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Clinical Characteristics are Not Significant Predictors of Advanced Obstructive Sleep Apnea in the Severely Obese

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Abstract

Introduction: Obstructive Sleep Apnea (OSA), present in 30-93% of bariatric patients, is an independent predictor of post-bariatric surgery complications. Universal screening with Polysomnography (PSG), the gold standard test for OSA, would be difficult to access and costly to perform. The purpose of this study was to identify clinically important, statistically significant predictors of moderate-to-severe OSA in a bariatric population that would enable providers to stratify or prioritize patients needing PSG.

Methods: A cross-sectional study was performed in patients referred for clinical suspicion of OSA. All patients underwent PSG. From a list of potential covariates deemed clinically important, multivariable binary logistic regression was used to identify statistically significant predictors ($p<0.05$) of moderate-to-severe OSA. Subjects were recruited from a bariatric specialty program in Edmonton, Alberta, with a central, region-wide, single-point-of-access referral system.

Results: Of 169 patients undergoing PSG, 161 (95.3%) had complete data. Mean age was 48.7 ± 9.1 years, 45(28%) were men, mean body mass index (BMI) was 49.5 ± 9.7 kg/m^2. 96(60%) patients had moderate-to-severe OSA and the mean Apnea-Hypopnea Index (AHI) was 27.0 ± 27.3.

The strongest predictors of OSA were neck circumference (OR 1.08; 95% CI 0.99-1.18) and hypertension (OR 1.95, 95% CI 0.93-4.09). However, no variable reached statistical significance.

Conclusion: Despite a model adequately powered to identify 16-32 statistically significant predictors, none was found. Given the high prevalence of OSA in patients undergoing bariatric care, the lack of identifiable predictors mandates that objective sleep testing be performed in all patients clinically suspected to have OSA.

Keywords: Obstructive sleep apnea; Clinical predictors; Morbid obesity; Bariatric care; Health status; Lung

Introduction

Obstructive sleep apnea (OSA) is a disorder resulting from pharyngeal collapse and causing repetitive episodes of absent (apneas) or diminished (hypopneas) airflow during sleep despite respiratory muscle effort [1]. OSA causes excessive daytime sleepiness, impaired quality of life, and has been linked to systemic hypertension, diabetes, and an increased incidence of cardiovascular events [1]. The Wisconsin Sleep Cohort Study reported a population-based OSA prevalence of 4% in middle-aged men and 2% in women in 1993 [2]. More recently, the prevalence of moderate-to-severe sleep apnea (AHI ≥15/h) has been estimated at 13% in men and 6% in women between the ages of 30-70 years [3].

Obesity is a major risk factor for the development of OSA and rising obesity prevalence rates very likely have contributed to the rise in OSA prevalence [4,5]. In severely obese individuals (body mass index or BMI ≥40 kg/m^2), OSA affects an estimated 60-98% [6-10] of patients undergoing bariatric surgery. Despite this high prevalence, many patients referred to bariatric clinics for management have undiagnosed OSA [7,8]. In addition, OSA in obese women, who are much more likely to undergo bariatric surgery than men, is more variable in its occurrence [1]. OSA is important to diagnose in the bariatric population as it has been associated with an increase in the composite endpoint of 30-days major adverse outcomes in a large, longitudinal assessment of perioperative safety [11]. A recent study by Proczko et al. found that patients undergoing bariatric surgery who had diagnosed OSA treated with CPAP had fewer complications and a shorter length of stay compared to patients with a high pre-test probability of OSA who were not on CPAP [12]. Detection of sleep apnea is thus important in these patients because OSA is a risk factor for complications post-bariatric surgery [13] and because effective treatment for OSA is available. Continuous positive airway pressure (CPAP) therapy is effective in reducing symptoms of sleepiness, improving quality of life, and reducing blood pressure [14,15]. In addition, there is increasing evidence that treatment of OSA with CPAP improves cardiovascular outcomes [16,17] and may improve perioperative risk.

Polysomnography (PSG) is the gold standard method for diagnosing OSA. Level 1 PSG is performed in a sleep laboratory with a technician in attendance; it measures respiratory, cardiovascular, and neurologic parameters. However, increasing demand and limited capacity to perform level 1 PSG have resulted in protracted wait times in publicly funded health care systems [18]. Level 3 PSG is performed using portable monitors and may be done in the patient's home. Unlike level 1 PSG, it is not able to detect non-respiratory sleep disorders nor does it typically measure stages of sleep, duration of sleep, or arousals. Despite these limitations, current guidelines recommend that level 3 PSG can be used to diagnose OSA in patients with a high pretest probability of moderate to severe OSA and who do not have significant comorbid cardiopulmonary or neurologic conditions [19]. However, a major barrier to accessing level 3 PSG in our provincially-funded health care system (Alberta, Canada) is the need for the patient to bear the cost of these studies.

One potentially useful way to overcome these limitations is to use clinical predictors to identify patients with increased likelihood of OSA and perform testing in only these patients or prioritize these patients for faster objective testing. This approach could potentially streamline use of PSG, decrease wait-times and reduce costs. Screening questionnaires, such as the Epworth Sleepiness Scale or the Berlin questionnaire are not sufficiently accurate to be used as stand-alone tools [20]. Previous studies aimed at deriving clinical prediction rules to inform the need for PSG have shown inconsistent results [21-23]. Therefore, no universally accepted and validated tool is currently being used in clinical practice.

The objective of this cross-sectional study was to identify clinical predictors of moderate-to-severe OSA in patients referred to a large Canadian bariatric care program. This program has a regional referral structure and is publicly funded; thus, the patient population is less highly selected than in previous studies [22,23]. We aimed to identify significant predictors of moderate-to-severe OSA and, to compare these with previous studies, and to generate a clinical prediction rule for this condition in a severely obese population. We postulated that this tool may be relevant to streamline referrals for PSG by identifying those that are most likely to have OSA (rather than sending all patients for PSG as is currently being suggested).

Methods

Approval to conduct this cross-sectional study was obtained from the University of Alberta Research Ethics Board (PRO0030092).

Participants and setting

Subjects were recruited from the Edmonton Weight Wise adult bariatric specialty clinic. This bariatric care clinic, established in 2005, serves as a catchment population of approximately 1.6 million residents and includes a central, region-wide, single-point-of-access referral system. Both medical and surgical treatments are provided to patients ≥18 years of age with BMI ≥35 kg/m^2 who have been unsuccessful with prior attempts at managing chronic obesity [24]. Approximately 800 new patients are seen annually, with over 200 surgeries performed each year [24].

Upon entry into Weight Wise, patients were assessed by a nurse case manager and, based upon clinical suspicion (i.e., daytime sleepiness, daytime fatigue, or excessive snoring) and screening with the adjusted neck circumference rule, were booked to see the sleep specialist. We performed a chart review of electronic medical records in 183 consecutive patients referred for specialist assessment and a PSG between August 2008 and February 2012. Fourteen patients were excluded because they declined to undergo PSG or had previously been diagnosed and treated for OSA. Of the remaining 169, 8 patients were subsequently excluded because of missing data, leaving 161 for the final analysis.

Data elements

Data collection included age, sex, weight, BMI, neck circumference, epworth sleepiness scale score, smoking history, and self-reported medical co-morbidities (hypertension, dyslipidemia, diabetes, hypothyroidism, GERD, arthritis, depression, rhino-sinusitis, history of lung disease).

Patients were formally tested with sleep testing with either a level 1 or a level 3 PSG. If both level 1 and level 3 PSG studies were available, data from the level 1 PSG were used for analysis. Moderate-to-severe OSA was defined as an apnea-hypopnea index (AHI) ≥15/h, from a level 1 PSG, or a respiratory disturbance index (RDI) ≥15/h from a level 3 PSG [20]. Data elements were collected via electronic medical record abstraction. For level 3 PSG, RDI was calculated using the method published by Vazquez et al. [1,21,22].

Statistical analyses

Descriptive analyses, consisting of means, medians, and proportions were first conducted and the prevalence of severe sleep apnea calculated. Multivariable binary logistic regression was then performed to identify independent predictors of moderate-to-severe sleep apnea (AHI ≥15/h). Medical comorbidities (hypertension, diabetes, dyslipidemia, depression, hypothyroidism, GERD, sinus disease, smoking, history of alcoholism, and history of lung disease) were selected based upon perceived clinical relevance to OSA and/or prior studies [1,21,22] and were classified as binary variables (present/absent). BMI, age, neck circumference, and ESS (as a composite proxy for daytime sleepiness symptoms) were analyzed as continuous variables. Age, sex, BMI (per unit increase), neck circumference, hypertension, diabetes, and ESS score were forced into all models a priori. Additional potential covariates from the variables listed above with p-values <0.2 on bivariate analyses were entered into the initial model. The final model was then created using a stepwise backwards selection method using a Wald Chi-square p-value of 0.05 as the threshold for inclusion. Data were complete for all variables. SAS (Version 9.3, Cary, NC) was used for all analyses.

Results

Baseline characteristics

Of 161 patients, 36 underwent level 1 PSG and the remainder underwent level 3 sleep testing. The treating physician ordered level 1 PSG if it was deemed necessary for patient care; otherwise, patients were diagnosed and treated based on level 3 study results. Table 1 shows baseline patient characteristics. The mean BMI was 49.5 ± 9.8 kg/m^2, mean age was 48.7 ± 9.1 (years), and 72% of patients were women.

Variable	All patients	Normal/mild OSA	Mod-severe OSA
	Mean (standard deviation) or No. (%)		
Number of patients	161	65	96
Age, years	48.7 (9.1)	48.7 (9.0)	48.6 (9.3)
Men, no (%)	45 (28.0)	16 (24.6)	29 (30.2)
Body mass index (BMI), kg/m^2	49.5 (9.8)	48.0 (9.3)	50.4 (10.0)
Epworth Sleepiness Scale Score	10.5 (5.5)	10.6 (5.7)	10.4 (5.5)
Neck Circumference, cm	44.2 (5.4)	43.0 (4.6)	45.0 (5.8)
Hypertension, no. (%)	90 (55.9)	32 (49.2)	58 (60.4)
Diabetes, no. (%)	51 (31.7)	21 (32.3)	30 (31.3)
Depression	47 (29.2)	17 (26.2)	30 (31.3)
Apnea-hypopnea index, number of events	27.9 (27.4)	9.5 (4.0)	40.2 (29.5)

Table 1: Baseline characteristics.

The mean AHI was 27.9 ± 27.4/h and 96 patients (60%) had moderate-to-severe OSA. The overall prevalence of OSA (AHI ≥5/h) was 94%; 56(34%) patients had mild OSA, 47(30%) had moderate OSA, and 49(30%) had severe OSA.

Symptoms of daytime somnolence were similar amongst all groups, with a mean ESS of 10.6 ± 5.7 in patients with mild or no OSA and 10.4 ± 5.5 in patients with moderate-to-severe sleep apnea.

Predictors of moderate-to-severe OSA

In the multivariable analysis, no statistically significant predictors of moderate-to-severe OSA were identified (Table 2). No additional variables were found to have a p-value less than 0.2 on univariate analysis. The strongest predictors were neck circumference (OR 1.08; 95% CI 0.99-1.18) and hypertension (OR 1.95, 95% CI 0.92-4.10), though neither met statistical significance. BMI, when analyzed as a continuous variable, was not associated with increasing risk of moderate-to-severe OSA (OR 0.99, 95% CI 0.95-1.03) in this cohort. The c statistic for the model including predictors forced in a priori or that had univariate p-values <0.2 was 0.64.

Variable	β-Coefficient	Odds ratio	95% Confidence interval
Age (per unit increase)	-0.01	0.99	0.95-1.03
Sex	-0.42	0.66	0.25-1.73
BMI (per unit increase)	0.02	1.02	0.98-1.06
Neck Circumference (per unit increase)	0.08	1.08	0.99-1.18
Hypertension	0.67	1.95	0.93-4.09
ESS (per unit increase)	-0.01	1.00	0.94-1.06
Diabetes	-0.51	0.60	0.28-1.30

Table 2: Logistic regression model predicting moderate-to-severe sleep apnea[1]. [1]Model c-statistic=0.64.

Discussion

In this study of 161 severely obese patients enrolled in a population-based regional obesity program and referred for PSG, we found that 60% had moderate-to-severe OSA. Amongst an initial list of 15 variables deemed clinically important, we were unable to find any statistically significant predictors of moderate-to-severe OSA. This null result was found despite a model adequately powered to identify 16-32 statistically significant predictors.

Our findings were unexpected given that age, male sex, increased BMI, and neck circumference are all established risk factors for OSA [1] including in studies examining patients undergoing bariatric surgery [21-23]. In 99 patients, Dixon et al. reported that age (≥38 years), BMI ≥45 kg/m^2, male sex, history of observed apneas, fasting plasma insulin ≥28 μmol/L, and hemoglobin A1C ≥6% were significant predictors of OSA [21]. A score of ≥3 of these variables predicted an apnea-hypopnea index (AHI) ≥15/h with a sensitivity and specificity of

89 and 91%. However, when this model was evaluated in a different sample of patients by Kolotkin et al., the sensitivity and specificity was found to be only 75% and 57%, respectively [22]. Instead, Kolotkin proposed a different 10-variable model consisting of neck circumference, systolic blood pressure, waist-hip ratio, waist, glucose, age, loud snoring, frequent snoring, BMI, and male sex. They reported a sensitivity and specificity of 77% for an AHI ≥15/h. These findings, together with the results of the present study, indicate that identifying a core set of variables that can consistently identify or exclude OSA in a high risk population may not be possible.

We found a very high prevalence of OSA in patients referred for bariatric care, a finding comparable to other published reports examining patients referred for bariatric surgery [6-10]. Given this high prevalence and the lack of a highly sensitive screening method, some authors have advocated for routine screening with Polysomnography (PSG) in all severely obese patients prior to undergoing bariatric surgery [23]. We concur with this recommendation, with the caveat that the present study can only be applied to patients initially suspected of having OSA (based upon a positive adjusted neck circumference, daytime sleepiness, or snoring). Stated another way, the pretest probability of OSA in bariatric populations may simply be too high and clinical predictors too non-specific to obviate the need for PSG testing in some of these patients.

Access-related barriers will limit the ability to perform PSG in all bariatric patients seen within our Weight Wise program. Approximately 1900 level 1 studies are performed annually for the entire Edmonton region (from all referral sources including Weight Wise), with wait times varying from an average of 14 months for routine referrals to under 4 weeks for urgent referrals. Given that 800 new patients are seen annually in the Weight Wise program, with most likely having some clinical suspicion of OSA, this program alone would likely account for over 40% of all available slots for the year. Thus, the majority of PSG studies will need to be of the level 3 variety; however cost is a barrier for the approximately 20% of Weight Wise patients who are of low income status [25]. Similar trends in other regions are occurring as revenue from level 1 polysomnography is being cut.

A major strength of this study is that the patients are derived from a population-based bariatric program, which limits referral bias. In addition, as discussed above, inadequate power is not a likely explanation for our findings. One limitation is that the data were not collected prospectively, but, rather in retrospective fashion via electronic chart review. A second limitation is that only patients suspected of having OSA based upon clinical symptoms or the Epworth score were included. Although this approach is justifiable based on clinical grounds, we cannot comment on the prevalence of completely asymptomatic OSA or generalize our results to this patient population. A third limitation is that level 1 sleep studies were not performed in all patients. Although level 1 PSG was traditionally considered the gold standard, level 3 studies are considered an acceptable alternative in a population where pretest probability is high [19].

Conclusion

Despite a model adequately powered to identify 16-32 statistically significant predictors of moderate-to-severe OSA, none was found. Given the high prevalence of OSA in severely obese patients undergoing bariatric care, this lack of an identifiable clinical prediction rule suggests that sleep testing be performed in all such patients clinically suspected to have OSA.

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RP had full access to the data and takes responsibility for the integrity of the data and accuracy of the data analysis. RP and LB developed the initial study concept, which was then refined by the remaining authors. CA and RP were responsible for statistical analysis. LB and RP wrote the initial draft of the manuscript. All remaining authors contributed to the final draft and approved the final submitted version of the manuscript.

Ethical approval for the study was obtained from the Research Ethics Office at the University of Alberta prior to starting the studyhave been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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