, Fagundes SC, Hoff LS, et al. Escala de Sonolência de Epworth: Versão em português. *J Bras Pneumol* 2009;35:877–83.
- [20] Zonato AI, Martinho FL, Bittencourt LR, et al. Head and neck physical examination: comparison between nonapneic and obstructive sleep apnea patients. *The Laryngoscope* 2005;115:1030–4.
- [21] Ng SK, Lee DLY, Li AM, et al. Reproducibility of clinical grading of tonsillar size. *Arch Otolaryngol Head Neck Surg* 2010;136:159–62.
- [22] Friedman M, Ibrahim H, Bass L. Clinical staging for sleep-disordered breathing. *Otolaryngol Head Neck Surg* 2002;127:13–21.
- [23] Godoy LBM, Palombini LO, Guilleminault C, et al. Treatment of upper airway resistance syndrome in adults: where do we stand? *Sleep Science* 2015;8:42–8.
- [24] Guilleminault C, Stoohs R, Clerk A, et al. A cause of excessive daytime sleepiness. The upper airway resistance syndrome. *Chest* 1993;104:781–7.
- [25] Ayappa I, Norman RG, Krieger AC, et al. Non invasive detection of respiratory effort-related arousals (RERA) by a nasal cannula/pressure transducer system. *Sleep* 2000;23:763–71.
- [26] Palombini L, Lopes MC, Tufick S, et al. Upper airway resistance syndrome: still not recognized and not treated. *Sleep Sci* 2011;4:7–8.
- [27] Collop N. Breathing related arousals: call them what you want, but please count them. *J Clin Sleep Med* 2014;10:125–6.
- [28] Lal D, Rounds AB, Divekar R. Gender-specific differences in chronic rhinosinusitis patients electing endoscopic sinus surgery. *Int Forum Allergy Rhinol* 2016;6:278–86.
- [29] Saxby AJ, Pace-Asciak P, Dar Santos RC, et al. The rhinological manifestations of women's health. *Otolaryngol Head Neck Surg* 2013;148:717–31.
- [30] Chen HJ, Xue H, Liu S, et al. Obesity trend in the United States and economic intervention options to change it: a simulation study linking ecological epidemiology and system dynamics modeling. *Public Health* 2018;161:20–8.
- [31] Berson SR, Klimczak J, Prezio EA, et al. Clinical associations between allergies and rapid eyes movement sleep disturbances. *Int Forum Allergy Rhinol* 2018;8:817–24.
- [32] Pedrosa RP, Maki-Nunes C, Midlej-Brito T, et al. Predictors of obstructive sleep apnea in consecutive patients with metabolic syndrome. *Metab Syndr Relat Disord* 2018;16:2–5.
- [33] Dokkedal-Silva V, Galduróz JCF, Tufick S, et al. Association of obesity, sleep apnea and hypothalamic inflammation: novel possibilities of research. *Eur J Intern Med* 2018;52:e17–8.
- [34] Dennis SK, Lam K, Luong A. A review of classification schemes for chronic rhinosinusitis with nasal polyposis endotypes. *Laryngoscope Investig Otolaryngol* 2016;1:130–4.
- [35] White DP. Advanced concepts in the pathophysiology of obstructive sleep apnea. Sleep-related breathing disorders. *Adv Otorhinolaryngol Basel* 2017;80:7–16.
- [36] Johansson L, Akerlund A, Holmberg K, et al. Prevalence of nasal polyps in adults: the Skovde population based study. *Ann Otol Rhinol Laryngol* 2003;112:625–9.
- [37] Eckert DJ, White DP, Jordan AS, et al. Defining phenotypic causes of obstructive sleep apnea: identification of novel therapeutic targets. *Am J Respir Crit Care Med* 2013;188:996–1004.