Sleep, 16(2):118–122

Predictive Value of Clinical Features in Diagnosing Obstructive Sleep Apnea

*V. Hoffstein and †J. P. Szalai

*Department of Medicine, St. Michael's Hospital, and
†Department of Research Design and Biostatistics, Sunnybrook Health Science Center,
University of Toronto, Toronto, Canada

Summary: We examined the predictive value of history and physical examination in the diagnosis of obstructive sleep apnea (OSA) syndrome. This was achieved by studying a set of 594 patients referred to the sleep clinic because of suspicion of sleep apnea. All patients were asked a set of standard sleep-related questions and all had nocturnal polysomnography. We used stepwise multiple linear regression analysis to examine the relationship between the apnea/hypopnea index (AHI), defined as the number of episodes of cessation of breathing per hour of sleep (dependent variable), and age, sex, body mass index (BMI) and replies to the sleep questionnaire (independent variables). We found that age, sex, body mass index, bed partner observation of apnea and pharyngeal examination were significant predictors of AHI, explaining 36% of the variability. Subjective impression of the examining clinician was also an independent significant predictor of AHI, accounting for 10% of the variability. Using a conventional cutoff value of 10 to divide patients into apneics (AHI > 10) and nonapneics (AHI ≤ 10), the sensitivity of subjective impression was 60% and the specificity 63%. We conclude that although clinical features obtained during history and physical examination explain a relatively high percent of the variability in AHI, subjective clinical impression alone is not sufficient to reliably identify patients with or without sleep apnea. **Key Words:** Obstructive sleep apnea—Clinical features—Predictive model.

Obstructive sleep apnea is a relatively common disorder, with prevalence estimated to lie between 0.3 and 1%, depending on the population studied (1–3). The diagnosis of this syndrome is usually made on the basis of characteristic clinical features and the results of nocturnal polysomnography demonstrating more than 10 episodes of complete or partial cessation of breathing per hour of sleep. Because the polysomnography is expensive and time-consuming, it is therefore of interest to determine whether sleep apnea syndrome can be predicted on the basis of history and physical examination alone. If an accurate prediction is possible, it would help to optimize the utilization of the sleep laboratory and to reduce the number of unnecessary sleep studies.

An earlier similar study (4) employed logistic regression analysis to show that in patients with high predicted probability of sleep apnea syndrome, subjective impression alone or any combination of clinical features is not a reliable screening test for this disorder. However, the logistic regression model treats the apnea/hypopnea index (AHI) as a dichotomous variable, which divides all patients into apneics and nonapneics based on the AHI of 10. This cutoff value of AHI is relatively arbitrary; some authors use the value of 5, others feel that a higher value (>15–20) is more appropriate, particularly in older patients. The results of logistic regression analysis obtained for one particular definition of sleep apnea (e.g. AHI cutoff of 10) cannot be applied to a different definition of sleep apnea (e.g. AHI cutoff of 20).

The present study is different in two respects. First, we examined a much larger set of patients (594) than in any previous study. Second, we treated AHI as a continuous, rather than discrete, variable and used multiple linear regression to determine whether subjective impression alone or any combination of clinical features serve as significant predictors of obstructive sleep apnea.

METHODS

Clinical assessment

Our study population consisted of 594 patients, all of whom were referred to the sleep disorders clinic because of suspicion of sleep apnea. All patients were

Accepted for publication November 1992.
Address correspondence and reprint requests to Dr. V. Hoffstein, St. Michael's Hospital, 30 Bond Street, Toronto, Ontario M5B 1W8, Canada.

interviewed and examined by only one of us (V.H.), who asked a series of standard questions (Table 1) about the presence of symptoms commonly thought to be associated with sleep apnea. These questions referred to snoring, nocturnal choking, excessive daytime sleepiness, morning symptoms (headaches, nausea, vomiting, tiredness, fatigue), daytime tiredness and fatigue, restless sleep, allergies, impotence, presence of concomitant disease (mainly hypertension, diabetes, cardiac disease or thyroid disease) and episodes of cessation of breathing at night. Whenever possible, patients' bedmates were asked to confirm snoring and apneic events. However, because we were not able to interview consistently all bedmates, we used patients', rather than bedmates', responses to questions regarding snoring, restless sleep and episodes of cessation of breathing at night.

Because pharyngeal abnormalities are known to play an important role in the pathogenesis of sleep apnea, the pharynx was examined in all patients and classified as normal or abnormal. The latter included such abnormalities as bulky or long uvula that failed to elevate from the base of the tongue during phonation, large tonsils compromising pharyngeal orifice or general appearance of the pharynx as being narrow and small. Based on the results of history and physical examination, a subjective impression regarding the presence or absence of sleep apnea was formed and recorded.

TABLE 1. *Clinical predictors of sleep apnea*

Symptom	OSA	Non-OSA	Chi-square	p
Snoring			10.8	0.001
Present	257	271		
Absent	18	48		
Nocturnal choking			4.7	0.031
Present	202	258		
Absent	73	61		
Excessive daytime sleepiness			9.4	0.002
Present	158	143		
Absent	117	176		
Morning symptoms			5.4	0.364
None	115	123		
Tiredness/fatigue	105	145		
Headaches	33	34		
Nausea/vomiting	13	10		
Any combination of above	9	7		
Restless sleep			0.3	0.558
Present	109	134		
Absent	166	185		
Impotence			14.4	0.001
Present	37	12		
Absent	198	224		
Bedpartner's observations			36.5	0.001
Stops breathing	206	162		
Does not stop breathing	69	157		
Allergies			1.9	0.166
Present	59	84		
Absent	216	235		
Daytime tiredness/fatigue			0.4	0.532
Present	126	138		
Absent	149	181		

Nocturnal polysomnography

In all patients, nocturnal polysomnography was performed and scored according to the standard criteria (5). Obstructive apneas were identified as episodes of cessation of airflow lasting more than 10 seconds and associated with paradoxical movements of the chest wall and abdomen. Hypopneas were defined as episodes of incomplete cessation of airflow lasting more than 10 seconds. During these episodes, the airflow was reduced to >50% of its magnitude during normal unobstructed breathing. The number of apneas and hypopneas per hour of sleep was defined as the apnea/hypopnea index (AHI). Obstructive sleep apnea was diagnosed if AHI was >10.

Statistical analysis

Students *t* test for unpaired observations and chi-square tests were used to compare age, body mass index (BMI) and frequency of various symptoms between the apneic and nonapneic patients.

Multiple stepwise regression analysis was employed to develop a predictive model of AHI scores for subjective impression and 14 other covariate variables collected during clinical assessment of the patient in the examining room. These variables included snoring, nocturnal choking, excessive daytime sleepiness, morning symptoms, daytime fatigue, restless sleep, bed partner's observation of apneas, impotence, allergies, concomitant medical illness, pharyngeal examination, age, sex and BMI.

Because subjective impression was rendered by a single physician with full knowledge of the other covariates for a subject, subjective impression's predictive relationship to AHI scores was assessed independently through a bivariate linear regression. The best-fitting model for the larger set of covariates was extracted through stepwise multiple linear regression (6) with $p = 0.05$ set as the upper limit to allow a covariate into the model and allowing it to remain in the model. For the predictive models, the studentized residuals, DFFITS and covariance ratios were scrutinized to identify observations producing overly large residuals or exerting extreme influence on parameter estimates. Observations producing a studentized residual with an absolute value >2 were deleted from the final model. For DFFITS and covariance ratios, size adjusted cutoffs were used to delete an observation from the final

TABLE 2. *Anthropometric and sleep data*

	All patients	Non-OSA	OSA	p
N	594	319	275	
Male : Female	471:123	236:83	235:40	0.0001
Age	47 ± 12	44 ± 12	50 ± 11	0.0001
BMI	29 ± 6	28 ± 5	31 ± 6	0.0001
AHI	19 ± 23	4 ± 3	36 ± 25	—

BMI—body mass index; AHI—apnea/hypopnea index, p-value refers to the difference between OSA and Non-OSA groups.

TABLE 3. *Subjective impression vs. objective diagnosis*

	Objective diagnosis		
	Non-OSA	OSA	Total
Subjective impression			
Apnea absent	225	135	360
Apnea present	94	140	234
Total	319	275	594

model (6–8). For the larger model, collinearity diagnostics were based on the scrutiny of the eigenvalues, condition indices and the proportions of variance accounted for by the principal components (6–8).

For all statistical tests, the 0.05 upper limit for a probability value was used in rejecting a null hypothesis and asserting statistically discernible relationships or effects.

All statistical computations were performed using the SAS software, release 6.04 (The SAS Institute, Gary, NC).

RESULTS

Table 2 shows the anthropometric data and the apnea/hypopnea index for the entire set of 594 patients as well as for the subsets of patients with and without sleep apnea. Patients with sleep apnea (AHI > 10) were significantly, but trivially, older and more obese than the nonapneic ones. Although in general there were more males than females, there was a significant male predominance among patients with sleep apnea, than among nonapneic controls (86% vs. 74%, chi-square = 11.8, df = 1, p = 0.001).

Patients with sleep apnea complained more frequently of snoring, nocturnal choking, excessive daytime sleepiness and impotence than nonapneic patients. They were frequently observed by their bedmates to stop breathing during sleep. Several of these differences were statistically significant, as may be seen from Table 1, which summarizes clinical symptoms and compares their frequencies between apneic and nonapneic patients.

Physical examination of the pharynx showed that 54% of patients with sleep apnea had abnormal pharynx vs. 35% of patients without sleep apnea, and this difference was statistically significant (chi-square = 22.6, df = 1, p < 0.0005).

Subjective impression identified correctly 51% of patients with obstructive sleep apnea (OSA) and 71% of patients without OSA (Table 3), resulting in the sensitivity of 60% and specificity of 63%.

Prior to using linear regression analysis with AHI as the dependent variable and clinical symptoms listed in Table 1 as the independent variables, we performed the Shapiro-Wilk statistics for the distribution of AHI. The results indicated statistically discernible deviation from a normal (Gaussian) distribution. Square root transformation reduced the deviation from normality. Therefore, all subsequent modeling through linear regression was conducted on square root-transformed values of AHI.

After the observations producing overly large studentized residuals and extreme influence statistics were deleted, 549 individuals provided data for the final model on the relationship between subjective impression and AHI scores. Linear regression analysis revealed a statistically significant ($r^2 = 0.1021$, p = 0.0001) relationship between subjective impression and AHI scores. However, the proportion of explained variance in AHI scores that is attributable to subjective impression was small, only 10%.

Initial modeling of the larger covariate model suggested multicolinearity for BMI and age. Therefore, the model was refitted with the product of body mass index (BMI) and age (BMI*AGE) as a covariate for each subject (9). This variable became a new, independent variable, describing the effect of age and obesity. The alternative would have been to delete either AGE or BMI from the model. We rejected this alternative because age and obesity are known to affect the severity of apnea. After overly influential observations were deleted, 534 individuals provided data for fitting the final model.

Table 4 displays the results of the stepwise multiple linear regression. BMI*AGE, sex (being male), spouse-reported snoring and abnormal pharyngeal examination were selected into the final model, indicating a direct relationship of the covariates to the AHI scores.

TABLE 4. *The results of stepwise multiple linear regression with selection from 14 covariates. Dependent variable: square root of apnea/hypopnea index (SQAHI)*

Independent variables	Partial r^2	Model r^2	p
BMI*AGE	0.2094	0.2094	0.0001
SPOUSREP	0.0798	0.2892	0.0001
SEX	0.0537	0.3429	0.0001
PHAREXAM	0.0156	0.3585	0.0004

The proportion of variance in AHI scores explained by the model was substantial, equal to 36% (r^2 = 0.3585).

Based on the results of the above model, the formula to calculate the predicted AHI score for a new patient is:

$$\text{Predicted AHI} = [-1.251428 + 0.002082\ \text{BMI*AGE} + 1.191770\text{SEX} + 0.0991152\text{SPOUSREP} + 0.53127\text{PHAREXAM}]^2$$

where SEX = 0 for females and 1 for males, SPOUSREP = 0 if apneas are not observed by bed partner and 1 if apneas are observed, PHAREXAM = 0 if pharyngeal examination is normal and 1 if it is abnormal.

DISCUSSION

This study shows that clinical features such as history, physical examination and subjective impression of a clinician can predict sleep apnea only in about 50% of patients suspected of having this disorder. The best correlates of the apnea/hypopnea index are body mass index, age, sex, pharyngeal examination and bed partner's observations regarding episodes of cessation of breathing.

One of the main reasons for this study was to test a hypothesis that clinical features can serve as a screening test in deciding whether to refer a particular patient for nocturnal polysomnography. The possibility of developing a reliable screening test is an attractive one, because sleep apnea is common (1–3), can lead to adverse medical consequences if left untreated (10,11) and its diagnosis requires expensive, labor-intensive and highly specialized sleep studies available in only a few centers.

Only a few previous studies attempted to examine this question. Kapuniai et al. (12) administered a questionnaire to 53 patients referred to a sleep disorder center and analyzed the responses using discriminant analysis. These authors found that loud snoring and observed episodes of cessation of breathing identified sleep apnea (AHI $\geq$ 10) 54–64% of the time. Adults without these symptoms are expected to have no sleep apnea 80–88% of the time. Crocker et al. (13) used 100 patients with suspected sleep apnea to develop a predictive model based on clinical features. These authors found that body mass index, age, apneas observed by bed partner and hypertension were significant correlates of the apnea/hypopnea index. When tested on a different set of 105 patients, this model yielded 92% sensitivity and 51% specificity. Stradling and Crosby (14) found that AHI correlated best with neck obesity, BMI, age and alcohol consumption. However, Scharf et al. (15) administered sleep questionnaires to 40 unselected subjects and found that neither the symptoms nor the age or BMI correlated with AHI. Because the incidence of snoring in the general population is about 40% and the incidence of apneas observed by bed partner is only 8% (16), it is possible that a set of 40 patients is simply not large enough to show significant correlations. Haponik et al. (17) found that bedside observation of patients with OSA has a sensitivity of 64%. However, neither the age nor BMI was included in the statistical analysis. Our present results, based on the largest set of patients studied to date, confirm that age and obesity are the strongest correlates of sleep apnea, with bed partners' observations of cessation of breathing being the next most common significant determinant of apnea.

Ever since the pioneering description of the sleep apnea syndrome by Guilleminault and Dement (18), it was thought that this disorder is associated with distinct and characteristic clinical features, such as obesity, snoring, excessive daytime sleepiness, restless sleep, impotence and morning headaches, among others. These symptoms were found to be present in up to 100% of patients with sleep apnea (18–20). Our results indicate that although these features are indeed very frequent in patients with sleep apnea, they are also very common in nonapneic snorers and cannot be used as a screening test in deciding whether a patient should undergo a sleep study. One factor requiring further investigation is the presence of concomitant disease. We have not found it to be a significant predictor of sleep apnea. However, in view of the findings of Crocker et al. (13), it is possible that had we considered only hypertension, rather than presence of concomitant disease in general, the result would have been different.

It is of interest to contrast the present result with the results of a model based on logistic regression analysis to develop a predictive model of sleep apnea (4). In this model, which treated the dependent variable AHI as dichotomous ($\leq$10), only age, sex, BMI and snoring were selected and retained as significant covariates. The present model, where AHI was treated as a continuous variable, also selected age, sex and BMI as significant predictors of sleep apnea. However, rather than snoring (which is very common in patients with and without sleep apnea), this model selected spousal observation of apnea and pharyngeal examination as other significant covariates. The choice of these particular features makes good clinical sense. We have already pointed out the predictive value of spousal observations of apnea found in previous investigations. It is also generally agreed that patients with sleep apnea have abnormal pharyngeal structure and function (21,22). We conclude that the continuous model

developed here is a more sensitive one than the logistic regression model. It selected a larger number of clinically relevant variables and, in doing so, was able to explain a relatively high percent (36%) of the variability in AHI. We are currently evaluating the predictive poser of the model prospectively in a new set of patients.

We conclude that clinical features obtained during the history and physical examination of patients suspected of having obstructive sleep apnea are not sensitive enough to identify patients with sleep apnea. It is possible that the sensitivity of clinical examination in picking up patients with this disease may be increased by combining clinical features with simple home or laboratory screening measurements (14,23,24). We also conclude that multiple linear regression with analysis of covariance is capable of explaining a significant part of the variability in AHI and provides a more sensitive predictive model of sleep apnea than logistic regression.

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