Original Article

Clinical Risk Assessment Model for Predicting Moderate to Severe Obstructive Sleep Apnea in Adult Thai Patients

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Objective: To develop a clinical assessment model for predicting moderate to severe obstructive sleep apnea (OSA).

Materials and Methods: All patients suspected of having OSA and undergoing the laboratory polysomnography (PSG) were enrolled. The clinical data, associated factors and PSG finding were reviewed. Significant risk factors for the model were chosen using multivariate logistic regression analysis. The predictive parameters of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated.

Results: Of the 929 patients, 580 (62.4%) had moderate to severe OSA. Patient ages ranged between 18 and 85 years, with the majority between 30 and 60 years (71.5%). Males were significantly prominent in the moderate to severe OSA group (76.4%). Forty-three percent had a body mass index (BMI) greater than 30 and 52% had a neck circumference (NC) greater than 40. Multivariate analysis showed the male gender, a BMI of 30 or greater, a NC of 40 or greater, a waist to height ratio (WHtR) of 0.5 or greater, the presence of hypertension (HT), and observed apnea were significant factors correlated with moderate to severe OSA. The clinical assessment model was created by using their estimated coefficients. The optimal cutoff points for predicting apnea-hypopnea index (AHI) of 15 or greater was 2, with sensitivity of 85.5% and specificity of 49.6%.

Conclusion: The present clinical risk assessment model appears to be a useful practical tool for identifying patients at risk for moderate to severe OSA, with acceptable predictive performance.

Keywords: Obstructive sleep apnea, Clinical assessment model, Predicting, Sleep apnea

Received 4 Jun 2019 | Revised 20 Apr 2020 | Accepted 27 Apr 2020

J Med Assoc Thai 2020;103(7):639-45
Website: http://www.jmatonline.com

Obstructive sleep apnea (OSA) is becoming increasingly prevalent in the middle-aged Asian population. The recent published studies reported the prevalence of OSA to be as high as 8.1% to 27% in adult Asians[1-8]. However, up to 82% to 93% of moderate to severe OSA remain undiagnosed[9]. Due to the partial or complete narrowing of the upper airway during sleep, it leads to disturbances in sleep quality and hypoxemia. As a result, people develop daytime symptoms of sleepiness, personality changes, and neurocognitive impairment. In addition, it diminishes the quality of life, and increases the risk of cardiovascular problems. Several studies have shown that untreated OSA is significantly associated with all-causes and cardiovascular mortalities[10,11]. In addition, the incidence of cardiovascular disease is being higher in moderate to severe OSA[11]. Moreover, untreated OSA patients are at a 2- to 10-fold increased risk of motor vehicle accidents[12].

The gold standard for diagnosis of OSA is the overnight laboratory polysomnography (PSG)[13]. Regarding this type of sleep study, it is costly, time-consuming, and has a long waiting list because of hospital limitations. Nowadays, a screening tool is necessary and used with a comprehensive sleep evaluation to identify patients at risk who require further investigation. The use of a screening tool identifies the low risk patients who do not urgently need PSG.

Today, various screening tools are used worldwide

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How to cite this article:

Tawaranurak K, Leelasawatsuk P, Chaiyarukjirakun V. Clinical Risk Assessment Model for Predicting Moderate to Severe Obstructive Sleep Apnea in Adult Thai Patients. J Med Assoc Thai 2020;103:639-45.

doi.org/10.35755/jmedassocthai.2020.07.10236

to assess patients at risk, all with different accuracies and validation. These are beneficial for prioritizing patients to undergo a sleep study as well as for the initiation of treatment. The prediction models, such as the morphometric model, the regression equation, or the clinical risk matrix have been reported to have both high sensitivity and specificity[14-16]. However, most of these are complicated to measure in routine clinical practice, and some require mathematical calculations, or even artificial intelligence systems. Thus, the simplified clinical screening instruments are more commonly used. The Epworth sleepiness scale (ESS) is a useful questionnaire to assess daytime sleepiness, however, it has no value in distinguishing habitual snorer from OSA[17-19]. Although the Berlin questionnaire was previously used with self-assessment and had a high sensitivity (76%) for detecting OSA, it was found to be relatively less sensitive in detecting moderate to severe OSA[20,21]. In contrast, the STOP Bang questionnaire was shown to have consistently high sensitivity in different severity levels and had an ability to rule out patients without OSA for surgical patients[21-24]. However, the risk factors and their cut-off points may not be so applicable for the Asian population, which are less obese and have differences in craniofacial morphology[25]. The objective of the present study was to develop a clinical risk assessment model, a simple clinical tool, for predicting moderate to severe OSA within Asian populations. It might help the clinicians' decision for submitting patients suspected of OSA for PSG.

Materials and Methods

Study population

The present study included all patients who were at least 18 years old, and had undergone the laboratory PSG, between March 2006 and December 2017, at Songklanagarind Hospital's sleep center, Songkhla, Thailand. The history and physical examination from computer-based medical records were reviewed. All data were collected, including age, gender, symptoms-related with OSA, ESS scores, and the findings from the physical examinations and the PSG. Type I PSG studies were conducted and consisted of electroencephalography (EEG), electrooculography (EOG), chin and leg electromyography (EMG), electrocardiography (ECG), thermistors and nasal pressure transducer for oronasal airflow, thoracic and abdominal belts for respiratory efforts, pulse oximetry for oxyhemoglobin level, tracheal microphone for snoring, and sensors for sleeping position. Additionally, these parameters' recordings were scored manually by use of standard criteria[13]. Moderate OSA was defined as an apnea-hypopnea index (AHI) score of 15 to 30, and severe OSA was defined as an AHI score of greater than 30[13]. The present retrospective study was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University (EC 56-129-13-1-3).

Statistical analysis

The categorical data were reported using number and percentage. Comparison between groups were performed with chi-square or Fisher's exact test for nominal variables, and Wilcoxon Mann Whitney test for ordinal variables. Logistic regression was used to analyze the significant factors in relation to OSA, and odds ratios (ORs) with 95% confidence intervals (CIs) were determined. The correlation was tested by Spearman correlation coefficients. Then, the clinical risk assessment model, for predicting moderate to severe, was developed by using the estimated coefficients. The cut-off point, identifying an AHI of greater than or equal to 15, was chosen to achieve a high sensitivity while preserving a moderate specificity, using the 2×2 contingency tables. The following parameters were calculated, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), negative likelihood ratio (LR–), and accuracy with their 95% CIs. All statistical analyses were performed using Epidata software (version 3.1), R software (version 3.5.1), and Amilia II software for imputing the missing data. A p-value of less than 0.05 was considered to be statistically significant.

Results

Of the 929 patients, 580 (62.4%) had moderate to severe OSA. Patient ages were between 18 and 85 years, with the majority between 30 and 60 years (71.5%). Males were significantly prominent in the moderate to severe OSA group, as high as 76.4%. In the AHI of 15 or greater group, 220 subjects (37.9%) were overweight, and 253 subjects (43.6%) were obese. Approximate 52% of this group had a neck circumference (NC) greater than 40 cm, compared with 18% of subjects with AHI of less than 15. Up to 96.2% of moderate to severe OSA patients had a waist to height ratio (WHtR) of 0.5 or more[26,27]. Among this group, the presence of choking or gasping, observed apnea, and morning headaches were greater. Moreover, 412 patients (71%) had Friedman tongue position (FTP) class 3 to 4[28], and

Table 1. Patients' characteristics in AHI <15 and AHI ≥15 groups (n=929)

Factors	AHI <15 group (n=349) n (%)	AHI ≥15 group (n=580) n (%)	p-value
Age (year)			0.388
<30	31 (8.9)	38 (6.6)	
30 to 60	248 (71.7)	416 (71.7)	
>60	70 (20.1)	126 (21.7)	
Sex			<0.001
Male	179 (51.3)	443 (76.4)	
Female	170 (48.7)	137 (23.6)	
Body mass index (kg/m^2)			<0.001
<23	77 (22.1)	41 (7.1)	
23 to 24.9	66 (18.9)	66 (11.4)	
25 to 29.9	136 (39)	220 (37.9)	
≥30	70 (20.1)	253 (43.6)	
Neck circumference (cm)			<0.001
<40	287 (82.2)	281 (48.4)	
≥40	62 (17.8)	299 (51.6)	
Waist circumference (cm)			<0.001
<90 in male, 80 in female	155 (44.4)	97 (16.7)	
≥90 in male, 80 in female	194 (55.6)	483 (83.3)	
Waist to height ratio			<0.001
<0.5	54 (15.5)	22 (3.8)	
≥0.5	295 (65.6)	558 (96.2)	
Friedman tongue position classification			0.011
Class 1 to 2	130 (37.2)	168 (29)	
Class 3 to 4	219 (62.8)	412 (71)	
Epworth sleepiness score			0.001
<10	199 (57.0)	267 (46.0)	
≥10	150 (43.0)	313 (54.0)	
Hypertension			<0.001
Yes	72 (20.6)	268 (28.8)	
No	277 (79.4)	661 (71.2)	
Habitual snoring			0.255
Yes	342 (98.0)	574 (99.0)	
No	7 (2.0)	6 (1.0)	
Choking or gasping			<0.001
Yes	212 (60.7)	421 (72.6)	
No	137 (39.3)	159 (27.4)	
Observed apnea			<0.001
Yes	187 (53.6)	405 (69.8)	
No	162 (46.4)	175 (30.2)	
Morning headache			0.044
Yes	228 (65.3)	339 (58.4)	
No	121 (34.7)	241 (41.6)	
Unrefreshing sleep			0.166
Yes	249 (71.3)	439 (75.7)	
No	100 (28.7)	141 (24.3)	
Neurocognitive impairment			0.516
Yes	229 (65.6)	367 (63.3)	
No	120 (34.4)	213 (36.7)	
Sleepiness-related accident			0.325
Yes	128 (36.7)	193 (33.3)	
No	221 (63.3)	387 (66.7)	

AHI=apnea-hypopnea index

313 patients (54%) had an ESS scores of 10 or more. Of the 580 patients, hypertension (HT) was presented in 28.8%. The demographic data along with the risk factors and symptoms are summarized in Table 1.

The univariate analysis showed that age, habitual snoring, symptoms of unrefreshing sleep, neurocognitive impairment, and sleepiness-related accidents had p-values greater than 0.05 and were not considered in the multiple logistic regression analysis. The remaining factors of gender, body mass index (BMI), NC, waist circumference (WC), WHtR, FTP, ESS, HT, choking or gasping, observed apnea, and morning headache were included in the multiple logistic regression. The coefficients, ORs, and their corresponding 95% CI were calculated (Table 2).

Men had 2.7 times higher odds for developing moderate to severe OSA than women (95% CI 1.9 to 3.77). BMI had a dose-response relationship with OSA, as BMI increased, the odds of having AHI of 15 or more increased. Subjects with BMI of 23 to 24.99, 25 to 29.99, and 30 or more had odds ratio of 1.9 (95% CI 1.13 to 3.13), 3.0 (95% CI 1.97 to 4.69), and 6.8 (95% CI 4.28 to 10.78), respectively, compared to subjects with BMI less than 23 kg/m^2. Patients having NC of 40 or more, or WHtR of 0.5 or more also had an odds ratio of 2.3 (95% CI 1.58 to 3.39) and 2.4

Table 2. Factors associated with moderate to severe OSA (AHI ≥15); multiple logistic regression analysis

Factors	Stepwise multivariate analysis			
	Coefficient	SE	p-value	Adjusted OR (95% CI)
Sex				
Male	0.99	0.17	<0.001	2.68 (1.9 to 3.77)
Female				1
BMI (kg/m^2)				
≥30	1.12	0.29	<0.001	6.79 (4.28 to 10.78)
25 to 29.99	0.26	0.26	0.318	3.04 (1.97 to 4.69)
23 to 24.99	0.04	0.29	0.879	1.88 (1.13 to 3.13)
<23				1
NC (cm)				
≥40	0.84	0.20	<0.001	2.31 (1.58 to 3.39)
<40				1
WHtR				
≥0.5	0.88	0.31	0.004	2.41 (1.32 to 4.43)
<0.5				1
Presence of HT				
Yes	0.41	0.18	0.019	1.51 (1.07 to 2.14)
No				1
Observed apnea				
Yes	0.74	0.16	<0.001	2.09 (1.53 to 2.87)
No				1

SE=standard error; OR=odds ratio; CI=confidence interval; BMI= body mass index; NC=neck circumference; WHtR=waist to height ratio; HT=hypertension

Table 3. Scoring scheme and the cut-off point for predicting of OSA

Factors	Scoring points
Sex	
Male	1.0
Female	0.0
BMI (kg/m^2)	
≥30	1.1
25 to 29.9	0.3
23 to 24.99	0.1
<23	0.0
NC (cm)	
≥40	0.8
<40	0.0
WHtR	
≥0.5	0.9
<0.5	0.0
Presence of HT	
Yes	0.4
No	0.0
Observed apnea	
Yes	0.7
No	0.0
Total score	Cut-off point >2

BMI=body mass index; NC=neck circumference; WHtR=waist to height ratio; HT=hypertension

(95% CI 1.32 to 4.43) compared to patients having NC less than 40 and WHtR less than 0.5. Patients stop breathing during sleep had an odds ratio of 2.09 (95% CI 1.53 to 2.87), compared to patients without breathing pause. Subjects who had HT had 1.5 times higher odds than subjects who did not.

The scoring scheme was developed, using the estimated coefficients of the six significant parameters from multiple logistic regression analysis, as shown in Table 3. The total scores were summed and calculated the cut-off points, which can then predict moderate to severe OSA. The authors used the cut-off scores of greater than 2 to predict patients at high risk of having AHI of greater than 15, with the sensitivity of 85.52%, and the specificity of 49.57%. Regarding predicting AHI greater than 30, the sensitivity was up to 90.80%, with the specificity of 42.44%. In addition, the scores of greater than 3.5 obtained higher specificity (89.97%) to identify patients who had moderate to severe OSA. The predictive performance of the clinical risk assessment model is shown in Table 4.

Discussion

The present study found that six significant parameters were able to predict patients as having moderate to severe OSA. These included the significant risk factors, that have been confirmed from most literatures, to correlate with OSA including male gender, obesity, and the presence of HT[29,30]. Besides these, observed apnea during sleep is also the most important record for patients suspected of OSA. The present study model can be used as a scoring scheme during routine clinical practice, which is easy to use and calculate, with high sensitivity (85.5%) and moderate specificity (49.6%), for predicting AHI of 15 or more in patients suspected of having OSA, at the cut-off point of more than 2. The higher score shows the higher risk to have severe severity. This model would enable the clinicians to detect the possibility of OSA during initial clinical visits, and help them to determine those patients at risk, and in

Table 4. Predictive parameters of cut-off points for screening of moderate to severe OSA

	AHI ≥15 events/hour		AHI >30 events/hour	
	Scores >2	Scores >3.5	Scores >2	Scores >3.5
Sensitivity (95% CI)	85.52% (82.39 to 88.28)	41.72% (37.68 to 45.86)	90.80% (87.59 to 93.41)	50.36% (45.43 to 55.29)
Specificity (95% CI)	49.57% (44.20 to 54.94)	89.97% (86.33 to 92.91)	42.44% (38.13 to 46.84)	86.63% (83.38 to 89.44)
PPV (95% CI)	73.81% (71.64 to 75.87)	87.36% (83.27 to 90.57)	55.80% (53.82 to 57.77)	75.09% (70.35 to 79.30)
NPV (95% CI)	67.32% (62.20 to 72.05)	48.16% (46.23 to 50.09)	85.21% (80.73 to 88.80)	68.56% (66.30 to 70.73)
LR+ (95% CI)	1.7 (1.52 to 1.89)	4.16 (3.00 to 5.78)	1.58 (1.46 to 1.71)	3.77 (2.96 to 4.79)
LR– (95% CI)	0.29 (0.23 to 0.37)	0.65 (0.60 to 0.70)	0.22 (0.16 to 0.30)	0.57 (0.52 to 0.64)
Accuracy (95% CI)	72.01% (69.01 to 74.88)	59.85% (56.62 to 63.02)	63.94% (60.76 to 67.03)	70.51% (67.46 to 73.42)
AUC	0.68	0.66	0.67	0.68

AHI=apnea-hypopnea index; CI=confidence interval; PPV=positive predictive value; NPV=negative predictive value; LR+=positive likelihood ratio; LR–=negative likelihood ratio; AUC=area under the curve

need of further investigation. Regarding the reliability, most parameters in the present model are objectively measured, so that a night-to-night variation would be low.

Several screening questionnaires have been validated worldwide. From the meta-analysis, the parameters involved in the screening questionnaires are various and the cut-off numbers used are also different, for example BMI, neck size, etc.[23]. Firstly, the Berlin questionnaire is widely used to evaluate patients with a history of suspected OSA in a primary care setting. This is a self-assessment of snoring behavior, sleepiness, and other risk factors of OSA. However, the Berlin questionnaires is shown to have high sensitivity for detecting OSA, estimated as 69% to 86%, but having relatively less sensitivity in detecting more severe cases[20,23,31]. Secondly, the STOP Bang questionnaire was beneficial for having consistently high sensitivity for identifying OSA in the different AHI cut-offs and severity levels. Regarding to the sensitivity in predicting AHI of 15 or more, and 30 or more as high as 93% and 100%, respectively, but the specificity declined to 43% and 37%, respectively[21-24,32]. Thus, this questionnaire is suitable to determine out-patients at risk for OSA in a perioperative setting. However, the present study has considerably less factors than those of the STOP Bang questionnaires. As well, the cut-off numbers are also different from the STOP Bang questionnaires. For the predictive performance, the present study model showed favorable results, which can predict moderate and severe OSA, coupled with high sensitivity (85.5% and 90.8%, respectively). The ESS questionnaire is the standard measurement of daytime sleepiness, by assessing eight common situations, however, its screening performance on the presence of OSA in a normal population is limited by low sensitivity of 65% and specificity of 54%[17-19,23]. Moreover, the increases of ESS scores do not correlate with the severity of OSA. Because of this, sleepiness may be ignored in some OSA cases, whereas some patients may be asymptomatic despite having severe OSA. For this reason, the subjective symptoms may be unreliable predictors of OSA in a public health system. Recently, a study on the four-variable screening tool is a simple screening instrument, that has been reported as having a sensitivity and specificity of 93% and 66%, respectively, to identify moderate to severe OSA, however, the present study did not use the standard PSG for OSA diagnosis. Therefore, its predictive performance may only be suitable for screening in low-risk populations[33]. Moreover, the morphometric model has been reported as having a very high, predictive performance in detecting patients with OSA, having a sensitivity of 98% and a specificity of 100%[16]. Another prediction model, using the artificial intelligence system, also showed the sensitivity and specificity of screening moderate to severe OSA patients, to be as high as 88% and 97%, respectively[15]. Although their predictive performances have a very high accuracy, these screening tools are quite complicated to use in a clinical practice setting.

Due to public health concerns, the authors decided to develop a simple, clinical assessment tool for detecting patients at risk for moderate to severe OSA. This tool consists of six items, including gender, BMI, NC, WHtR, presence of HT, and a notice of breathing pauses during sleep. These are easily, objective measures for healthcare providers.

Additionally, its cutoff number is quite applicable for Asian people. In addition, its diagnostic performance using the cutoff of more than 2 is also acceptable, and similar to many screening tools that are more complex. The limitation of the present study was referral bias, resulting from the high-risk population, and it has not been validated on different target populations. Thus, additional improvements of this model are needed to be more feasible for people to use as an early self-screening tool.

Conclusion

There is a high prevalence of undiagnosed OSA within the high-risk populations. Untreated disease leads to secondary cardiovascular consequences, and public health problems. The present clinical assessment model appears to be useful and practical tool for identifying patients at risk for moderate to severe OSA, with an acceptable predictive performance. In addition, it might help with the clinicians' decision to prioritize patients for PSG.

What is already known on this topic?

Many sleep screening tools are adjunctively used to evaluate patients at risk for OSA with different accuracies. However, the risk factors and their cut-off points may not be applicable for the Asian population.

What this study adds?

The authors identify some significant risk factors to develop a model for predicting moderate to severe OSA. It will help the clinicians' decision to submit patients at risk for PSG.

Acknowledgement

The authors would like to thank the Faculty of Medicine, Prince of Songkla University for funding, and Nannapat Pruphetkaew for data analysis.

Funding disclosure

This study was funded by the Faculty of Medicine, Prince of Songkla University.

Conflicts of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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