Auris Nasus Larynx xxx (xxxx) xxx

Contents lists available at ScienceDirect

Auris Nasus Larynx

journal homepage: www.elsevier.com/locate/anl

# Utility of acoustic pharyngometry for screening of obstructive sleep apnea

Boo-Young Kim[a], Jung-Hae Cho[b], Do Hyun Kim[c], Sung Won Kim[c], Soo Whan Kim[c], Byung Guk Kim[d], Yong Jin Park[b,*]

[a] *Department of Otolaryngology-Head and Neck Surgery, Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea*
[b] *Department of Otolaryngology-Head and Neck Surgery, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea*
[c] *Department of Otolaryngology-Head and Neck Surgery, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea*
[d] *Department of Otolaryngology-Head and Neck Surgery, St. Paul's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea*

ARTICLE INFO

*Article history:*
Received 30 May 2019
Accepted 24 October 2019
Available online xxx

*Keywords:*
Acoustic pharyngometry
Cephalometry
Obstructive sleep apnea

ABSTRACT

*Objective:* To determine whether combining acoustic pharyngometric parameters with cephalometric and clinical parameters could improve the predictive power for significant obstructive sleep apnea (OSA) in a Korean population.

*Methods:* A total of 229 consecutive adult patients with suspected OSA were enrolled. The predictability for significant OSA using acoustic pharyngometric or cephalometric parameters or combining these parameters and clinical factors was calculated and compared using multivariate logistic regression and receiver operating characteristic (ROC) curves.

*Results:* In multivariate logistic regression, age, sex, minimum upper airway cross-sectional area (UA-CSA), and mandibular plane to hyoid distance (MPH) were all significant independent predictors of significant OSA. The minimum UA-CSA of 0.85 $cm^2$ provided fair discrimination for OSA [area under the curve (AUC): 0.60, 95% confidence interval (CI): 0.52–0.67]. The MPH of 18.75 mm provided fair discrimination for OSA (AUC; 0.65, 95% CI: 0.58–0.72). The discriminative ability of the final model of multivariate ROC curve analyses that included the minimum UA-CSA, age, sex, body mass index (BMI), and MPH was better than the minimum UA-CSA alone (AUCs: 0.77 vs. 0.60). Optimal cut-off values of predictors for discriminating significant OSA were as follows: male for sex, 40 years for age, 25.5 $kg/m^2$ for BMI, 1.06 $cm^2$ for minimum UA-CSA, and 18 mm for MPH.

*Conclusion:* Minimum UA-CSA measured using acoustic pharyngometry while sitting might be a useful method to predict OSA. Combining minimum UA-CSA with age, sex, BMI and MPH improved the predictive value for significant OSA.



## 1. Introduction

The current gold-standard method of diagnosing obstructive sleep apnea (OSA) is in-laboratory polysomnography

* Corresponding author. Present address: 93 jungbu dearo, paldalgu, Suwon, Gyeonggi-do 16247, Republic of Korea.
*E-mail address:* yp@catholic.ac.kr (Y.J. Park).

https://doi.org/10.1016/j.anl.2019.10.007
0385-8146/© 2019 Oto-Rhino-Laryngological Society of Japan Inc. Published by Elsevier B.V. All rights reserved.

(PSG) which can be complicated and expensive. Given that OSA causes several medical complications, it would be very useful if clinicians have predictive tools to identify patients whose classic PSG is vital. Most Korean studies on predictors of OSA have focused on clinical features and anthropometric measurements that have limitations in accurately predicting OSA [1–3]. Cephalometric radiographs have been used for diagnostic study of OSA due to their low cost and easy method. A meta-analysis has recently reported that mandibular plane to hyoid bone distance (MPH) is one of the most reliable parameters for predicting Apnea-Hypopnea Index (AHI) [4]. Several Korean studies have also reported that MPH is positively correlated with AHI [5,6].

Acoustic pharyngometry is a noninvasive and cost effective method that uses sound reflection to quickly assess the upper airway cross-sectional area (UA-CSA) [7]. Despite its limitation of testing while awake, previous studies using acoustic pharyngometry have shown a significant difference in UA-CSA measurements between subjects with OSA and those without OSA [8,9]. However, considering interracial differences in acoustic pharyngometric measurements [10,11], it is important to ascertain the effectiveness of such method with Asian populations including Koreans. It can be more useful if the presence of OSA can be triaged, especially when acoustic pharyngometry is combined with other techniques.

Thus, the purpose of this study was to assess the predictability of acoustic pharyngometry as a screening method to discriminate the presence of significant OSA defined as an obstructive apnea index (OAI) $\geq$ 5 in Koreans with suspected OSA, and determine whether combining acoustic pharyngometric parameters with cephalometric parameters and clinical factors such as age, sex, and body mass index (BMI) could improve the predictive power for significant OSA.

## 2. Materials and methods

### 2.1. Subjects and study design

We conducted a retrospective review of medical data and records of consecutive adult Korean patients (age $\geq$ 18 years) with suspected OSA who had undergone standard overnight laboratory PSG, acoustic pharyngometry, and lateral cephalometry between April 2003 and January 2006 at the Department of Otolaryngology-Head and Neck Surgery of St. Vincent's Hospital, Republic of Korea. All acoustic pharyngometry and cephalometry studies were performed by the same examiner respectively within three weeks before PSG was performed. The following information was collected for analysis purposes: patients demographics (age, sex, BMI), PSG measures, acoustic pharyngometric and cephalometric measurements. A total of 243 subjects were selected, of whom 14 were excluded, resulting in a study population of 229. The reasons for exclusion are as follows: 1 had brain tumor; 9 had low sleep efficiency (< 70%); and 4 had poor-quality acoustic pharyngometry tracings. A poor-quality acoustic pharyngometry tracing was defined as a tracing that was poorly reproducible with a coefficient of variation greater than 10%. We arbitrarily defined the likelihood of significant OSA as an OAI $\geq$ 5 events/h. All subjects were divided into two groups: significant OSA (OAI $\geq$ 5; 124 patients) and low OAI (OAI < 5; 105 patients). Ethical approval was obtained from Institutional Review Board of our hospital (approval number: VC18RESI0034).

### 2.2. Polysomnography

Overnight hospital recordings were performed using a computerized 18-channel polygraph (Embla, Flaga hf. Medical Devices, IS-105 ReykjaVik, Iceland). All data were manually scored by a blinded certified scorer using American Academy of Sleep Medicine criteria. Apnea was defined as the absence of nasal flow for at least 10 s. Hypopnea was defined as a reduction in amplitude of airflow of greater than 50% of baseline for more than 10 s. These events were defined as obstructive if they occurred in associated with thoracoabdominal wall movement. OAI was defined as the number of obstructive apnea averaged per hour of sleep. Only those patients whose sleep files had sleep efficiency of at least 70% or more during a period of sleep of at least 6 h were included.

### 2.3. Acoustic pharyngometry

Pharyngeal structure was assessed by measurements of pharyngeal volume, mean CSA, and minimal CSA from the velopharyngeal junction to the glottis at a relaxed end-expiration during normal tidal breathing [at functional residual capacity (FRC)] using an acoustic pharyngometer (Eccovision; E. Benson Hood Laboratories, Pembroke, MA, USA). The exclusion criteria for the performance of acoustic pharyngometry included severe lung disease. To standardize the operating technique of this equipment, we examined 27 normal volunteers (13 males and 14 females) as a pre-study. All volunteers gave no history of snoring, apparent facial skeletal anomalies, and BMI more than 25.4 kg/m$^2$.

While awake seated in an upright and comfortable position on a straight-back chair, subjects were requested to keep head and neck erect and fix their gaze at a point in the opposite space. Subjects breathed orally through a pharyngometer with the aid of a nose clip. They were requested to think a silent "oooh", set the tongue in a relaxed, neutral position, and keep the velum closed to prevent acoustic leak through the nose.

Pharyngometry data were collected and analyzed by the same trained examiner. For each subject, four graphs were obtained by adopting the Ecovision operating protocol. At least four consecutive measurements were performed to obtain one same graph. These measurements were used with a coefficient of variation of less than 10% for each study. The CSA (on the *Y*-axis) at each distance point (on the *X*-axis) was read and then averaged to obtain the mean CSA for the analysis segment of pharyngeal length of each volunteer, and an averaged standard curve for all normal volunteers was produced as error bar and line of mean.

### 2.4. Lateral cephalometry

Lateral cephalometric radiographs were taken with patients while standing in upright position. Patient's eyes were di-

Please cite this article as: B.-Y. Kim, J.-H. Cho and D.H. Kim et al., Utility of acoustic pharyngometry for screening of obstructive sleep apnea, Auris Nasus Larynx, https://doi.org/10.1016/j.anl.2019.10.007

**Table 1**
Demographic and polysomnographic characteristics of subjects with and without obstructive sleep apnea.

| Characteristics | Total ($n=229$) | OSA (OAI $\geq$ 5, $n=124$) | Low OAI (OAI $<$ 5, $n=105$) | $p$-Value |
|---|---|---|---|---|
| Demographics | | | | |
| Age, year | 42.8 ± 10.6 | 45.1 ± 10.5 | 40.1 ± 10.2 | <0.0001 |
| Male sex, $n$ (%) | 183 (80%) | 111 (90%) | 72 (69%) | <0.0001 |
| BMI, kg/m$^2$ | 26.5 ± 3.5 | 27.2 ± 3.3 | 25.7 ± 3.5 | 0.001 |
| Polysomnography | | | | |
| Sleep efficiency, % | 93.0 ± 6.7 | 93.2 ± 6.0 | 92.7 ± 7.4 | 0.60 |
| OAI, events/h | 13.4 ± 17.8 | 23.6 ± 19.0 | 1.3 ± 1.5 | <0.0001 |
| AHI, events/h | 27.3 ± 23.7 | 41.9 ± 22.4 | 10.1 ± 9.4 | <0.0001 |
| Mean $SaO_2$, % | 94.8 ± 0.2 | 93.8 ± 3.5 | 96.0 ± 1.6 | <0.0001 |
| Lowest $SaO_2$, % | 80.4 ± 10.1 | 75.3 ± 10.3 | 86.3 ± 5.8 | <0.0001 |

Data are presented as mean ± standard deviation for continuous variables and number (percent) for sex.
$p$-Values were calculated by independent $T$ test for continuous variables and chi-square test for sex.
Definition of abbreviations: OSA = obstructive sleep apnea; OAI = obstructive apnea index; AHI = apnea–hypopnea index; BMI = body mass index; $SaO_2 = O_2$ saturation.

rected forward in a natural head position so that the gaze was parallel to the floor. Radiographs were obtained at the end expiratory phase without swallowing. The mouth was closed with lips relaxed. The following cephalometric indices of soft tissues and bony framework of the skull were included: SNA to maxillary prognathism = angle measurement from sella (S) to nasion (N) to point A (subspinale); SNB to mandibular prognathism = angle measurement from S to N to point B (supramentale); ANS-Gn to anterior lower facial height = vertical measurement from anterior nasal spine (ANS) to gnathion (Gn); MPH to perpendicular distance from mandibular plane (MP) to hyoid bone (H); PNSP to distance from posterior nasal spine (PNS) to the tip of the soft palate (P); and PAS to posterior airway space = distance between the base of the tongue and the posterior pharyngeal wall along the line from the supramentale to the gonion. Cephalograms were interpreted by two ENT doctors under an orthodontist's guidance.

### 2.5. Statistics

All statistical analyses except receiver operating characteristic (ROC) curve analysis were performed using SPSS (Version 21, IBM, KOREA). ROC curves analyses were performed using Web-R.org. $P < 0.05$ was considered statistically significant. Quantitative data are expressed as the mean ± standard deviation and categorical data as number or percentage. Characteristics of subjects who were diagnosed with significant OSA (OAI ≥ 5) versus those who were not were compared using independent $T$ test for continuous variables or chi-square test for categorical variables. Univariate binary logistic regression was used to evaluate the relation between clinical, acoustic pharygometric and cephalometric parameters and the presence of significant OSA. Multivariate analysis was performed with the binary logistic regression test to determine the independent predictor of the presence of significant OSA. Hosmer–Lemeshow test was used to determine the goodness of fit of the logistic regression. The predictive power of clinical factors, acoustic pharygometric and cephalometric parameters, and combining clinical factors and acoustic pharygometric and cephalometric parameters for discriminating significant OSA was tested by ROC curve analysis. Predefined rules were used to assess the classification performance according to area under the ROC curve (AUC) values [12]. The minimum UA-CSA and MPH values that provided optimal discrimination based on the sum of sensitivity and specificity were determined. Positive and negative predictive values were also calculated. The two correlated ROC curves in Web-R.org were compared automatically using DeLong's test [13]. When we put several predictors in 'Models with several predictors' to quantify improvement in discrimination ability associated with UA-CSA or MPH, multiple logistic regression with stepwise backward elimination was performed automatically. Multiple regression Model ROC Curves with several predictors and final Model ROC Curves were drawn and compared through a stepwise regression process.

## 3. Results

### 3.1. Standard curve

The averaged standard curve for all normal volunteers is shown in Fig. 1. The mean and minimum pharyngeal CSA at FRC when sitting was 2.06 ± 0.30, 1.20 ± 0.23 (cm$^2$, mean ± SD) respectively.

### 3.2. Characteristics of subjects

Among 229 Korean subjects (183 males, 46 females; age, 18–70 years) studied, 124 patients had significant OSA (OAI ≥ 5). Table 1 lists demographic and polysomnographic variables showing significant differences between OSA and low OAI groups. A statistically significant difference in sleep efficiency was not observed. Table 2 lists acoustic pharyngometric and lateral cephalometric variables showing significant differences between OSA and low OAI groups. Compared with the low OAI group, the minimum UA-CSA was significantly ($P = 0.045$) smaller in the OSA group. MPH and PNSP were

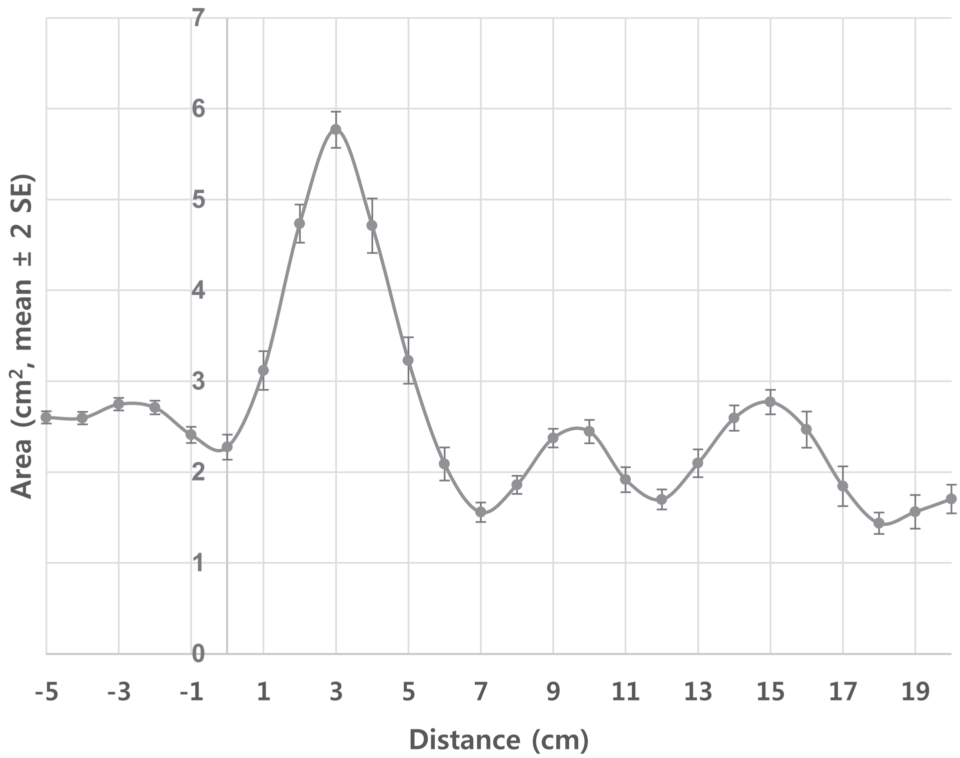


**Fig. 1.** Normal standard curve (error bar).

**Table 2**
Acoustic pharyngometric and cephalometric variables of subjects with and without obstructive sleep apnea.

| Characteristics | Total ($n = 229$) | OSA (OAI $\geq$ 5, $n = 124$) | Low OAI (OAI < 5, $n = 105$) | $p$-Value |
|---|---|---|---|---|
| UA-CSA at FRC while sitting, $cm^2$ | | | | |
| Minimum | 0.98 ± 0.29 | 0.94 ± 0.29 | 1.02 ± 0.30 | 0.045 |
| Cephalometry data, mm | | | | |
| MPH | 18.57 ± 6.44 | 20.11 ± 6.29 | 16.76 ± 6.18 | < 0.0001 |
| PNSP | 38.34 ± 6.94 | 39.64 ± 6.23 | 36.79 ± 7.44 | 0.002 |

Data are presented as mean ± standard deviation. $p$-Values were calculated by independent $T$ test for continuous variables.
Definition of abbreviations: OSA = obstructive sleep apnea; OAI = obstructive apnea index; UA-CSA = upper airway cross-sectional area; FRC = functional residual capacity; MPH = perpendicular distance from the mandibular plane to hyoid bone; PNSP = distance from posterior nasal spine to the tip of the soft palate.

significantly longer in the OSA group than those in the low OAI group ($P < 0.0001$ and $P = 0.002$, respectively).

### 3.3. Logistic regression approach

In multivariate logistic regression analysis, we included the following variables that showed significant ($p < 0.05$) differences between the two groups in several univariate logistic regression analyses: age, sex, BMI, minimum UA-CSA, MPH, and PNSP. Results of multivariate logistic regression models are shown in Table 3. Age, sex, minimum UA-CSA, and MPH were all significant independent predictors of significant OSA (OAI $\geq$ 5). The odds of OSA significantly increased for every 0.5 $cm^2$ decrease in the minimum UA-CSA [OR (odds ratio): 3.23, 95% confidence interval (CI): 1.37–7.63, $P = 0.008$] after controlling for age, sex and MPH. Also, after controlling for age, sex and minimum UA-CSA, the odds of OSA significantly increased for every 10 mm increase in MPH (OR: 3.28, 95% CI: 1.33–8.09, $P = 0.010$).

### 3.4. Receiver operating characteristic curve approach

Results of ROC curve analyses are shown in Fig. 2. Fair discriminative ability was observed for different cut points of the minimum UA-CSA and MPH. The minimum UA-CSA of 0.85 $cm^2$ provided fair discrimination for OSA (sensitivity, 45.2%; specificity, 77.1%; AUC: 0.60, 95% CI: 0.52–0.67, $P < 0.001$) with positive predictive value of 45.6% and negative predictive value of 30.0%. The MPH of 18.75 mm provided fair discrimination for OSA (sensitivity, 60.5%; specificity, 62.9%; AUC: 0.65, 95% CI: 0.58−0.72, $P < 0.001$) with positive predictive value of 42.6% and negative predictive value of 34.2%. No significant difference in discriminatory abil-

Please cite this article as: B.-Y. Kim, J.-H. Cho and D.H. Kim et al., Utility of acoustic pharyngometry for screening of obstructive sleep apnea, Auris Nasus Larynx, https://doi.org/10.1016/j.anl.2019.10.007

**Table 3**
Multivariate logistic regression results for predicting obstructive sleep apnea.

| Predictor | B | S.E. | OR (95% CI) | *p*-Value |
|---|---|---|---|---|
| Age, years | 0.058 | 0.015 | 1.060 (1.029–1.093) | $< 0.001$ |
| Sex (male) | 1.342 | 0.411 | 3.826 (1.710–8.562) | 0.001 |
| Per 0.5 $cm^2$ decrease in minimum UA-CSA | 1.172 | 0.439 | 3.229 (1.366–7.628) | 0.008 |
| Per 10 mm increase in MPH | 1.186 | 0.461 | 3.275 (1.326–8.087) | 0.010 |

Definition of abbreviations: B = regression coefficient; S.E. = standard error; OR =odds ratio; CI = confidence interval; BMI = body mass index; UA-CSA = upper airway cross-sectional area; MPH = perpendicular distance from the mandibular plane to hyoid bone.

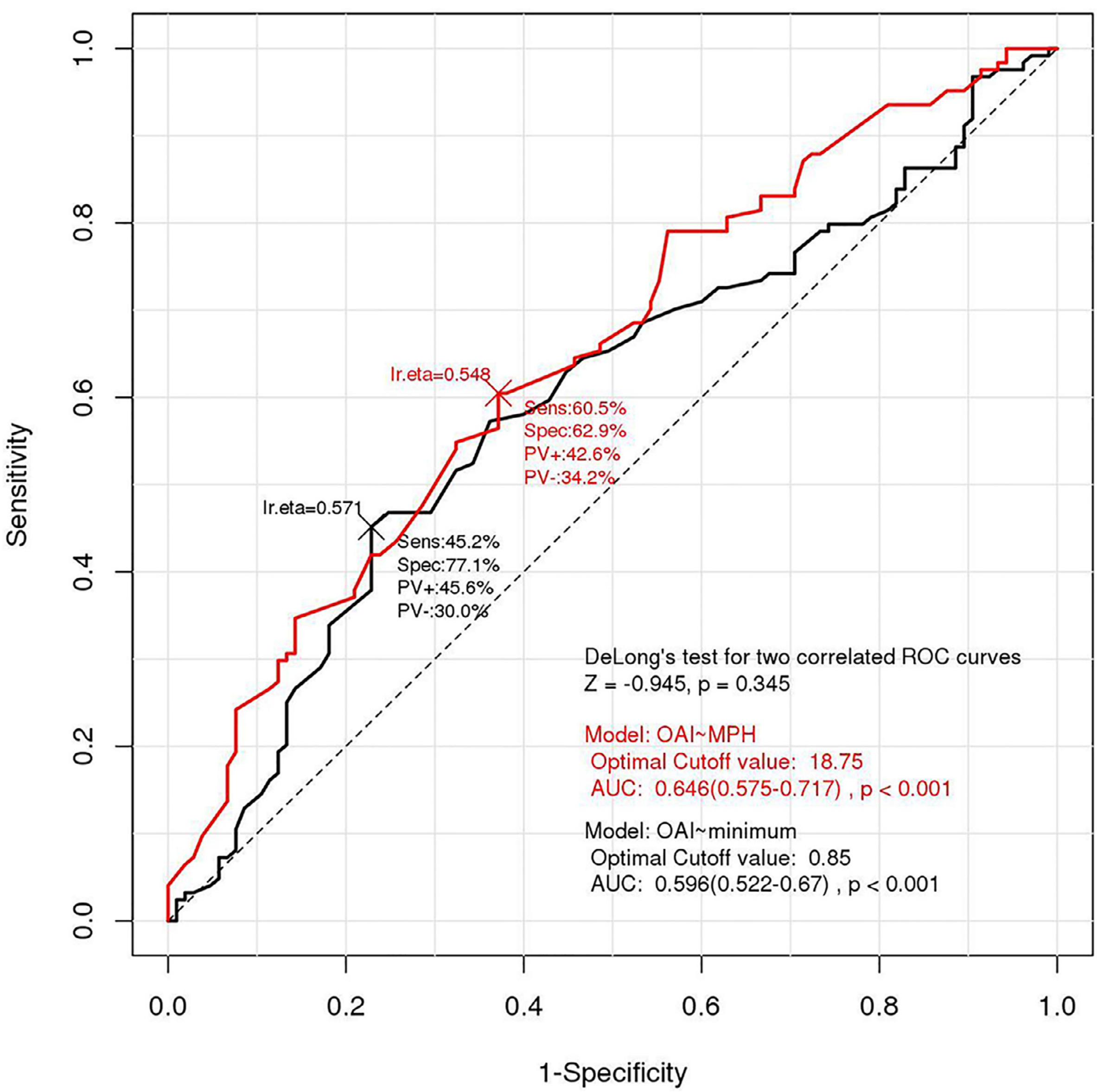


**Fig. 2.** Results of receiver operating characteristic curve analyses: ability between the minimum upper airway cross-sectional area and MPH to discriminate subjects with and without a diagnosis of obstructive sleep apnea (OAI $\geq$ 5).
Definition of abbreviations: Ir.eta=the place where the sum of specificity and sensitivity is maximized. optimal cut off value from logistic regression model; Sens=sensitivity; Spec=specificity; PV+ =positive predictive value; PV−=negative predictive value; OAI=obstructive apnea index; MPH=perpendicular distance from the mandibular plane to hyoid bone; AUC=area under the receiver operating characteristic curve; minimum = minimum upper airway cross-sectional area.

**Table 4**
Results of multivariate receiver operating characteristic curve analyses.

| Predictors | AUC |
|---|---|
| Age + Sex + BMI | 0.71 |
| Age + Sex + BMI + MPH | 0.74 |
| Age + Sex + BMI + Minimum | 0.74 |
| Age + Sex + BMI + MPH + Minimum | 0.77 |

Definition of abbreviations: AUC=area under the receiver operating characteristic curve; BMI=body mass index; MPH=perpendicular distance from the mandibular plane to hyoid bone; Minimum=minimum upper airway cross-sectional area.

ity between the minimum UA-CSA and MPH was observed ($P = 0.345$).

Results of multivariate ROC curve analyses are shown in Table 4. When minimum UA-CSA, MPH, or minimum UA-CSA and MPH were added to clinical factors including age, sex, and BMI, these measurements showed better discriminative ability (AUCs range: 0.71 to 0.77). The discriminative ability of the model that included clinical factors only was better than the minimum UA-CSA alone (AUCs: 0.71 vs. 0.60). The discriminative ability of the final model that included the minimum UA-CSA, age, sex, BMI, and MPH was also better than the minimum UA-CSA alone (AUCs: 0.77 vs. 0.60). Results of multiple regression Model ROC curves with several predictors and final Model ROC curves are shown in Fig. 3. Optimal cut-off values of predictors for discriminating significant OSA (OAI $\geq$ 5) were as follows: male for sex, 40 years for age, 25.5 kg/m$^2$ for BMI, 1.06 cm$^2$ for minimum UA-CSA, and 18 mm for MPH.

## 4. Discussion

Cost limitations contribute to significant delays in the testing of patients for OSA with standard PSG. Thus, a cheaper, noninvasive, more easily repeatable screening tool such as

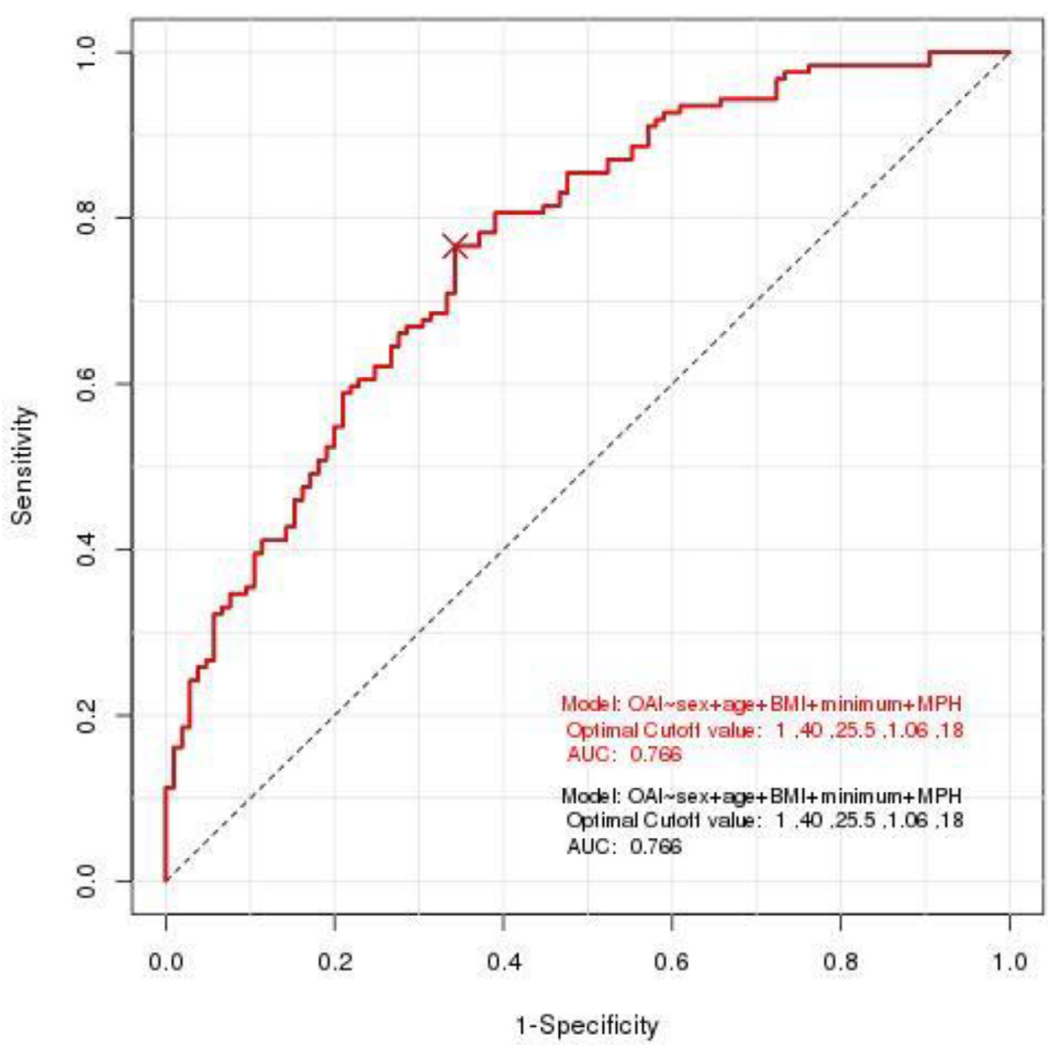


**Fig. 3.** Results of multiple regression Model ROC Curves with several predictors and final Model ROC Curves: the optimal cut-off values of predictors for discriminating significant OSA (OAI $\geq$ 5) were as follows: male for sex, 40 years for age, 25.5 kg/m$^2$ for BMI, 1.06 cm$^2$ for minimum UA-CSA, 18 mm for MPH.
Definition of abbreviations: OAI=obstructive apnea index; BMI=body mass index; minimum= minimum upper airway cross-sectional area; MPH=perpendicular distance from the mandibular plane to hyoid bone; AUC=area under the receiver operating characteristic curve.

Please cite this article as: B.-Y. Kim, J.-H. Cho and D.H. Kim et al., Utility of acoustic pharyngometry for screening of obstructive sleep apnea, Auris Nasus Larynx, https://doi.org/10.1016/j.anl.2019.10.007

acoustic pharyngometry may help primary physician decide which patient is at high risk OSA who should be referred to sleep centers for further evaluation and treatment of OSA.

To the best of our knowledge, this is the first study to date performed in Koreans with suspected OSA to examine the predictive and discriminative ability of acoustic pharyngometric measurements in combination with cephalometric measurements and objective clinical factors such as age, sex, and BMI. We found that age, sex, minimum UA-CSA, and MPH were all significant independent predictors of significant OSA (OAI $\geq$ 5).

The present study demonstrated that the minimum UA-CSA that was measured using acoustic pharyngometry at FRC while sitting was a significant independent predictor of OSA when we controlled for several predictors using logistic regression. However, using an ROC approach, we found that the discriminative validity of minimum UA-CSA for identifying significant OSA was fair (AUC: 0.60). A previous study by DeYoung et al. has reported that the AUC for the minimum UA-CSA predicting an AHI less than 15 per hour is 0.85 [14]. The difference for observed AUCs between DeYoung's et al. study and our study might be due to their smaller sample size (60 vs. 229 subjects) and, data collected from suspected OSA and control subjects (51 and 9, respectively) versus data collected from suspected OSA subjects only (229). A study by Kendzerska et al. has shown that the AUC for the mean UA-CSA predicting an AHI greater than or equal to 5 is 0.60 [15], similar to the AUC for the minimum UA-CSA in our study. However, we did not demonstrate a significant difference in the mean UA-CSA, unlike their study. Such difference might be attributable to interethnic differences in upper airway anatomy and craniofacial structure. The importance of this minimum UA-CSA has also been found in a dynamic multidetector CT (MD-CT) study on the correlation between severity of OSA and upper airway morphology [5].

An inter-ethnic study by Lee et al. has reported that Chinese patients with the same degree of obesity as Caucasians have more severe OSA and more craniofacial bony restriction [16]. Consistent with prior studies [5,6], we also found that MPH was the most significant cephalometric predictor of significant OSA when we controlled for confounders using logistic regression. An inferiorly displaced hyoid bone measured by MPH could lead to an increase in pharyngeal length, defined as the distance from the posterior nasal spine to the epiglottis base attached to the hyoid. A longer pharynx is more collapsible, which can predispose to OSA. A longer upper airway length (UAL) has been reported to be associated with OSA severity assessed by upper airway collapsibility and AHI [17–19]. Men with OSA have been found to have longer UAL than women with OSA [20,21]. Aging is also found to be associated with longer UAL and increased upper airway collapsibility during sleep [19,22]. Our results using ROC approach demonstrated that the AUC for MPH predicting a significant OSA was 0.65, similar to the AUC (0.60) for minimum UA-CSA. Fair discriminative ability of these two techniques found in our study might be explained by multifactorial mechanisms responsible for OSA. These factors include a narrow, crowded, or collapsible upper airway and non-anatomical causes such as ineffective pharyngeal dilator muscle function during sleep, a low threshold for arousal to airway narrowing during sleep, and unstable control of breathing [23]. Our current study also showed that age and male sex were significant predictors for OSA, similar to results of previous studies [1,6,24,25].

Increased tongue fat deposition by obesity can also lead to tongue enlargement, inferiorly displacing the hyoid bone and epiglottis [25]. Inferiorly displacement of the hyoid bone and epiglottis can increase UAL. Therefore, it can be said that male sex and obesity share a similar mechanism that can increase the upper airway collapsibility by increasing UAL. Although our study found that BMI was not a significant predictor for OSA in multivariate logistic regression analysis, obesity is generally accepted as an OSA determinant. Therefore, BMI was included in the multivariate ROC curve analysis of our study. The final discriminative value of the model including age, sex, and BMI only provided acceptable discrimination for OSA (AUC: 0.71). Our results for BMI differed from the result of one study performed on Hong Kong Chinese subjects, reporting that BMI did not provide additional benefits to predictions of OSA [26]. The current World Health Organization (WHO) BMI cut-off values for Asian populations are 25 kg/m$^2$ or higher for being overweight and 27.5 kg/m$^2$ or higher for having high risk of obesity [27].

In the analysis of multivariate ROC curves, we found that the minimum UA-CSA had fair discriminant value. However, after adding age, sex, BMI, and MPH to the model, AUC was increased from 0.60 to 0.77. Results from final Model ROC Curves demonstrated that no single method could reliably predict significant OSA (OAI $\geq$ 5). In the present study, optimal cut-off values for predictors as a significant OSA determinant were as follows: male for sex, 40 years for age, 25.5 kg/m$^2$ for BMI, 1.06 cm$^2$ for minimum UA-CSA, and 18 mm for MPH. The cut-off value of BMI found in this study was similar to that reported in a previous study of the Korean population [2].

The present study has several limitations. First, our study was conducted through a cross-sectional analysis of male-dominated OSA suspected patients at a single center in Korea. Thus, our results should be applied cautiously to the general population. Second, acoustic pharyngometry and cephalometry performed during wakefulness and in the upright position might not accurately predict the upper airway soft tissues structures during sleep. In addition, we did not assess the upper airway collapsibility. Third, we did not objectively evaluate anthropometric indices such as neck circumference or waist-to-hip ratio that could reflect upper airway and central fat deposition. Inclusion of these indices might be able to improve the predictive ability of our model. Finally, this technique cannot be standard tool to evaluate sleep apnea patients clinically. However, we analyzed this data for screening tool for OSA not for diagnostic tool. Despite these limitations, our results suggest that analysis of acoustic pharyngometry in combination with cephalometry and objective clinical factors might provide useful information for a presumptive diagnosis for significant OSA patients, especially for whom PSG could not be performed easily such as old men and disable people. Moreover, the cut-off values selected from the final Model ROC Curves can be easily applied when a classic PSG is required to identify high risk OSA patients from primary care.

## 5. Conclusion

The present findings suggest that the minimum UA-CSA measured using acoustic pharyngometry at FRC while sitting might be a useful method to predict significant OSA risk. Minimum UA-CSA combined with age, sex, BMI and MPH in particular improved the predictive power for significant OSA. In addition, this study demonstrated the cut-off values of age, sex, BMI, minimum UA-CSA and MPH that might increase the OSA risk.

## Declaration of Competing Interest

None of the authors have any conflicts of interest.

## Acknowledgments

The authors thank the staff of the Department of Biostatistics of the Catholic Research Coordinating Center for their technical support.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.anl.2019.10.007.

## References

[1] Kim J, In K, Kim J, You S, Kang K, Shim J, et al. Prevalence of sleep-disordered breathing in middle-aged Korean men and women. Am J Respir Crit Care Med 2004;170(10):1108–13.
[2] Kang HH, Kang JY, Ha JH, Lee J, Kim SK, Moon HS, et al. The associations between anthropometric indices and obstructive sleep apnea in a Korean population. PLoS One 2014;9(12):e114463.
[3] Kim SW, Kim BY, Han JJ, Hwang JH, Jung K, Kim M, et al. Major factors affecting severity of obstructive sleep apnea. Indian J Otolaryngol Head Neck Surg 2015;67(Suppl 1):114–18.
[4] Armalaite J, Lopatiene K. Lateral teleradiography of the head as a diagnostic tool used to predict obstructive sleep apnea. Dentomaxillofac Radiol 2016;45(1):20150085.
[5] Heo JY, Kim JS. Correlation between severity of sleep apnea and upper airway morphology: cephalometry and MD-CT study during awake and sleep states. Acta Otolaryngol 2011;131(1):84–90.
[6] Kim ST, Park KH, Shin SH, Kim JE, Pae CU, Ko KP, et al. Formula for predicting OSA and the Apnea-Hypopnea Index in Koreans with suspected OSA using clinical, anthropometric, and cephalometric variables. Sleep Breath 2017;21(4):885–92.
[7] Kamal I. Test-retest validity of acoustic pharyngometry measurements. Otolaryngol Head Neck Surg 2004;130(2):223–8.
[8] Bradley TD, Brown IG, Grossman RF, Zamel N, Martinez D, Phillipson EA, et al. Pharyngeal size in snorers, nonsnorers, and patients with obstructive sleep apnea. N Engl J Med 1986;315(21):1327–31.
[9] Kamal I. Acoustic pharyngometry patterns of snoring and obstructive sleep apnea patients. Otolaryngol Head Neck Surg 2004;130(1):58–66.
[10] Patel SR, Frame JM, Larkin EK, Redline S. Heritability of upper airway dimensions derived using acoustic pharyngometry. Eur Respir J 2008;32(5):1304–8.
[11] Monahan K, Kirchner HL, Redline S. Oropharyngeal dimensions in adults: effect of ethnicity, gender, and sleep apnea. J Clin Sleep Med 2005;1(3):257–63.
[12] Hosmer DW, Lemeshow S. Assessing the fit of the model. Applied logistic regression Wiley series in probability and statistics. 2nd ed. New York: Wiley; 2000. p. 143–202.
[13] Robin X, Turk N, Hainard A, Tiberti N, Lisacek F, Sanchez JC, et al. pROC: an open-source package for R and S+ to analyze and compre ROC curves. BMC Bioformatics 2011;12:77.
[14] DeYoung PN, Bakker JP, Sands SA, Batool-Anwar S, Connolly JG, Butler JP, et al. Acoustic pharyngometry measurement of minimal cross–sectional airway area is a significant independent predictor of moderate-to-severe obstructive sleep apnea. J Clin Sleep Med 2013;9:1161–4.
[15] Kendzerska T, Grewal M, Ryan CM. Utility of acoustic pharyngometry for the diagnosis of obstructive sleep apnea. Ann Am Thorac Soc 2016;13(11):2019–26.
[16] Lee RW, Vasudavan S, Hui DS, Prvan T, Petocz P, Darendeliler MA, et al. Differences in craniofacial structures and obesity in Caucasian and Chinese patients with obstructive sleep apnea. Sleep 2010;33(8):1075–80.
[17] Sforza E, Bacon W, Weiss T, Thibault A, Petiau C, Krieger J, et al. Upper airway collapsibility and cephalometric variables in patients with obstructive sleep apnea. Am J Respir Crit Care Med 2000;161(2 Pt 1):347–52.
[18] Hirata RP, Schorr F, Kayamori F, Moriya HT, Romano S, Insalaco G, et al. Upper airway collapsibility assessed by negative expiratory pressure while awake is associated with upper airway anatomy. J Clin Sleep Med 2016;12(10):1339–46.
[19] Yamashiro Y, Kryger M. Is laryngeal descent associated with increased risk for obstructive sleep apnea? Chest 2012;141(6):1407–13.
[20] Segal Y, Malhotra A, Pillar G. Upper airway length may be associated with the severity of obstructive sleep apnea syndrome. Sleep Breath 2008;12(4):311–16.
[21] Godoy IR, Martinez-Salazar EL, Eajazi A, genta PR, Bredella MA, Torriani M. Fat accumulation in the tongue is associated with male gender, abnormal upper airway patency and whole-body adiposity. Metabolism 2016;65(11):1657–63.
[22] Eikermann M, Jordan AS, Chamberlin NL, Gautam S, Wellman A, Lo YL, et al. The influence of aging on pharyngeal collapsibility during sleep. Chest 2007;131(6):1702–9.
[23] Osman AM, Carter SG, Carberry JC, Eckert DJ. Obstructive sleep apnea: current perspectives. Nat Sci Sleep 2018;10:21–34.
[24] Bouloukaki I, Kapsimalis F, Mermigkis C, Kryger M, Tzanakis N, Panaqou P, et al. Prediction of obstructive sleep apnea syndrome in a large Greek population. Sleep Breath 2011;15(4):657–64.
[25] Kim AM, Keenan BT, Jackson N, Chan EL, Staley B, Poptani H, et al. Tongue fat and its relationship to obstructive sleep apnea. Sleep 2014;37(10):1639–48.
[26] Sutherland K, Lee RW, Petocz P, Chan TO, Nq S, Hui DS, et al. Craniofacial phenotyping for prediction of obstructive sleep apnea in a Chinese population. Respirology 2016;21(6):1118–25.
[27] WHO Expert Consultation Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363(9403):157–63.