

# Evaluation of the efficiency of anthropometric parameters and submental ultrasonographic indices as predictors for screening of obstructive sleep apnea and its severity

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**Background** Obstructive sleep apnea (OSA) syndrome is a chronic disease characterized by episodes of upper airway collapse, and has been associated with increased cardiovascular morbidity. Clinical and epidemiological studies have shown that OSA and obesity are strongly associated.

**Aim** The aim of this study was to demonstrate probable positive predictive anthropometric indices and ultrasonic parameters (anatomical and dynamic) and their possible cutoff values for the diagnosis of OSA and its severity.

**Patients and methods** A total of 80 adult patients with at least one of the major OSA symptoms were included in this study, and polysomnography was performed to confirm diagnosis and classify patients according to apnea–hypopnea index into mild, moderate, and severe groups. Anthropometric indices such as abdominal circumference, hip circumference, and neck circumference (NC) were measured for all included patients. Submental ultrasound was performed to measure retropalatal diameter, distance between lingual arteries, retroglossal airspaces, and tongue base thickness.

**Results** The cutoff values of 39.5 cm for NC (sensitivity of 80% and specificity of 77%) and of 25 mm for retropalatal

diameter during Muller maneuver (sensitivity of 80% and specificity of 82%) showed the most predictive value for both the presence and the severity of OSA, especially when used concomitantly (with 100% sensitivity and 90% specificity).

**Conclusion** Concomitant submental ultrasonography and NC may be a promising tool for screening of OSA and its severity for possible early intervention.

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**Keywords:** anthropometric, obstructive sleep apnea, outcome, predictors, ultrasonography

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## Introduction

Obstructive sleep apnea syndrome (OSAS) is a chronic disease characterized by episodes of partial or complete upper airway collapse that result in oxygen desaturation and microarousals, causing symptoms varying from snoring to excessive daytime sleepiness [1]. Obstructive sleep apnea (OSA), which is the most severe form of sleep-related breathing disorders, is characterized by reduction or complete cessation of airflow due to repeated upper airway collapse during sleep [2]. Obesity, particularly central obesity, is significantly associated with an increased prevalence of OSA in the general population, because it causes enlargement of the soft tissue structures within and surrounding the airway, thus contributing significantly to pharyngeal airway narrowing or collapse [3]. However, several epidemiologic studies found that 60% of patients with OSA were not obese. Recent estimates suggest that 60% of the adult population in industrialized countries is overweight (BMI > 25 kg/m<sup>2</sup>) and at least 30% is obese (BMI > 30 kg/m<sup>2</sup>) [4]. There are many anthropometric measures for screening and grading obesity and consequently OSA, such as BMI, neck circumference (NC), abdominal circumference (AC), and hip circumference (HC). Among anthropometric measurements, NC has been

suggested to be a predictive risk factor for OSA [5]. Body fat distribution seems to be of importance in relation to OSA. However, some authors have demonstrated that BMI correlates with OSA better than NC. The criteria of obesity are dependent on sex and ethnicity [6], and the relationship between obesity and OSA is unclear. Obesity is classified as visceral and peripheral, of which visceral obesity correlates more closely with obstructive sleep apnea hypopnea syndrome (OSAHS) compared with peripheral [7]. Although polysomnography (PSG) is an essential gold standard tool for the diagnosis of OSA, it is costly, complex, is not readily available, especially in underdeveloped countries, requires expert technical service, and in many countries it is difficult to access. For better prediction of OSA, radiographic modalities including MRI, computed tomography, and ultrasonography (US) have been applied to assess the upper airway anatomy in OSA patients [8]. However, MRI and computed tomography cannot be widely applied due to the high

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costs and radiation exposure. However, US is less expensive, available, radiation-free, and portable, thereby allowing for high accessibility for screening and can demonstrate the vocal cords and air column of the upper airway clearly, and thus capable for detecting anatomic risk factors for OSA, including parapharyngeal space and tongue. Therefore, a simpler and less costly method is needed as a screening method to detect and pick up patients who are at a high risk for OSA when considering the use of full overnight PSG to confirm the diagnosis of OSA [9]. However, no studies suggest anthropometric measurements except for NC as a risk factor for OSA. Chronic inflammation in OSAS may play an important role in the progression of atherosclerosis and cardiovascular disease [10,11]. The hypothesis of a correlation between anthropometric measurements and OSAHS was the basis of the present study that aimed to investigate this correlation and demonstrate probable positive predictive anthropometric indices and ultrasonic parameters (anatomical and dynamic) and their cutoff values for suspecting the diagnosis of OSAHS and its severity compared with PSG parameters.

## **Patients and methods**

### **Inclusion criteria**

A total of 80 adult patients with at least one of the major OSA symptoms, including snoring, daytime sleepiness, nocturnal gasping or choking, and witnessed apnea in their first medical visit were included in this study that was conducted between January 2012 and January 2015 at Departments of Endocrinology, Chest, Physiotherapy, and ENT, Faculty of Medicine, Ain Shams University Hospitals and Misr University for Science and Technology. This study was approved by IRB/ethics committee. The purpose of the study was explained and written informed consent was obtained from all participants. Full medical history along with clinical examination was performed for all patients (demographic data for all participants was noted along with the physiological parameters such as blood pressure, respiratory rate, and pulse rate). Patients were assessed for any cardiovascular disease risk factors, including the presence or absence of medically diagnosed hypertension, diabetes mellitus, dyslipidemia, and current smoking status.

### **Exclusion criteria**

Patients with previous diagnosis of OSA, continuous positive airway pressure treatment, or bilevel positive airway pressure therapy, known cases of type 2 diabetes mellitus, hypertension, neurologic disorders,

hypothyroidism, Cushing syndrome, pregnancy, malignancy, congestive heart failure, psychotic disorder, nephrotic syndrome, or chronic renal failure, chronic liver failure, and also patients with respiratory infection and/or failure were excluded from the study. Patients with critical illness with poor functional status, those with a history of heart failure, history of acute coronary syndrome, myocardial infarction, and/or any revascularization procedure and refractory arrhythmia were also excluded from the study. Participants not able to stand/nonambulatory, participants not willing to participate were also excluded.

### **Anthropometric profile**

Body weight of all participants was recorded in erect position without shoes and wearing only light indoor clothes, with a bathroom weighing scale. Height was measured to the nearest 1 cm and BMI was calculated as body weight/height<sup>2</sup> (kg/m<sup>2</sup>). The circumferences were measured and assessed with the aid of nonelastic nonflexible measuring tape and recorded in centimeters. WC (AC) was measured (with patients in the standing position) midway between the lower rib cage margin and the anterior superior iliac spine. The reading was taken at the end of a normal exhalation. HC was measured with patients in the standing position at the maximum circumference of the buttocks (along a horizontal line at the femoral greater trochanter) with the participant standing with feet placed together. Waist-hip ratio (WHR) was calculated by dividing the waist circumference by the HC. NC was measured along a horizontal line across the midline of the thyroid cartilage (at the level of the cricothyroid membrane). Anthropometric measurements were based on the National Health and Nutrition Examination Survey guidelines [5].

### **Polysonnography**

An overnight PSG evaluation with a Somnostar Pro 7-3a (Cardinal Health Inc., Dublin, Ohio, USA) was performed for all patients suspected to have OSA at Cairo Sleep Center. A transducer system connected to a nasal cannula was used to record and detect all respiratory events. Snoring was monitored with a microphone placed on the larynx at the anterosuperior portion of the neck. Full-night video recordings were also performed during the sleep test period. All of the evaluations were terminated after the final waking in the morning. The PSG data were collected in a computerized PSG system, and the scoring process was performed manually. Respiratory events were scored according to the updated criteria of

the American Academy of Sleep Medicine. Apnea was defined as a cessation of airflow lasting at least 10 s. Hypopnea was defined by more than 4% drop in oxygen saturation in addition to more than 30% drop in airflow for more than 10 s [12].

The apnea-hypopnea index (AHI) was defined as the number of apnea and hypopnea events that occurred per hour of sleep. The AHI, when associated with typical symptoms was scored and classified as follows: AHI of at least 5 events/h was diagnosed as OSA, of which  $15 > \text{AHI} \geq 5$  events/h was considered mild,  $30 > \text{AHI} \geq 15$  events/h was classified as moderate, and more than or equal to 30 events/h was considered as severe OSA. Those who had an AHI less than 5 were included in the study as the non-OSA group.

#### Submental ultrasonography

Submental US was performed by an independent operator who was blinded to the PSG results. Submental US was performed using a Toshiba Aplio 500 Platinum platform (Toshiba, Otawara, Japan) using a 1–6-MHz convex transducer. The following measurements were evaluated: distance between lingual arteries (DLA), retropalatal diameter (RPD) in the transverse dimension, retroglossal (RG) airspaces, and tongue base thickness in the sagittal plane. The RPD and RG were measured during the resting state and under Muller's maneuver (MM) (which was performed by an attempt at vigorous inhalation with the mouth and nose closed). With the patient in a seated position, the transducer was introduced to the skin of the neck in the submental region coronally, immediately cephalad to the body of the hyoid bone, and midsagittally (i.e. in the area between the hyoid bone and the symphysis of the mandible).

#### Laboratory measurements

The biochemical parameters analyzed included total cholesterol, triglyceride, fasting blood glucose, HbA1c, erythrocyte sedimentation rate, high sensitivity C-reactive protein, and complete blood cell count. The platelet lymphocyte ratio was calculated by dividing the lymphocyte from the platelet.

#### Statistical analysis

Statistical analysis was performed manually as well as using statistical package for the social sciences (SPSS; Shandong Weigao Group Medical Company, China), version 21. Patient's demographic data – that is, age, sex, BMI, height, and weight distribution – were analyzed and expressed as mean $\pm$ SD for continuous

variables and as numbers and percentages, for categorical variables. Correlation coefficient was used to find the strength of association between numerical variables – that is, anthropometric measurements, submental US measurements, and PSG parameters. Continuous variables were compared with Student's *t*-tests, and categorical variables were compared with a  $\chi^2$ -test or Fisher's exact test, as appropriate. After adjusting for age, sex, and smoking status, a logistic regression analysis was used to evaluate the significance of the individual anthropometric indices for the presence of OSA. Linear regression analysis was performed to evaluate the significance of the individual anthropometric indices for the severity of OSA. *P* values less than 0.05 were considered statistically significant. Receiver operating characteristics (ROC) analysis was used to determine the optimal cutoff values of the individual anatomical and dynamic US indices and individual anthropometric indices for predicting and screening for OSA using computer-generated randomization of the OSA patients with complete data, multivariate analysis of the patient group. The analysis of variance test was used for independent measures to compare the means of more than two independent samples. The distribution of data was assessed using the Kolmogorov–Smirnov test of normality.

#### Results

Fifty-two (65%) of the included 80 patients with suspected OSAS were confirmed to have the disease using PSG with AHI more than or equal to 5 (the OSA group), whereas it was excluded in the remaining 28/80 (35%) with AHI less than 5 (the non-OSA group). There was a highly significant statistical increase in NC, WC, HC, and WHR in patients with OSA than in those without. As regards US findings, anatomical parameters showed a highly statistically significant increase in both resting tongue base thickness and DLA among OSA patients than among those without. Moreover, there was a highly significant statistical decrease or shortening in the RPD as regards resting measure and MM in the OSA group than among patients in whom OSA was not confirmed along with shortening of the retroglossal diameter (RGD) (as regards resting measure and MM) in OSA patients as well than among those without, but in a nonsignificant manner. As regards dynamic ultrasound parameters, changes in RPD as regards % MM showed a highly statistically significant increased percentage of shortening and narrowing among patients with OSA. Although RGD showed increased percentage of shortening and narrowing as

**Table 1** Baseline characteristics, demographic data, polysomnographic and ultrasonic parameters, and laboratory values among the studied participants

Variables	AHI $\geq 5$ (OSA group) (mean $\pm$ SD)	AHI $<5$ (non-OSA group) (mean $\pm$ SD)	P value
n/N (%)	52/80 (65)	28/80 (35)	–
Smoking [n/N (%)]	22/52 (42.3)	8/28 (28.6)	0.013
Age (years)	49.97 $\pm$ 11	42.32 $\pm$ 16	0.012
Sex [n/N (%)]			<0.001
Male	39/52 (75)	14/28 (50)	
Female	13/52 (25)	14/28 (50)	
Hypertension [n/N (%)]	17/52 (32.7)	3/28 (10.7)	<0.001
BMI (kg/m <sup>2</sup> )			<0.001
Male	28.3 $\pm$ 2.35	25.3 $\pm$ 2.14	
Female	25.7 $\pm$ 3.28	23.4 $\pm$ 1.21	
NC (cm)			<0.001
Male	39.93 $\pm$ 4.11	34.21 $\pm$ 3.8	
Female	35.13 $\pm$ 2.14	31.01 $\pm$ 1.7	
AC (WC) (cm)			<0.001
Male	103.87 $\pm$ 18.35	90.93 $\pm$ 16.11	
Female	90.9 $\pm$ 15.45	86.65 $\pm$ 22.31	
HC (cm)			<0.001
Male	114.15 $\pm$ 18.34	99.32 $\pm$ 12.43	
Female	99.36 $\pm$ 14.23	95.17 $\pm$ 21.39	
AHR (WHR)			<0.001
Male	95.6	91.3	
Female	92.7	88.4	
Apnea index (/h)	24.0 $\pm$ 33.5	0.7 $\pm$ 21.4	<0.001
Hypopnea index (/h)	16.7 $\pm$ 1.26	1.1 $\pm$ 3.32	<0.001
AHI (/h)	33.7 $\pm$ 16.5	1.9 $\pm$ 23.7	<0.001
Mean SaO <sub>2</sub> (%)	92 $\pm$ 14.0	95.9 $\pm$ 1.5	0.325
FBS (mg/dl)	115.21 $\pm$ 31.17	90.32 $\pm$ 25.22	0.01
HbA1c (%)	6.79 $\pm$ 0.65	5.13 $\pm$ 0.40	0.01
Total serum cholesterol (mg/dl)	189.3 $\pm$ 35.7	168.9 $\pm$ 32.1	0.13
TG (mg/dl)	158.65 $\pm$ 54.3	139.89 $\pm$ 63.2	0.53
ESR (mm/h)	19.87 $\pm$ 25.4	9.84 $\pm$ 21.5	0.21
hs-CRP (mg/l)	1.13 $\pm$ 1.24	0.65 $\pm$ 1.47	0.43
WBC ( $\times 10^6/l$ )	75934 $\pm$ 235	6637 $\pm$ 174	0.13
Neutrophil (%)	59.98 $\pm$ 14.5	52.41 $\pm$ 13.4	0.01
Lymphocyte (%)	27.4 $\pm$ 8.35	36.1 $\pm$ 9.87	<0.001
Eosinophil (%)	2.60 $\pm$ 1.99	2.24 $\pm$ 1.66	0.217
Monocyte (%)	8.51 $\pm$ 5.96	7.91 $\pm$ 2.54	0.234
Hb (g/dl)	14.3 $\pm$ 2.8	13.2 $\pm$ 1.6	0.001
Hct (%)	42.98 $\pm$ 1.67	40.31 $\pm$ 3.85	0.01
RBC ( $\times 10^9/l$ )	4687 $\pm$ 282.7	4523 $\pm$ 326.1	0.17
RDW (%)	13.0 $\pm$ 0.34	13.1 $\pm$ 1.42	0.62
Platelet ( $\times 10^9/l$ )	245.7 $\pm$ 60.96	236.5 $\pm$ 32.73	0.001
PLR	127.98 $\pm$ 74.53	97.75 $\pm$ 84.21	<0.001
PDW (%)	16.4 $\pm$ 0.99	15.9 $\pm$ 1.12	0.001
US parameters (mm)			
Resting tongue base thickness	44.23 $\pm$ 7.1	38.46 $\pm$ 2.4	<0.001
DLA	33.72 $\pm$ 17.9	26.93 $\pm$ 13.4	<0.001
RPD (mm)			
Resting	29.43 $\pm$ 17.13	34.61 $\pm$ 14.11	<0.001
Muller maneuver	22.34 $\pm$ 5.34	27.21 $\pm$ 3.41	<0.001
Change at Muller maneuver (%)	32	25	<0.001
RGD (mm)			
Resting	32.32 $\pm$ 1.2	33.12 $\pm$ 3.4	0.213
Muller maneuver	24.23 $\pm$ 4.0	25.14 $\pm$ 1.7	0.192
Change at Muller maneuver (%)	33	32	0.154

AC, abdominal circumference; AHI, apnea–hypopnea index; AHR, abdominal hip ratio; DLA, distance between lingual arteries; DLA, distance between lingual arteries; ESR, erythrocyte sedimentation rate; FBS, fasting blood sugar; Hb, hemoglobin; HbA1c, hemoglobin A1c; HC, hip circumference; Hct, hematocrit; hs-CRP, high sensitivity C-reactive protein; NC, neck circumference; OSA, obstructive sleep apnea; PDW, platelet volume distribution width; per deciliter; PLR, platelet lymphocyte ratio; RBC, red blood cell; RDW, red cell distribution width; RGD, retroglossal diameter; RPD, retropalatal diameter; SaO<sub>2</sub>, oxygen saturation; TG, triglyceride; US, ultrasonography; WBC, white blood cell; WC, waist circumference; WHR, waist–hip ratio.



well among OSA group patients, it was in a nonsignificant manner (Table 1).

In the present study, 13/52 (25%) of the diagnosed OSA patients were found to have mild OSA, 15/52 (28.8%) had moderate OSA, and the remaining 24/52 (46.2%) were diagnosed with severe OSA (Table 2).

There was a highly significant statistical increase in NC, WC, HC, and WHR among male patients than among female patients. Despite being younger, the severity of OSA was significantly higher in men compared with women as they had significantly higher AHI compared with female patients. There was a nonsignificant statistical increase in BMI among male patients than among female patients. Age was significantly higher among female patients than among male patients (Table 3).

Statistically significant increase in age, BMI, and WC (AC) with increased OSA severity as regards AHI was found. Highly significant statistical increase in NC with increased AHI was found among OSA patients, but

**Table 2 Severity of obstructive sleep apnea among the studied diagnosed 52 patients according to apnea-hypopnea index**

Variables	Mild OSA	Moderate OSA	Severe OSA
n/N (%)	13/52 (25)	15/52 (28.8)	24/52 (46.2)

OSA, obstructive sleep apnea.

**Table 3 Comparison between sex and anthropometric values among obstructive sleep apnea patients**

Variables	Male (mean±SD)	Female (mean±SD)	P value
n/N (%)	39/52 (75)	13/52 (25)	
Age (years)	45.1±23.4	54.4±21.3	<0.001
BMI (kg/m <sup>2</sup> )	28.3±2.35	25.7±3.28	0.229
NC (cm)	39.93±4.11	35.13±2.14	<0.001
WC (AC) (cm)	103.87±18.35	90.9±15.45	<0.001
HC (cm)	114.15±18.34	99.36±14.23	<0.001
WHR (AHR)	95.6	92.7	<0.001
AHI (/h)	34.45±9.17	23.32±3.11	<0.001

AC, abdominal circumference; AHI, apnea-hypopnea index; AHR, abdominal hip ratio; HC, hip circumference; NC, neck circumference; WC, waist circumference; WHR, waist-hip ratio.

**Table 4 Comparison between anthropometric indices and obstructive sleep apnea severity**

Variables	Mild OSA (mean±SD)	Moderate OSA (mean±SD)	Severe OSA (mean±SD)	P value
Age (years)	43.2±11.21	45.3±12.45	48.6±18.52	0.01
BMI (kg/m <sup>2</sup> )	25.12±29.65	25.99±31.21	27.35±22.73	0.01
NC (cm)	36.1±33.5	37.5±29.87	39.4±45.22	<0.001
WC (AC) (cm)	95.2±12.45	99.5±18.92	104.1±14.56	0.01
HC (cm)	99.9±45.8	104.8±32.3	107.2±21.6	0.123
WHR (AHR)	93.2	93.4	94.2	0.249

AC, abdominal circumference; AHR, abdominal hip ratio; HC, hip circumference; NC, neck circumference; OSA, obstructive sleep apnea; WC, waist circumference; WHR, waist-hip ratio.

nonsignificant statistical increase was found as regards HC and WHR with increased severity of OSA in patients with OSA diagnosis (Table 4).

After adjusting for age, sex, and smoking, a logistic regression model that was used to evaluate the significance of the individual anthropometric indices for the presence of OSA showed highest significant correlation between NC and the diagnosis and presence of OSA. Lesser significance was found between BMI and HC and OSA diagnosis. However, no significant correlation was found between HC or WHR and the presence of OSA (Table 5).

In the ROC analysis that was used to determine the optimal cutoff values of the individual anthropometric indices for predicting OSA, the cutoff value of 39.5 cm for NC (sensitivity of 80% and specificity of 77%) showed the most predictive value for both the presence and the severity of OSA, followed by 94.4 cm for WC (sensitivity of 69% and specificity of 75%), and 26.98 kg/m<sup>2</sup> for BMI as the least predictive diagnostic index and for severity as well (sensitivity of 67% and specificity of 66%) and were optimal for male patients. However, the values of 37.3 cm for NC (sensitivity of 83% and specificity of 84%), followed by 88.9 cm for WC (sensitivity of 74% and specificity of 65%), and 25.23 kg/m<sup>2</sup> for BMI, which had the least predictive value for diagnosis and severity of OSA (sensitivity of 58% and specificity of 59%), were optimal for female patients (Table 6 and Fig. 1).

As regards anatomical US parameters, there was a highly significant statistical positive correlation between resting tongue base thickness and OSA severity. There was also highly significant statistical positive correlation between DLA and OSA severity. Highly significant progressive shortening and narrowing was found for RPD with progression of OSA severity and AHI in both resting position and MM, being longest in mild OSA and became narrower in moderate OSA to reach the shortest and narrowest values. In severe OSA, nonsignificant progressive

**Table 5 Evaluation of the correlation and significance of the individual (univariate) anthropometric indices for diagnosis of obstructive sleep apnea**

Variables	Presence of OSA		P value
	Odd ratio	Confidence interval (95% CI)	
BMI (kg/m <sup>2</sup> )	1.245	1.31–1.63	0.01
NC (cm)	1.312	1.22–1.82	<0.001
WC (AC) (cm)	1.231	1.15–1.26	0.01
HC (cm)	1.104	1.04–1.10	0.132
WHR (AHR)	1.113	1.02–1.12	0.241

AC, abdominal circumference; AHR, abdominal hip ratio; CI, confidence interval; HC, hip circumference; NC, neck circumference; WC, waist circumference; WHR, waist–hip ratio.

**Table 6 Accuracy, sensitivity, and specificity of the possible optimal cutoff values of the individual anthropometric indices for predicting the presence and severity of obstructive sleep apnea**

Variables	Cutoff values	Sensitivity (%)	Specificity (%)
BMI (kg/m <sup>2</sup> )			
Male	26.98	67	66
Female	25.23	58	59
NC (cm)			
Male	39.5	80	77
Female	37.3	83	84
WC (AC) (cm)			
Male	94.4	69	75
Female	88.9	74	65

AC, abdominal circumference; NC, neck circumference; WC, waist circumference.

shortening and narrowing was found in RGD with progression of OSA severity and AHI in both resting position and MM. However, dynamic US parameters revealed highly statistically significant increased percentage of shortening and narrowing in RPD at %MM with progressive OSA severity and AHI. However, there was a nonsignificant statistically increased percentage of shortening and narrowing in RGD at %MM with progressive OSA severity and AHI (Table 7).

After adjusting for age, sex, and smoking, a logistic regression model that was used to evaluate the significance of the individual (univariate) anatomical and dynamic US indices for the presence of OSA showed highest significant correlation between all RPD indices (mostly on MM and also the change at %MM and the least was the measures at resting position) and DLA and the diagnosis or screening for the presence of OSA. Lesser significance was found between resting tongue base thickness and OSA diagnosis. However, no significant correlation was found between all RGD indices (with resting position, on MM, and also the change at %MM) and the presence of OSA (Table 8).

In the ROC analysis that was used to determine the optimal cutoff values of the individual anatomical and

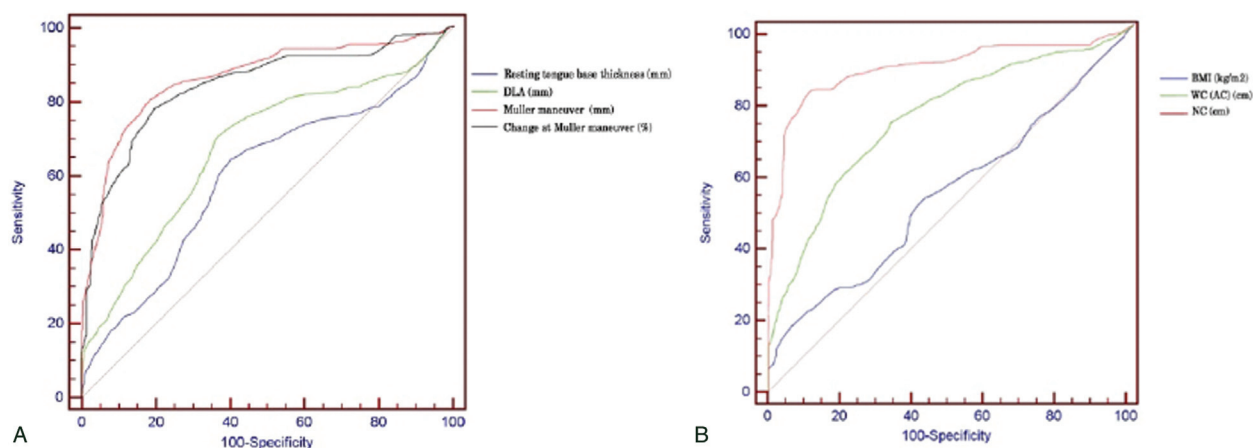
dynamic US indices for predicting and screening for OSA, the cutoff value of 25 mm for RPD during MM (sensitivity of 80% and specificity of 82%) showed the most predictive value for both the presence and the severity of OSA, followed by a cutoff value of 20% change at %MM (sensitivity of 79% and specificity of 80%), 30 mm cutoff value for the distance between lingual arteries (DLA) (sensitivity of 70% and specificity of 64%) and the least predictive index was that for resting tongue base thickness with a cutoff value of 40 mm with a sensitivity of 64% and specificity of 59% for screening of OSA and its severity (Table 9 and Fig. 2).

In the ROC analysis the optimal cutoff values of the individual anatomical and dynamic US indices for predicting and screening for OSA were used. Using computer-generated randomization of the OSA patients with complete data, multivariate analysis of the patients group identified %RP shortening on MM as independent predictors of screening and severity OSA. With these two factors, the probability [logit (*P*)] was generated using the following formula:  $\text{logit } (P) = 215.801 + 0.321 \times \text{NC} + 0.083 \times (\% \text{RP shortening at MM})$ . The outline of probabilities was generated using the quartiles of NC and %RP shortening on MM. The optimal cutoff value for probability was calculated based on the most significant cutoff values in each univariate analysis. Multivariate analyses probability was found to be highest when combined NC and RPD (%MM change) were plotted with each other, raising both sensitivity and specificity for both screening of OSA patients and severity than each used individually as univariate index or value. Therefore, combined NC and a decreased proportion of Muller's RPD had the best diagnostic probability, sensitivity, and specificity in the diagnosis of OSA and predicting its severity OSA probability was predicted with 100% sensitivity and 90% specificity (Table 10).

## Discussion

OSA is considered the most severe form of sleep-related breathing disorders [2]. Obesity, particularly

Fig. 1



Receiver operating characteristic (ROC) analysis to determine the optimal cutoff values of the individual anthropometric indices for predicting obstructive sleep apnea (OSA) in (a) male and in (b) female patients

**Table 7 Comparison between ultrasonography anatomical and dynamic changes and obstructive sleep apnea severity**

US parameters	Mild OSA (mean±SD)	Moderate OSA (mean±SD)	Severe OSA (mean±SD)	P value
Resting tongue base thickness (mm)	41.31±2.33	49.1±3.41	58.2±6.62	<0.001
DLA (mm)	31.32±9.7	35.45±5.1	40.96±8.5	<0.001
RPD				
Resting (mm)	34.14±19.33	23.12±11.78	28.54±16.23	<0.001
Muller maneuver (mm)	27.42±12.56	22.43±16.43	17.05±19.53	<0.001
Change at Muller maneuver (%)	23	38	56	<0.001
RGD				
Resting (mm)	39.87±3.3	38.65±1.5	35.27±2.8	0.243
Muller maneuver (mm)	28.9±1.6	26.8±3.9	23.9±2.4	0.156
Change at Muller maneuver (%)	37	38	40	0.467

AHI, apnea-hypopnea index; DLA, distance between lingual arteries; MM, Muller maneuver; OSA, obstructive sleep apnea; RGD, retroglossal diameter; RPD, retropalatal diameter; US, ultrasonography.

**Table 8 Evaluation of the correlation and significance of the individual (univariate) anatomical and dynamic ultrasonography indices for diagnosis of obstructive sleep apnea**

US parameters	Presence of OSA		P value
	Odd ratio	Confidence interval (95% CI)	
Resting tongue base thickness (mm)	1.142	1.035–1.213	0.001
DLA (mm)	1.321	1.117–1.602	<0.001
RPD			
Resting (mm)	0.746	0.691–0.851	0.001
Muller maneuver (mm)	0.854	0.805–0.987	<0.001
Change at Muller maneuver (%)	1.431	1.011–1.726	<0.001
RGD			
Resting (mm)	0.887	0.816–0.975	0.513
Muller maneuver (mm)	0.832	0.763–0.998	0.145
Change at Muller maneuver (%)	1.157	0.954–1.218	0.124

CI, confidence interval; DLA, distance between lingual arteries; OSA, obstructive sleep apnea; RGD, retroglossal diameter; RPD, retropalatal diameter; US, ultrasonography.

central obesity, is significantly associated with an increased prevalence of OSA. Although PSG is considered as an essential gold standard tool for screening and diagnosing OSA, it is costly, complex, not readily available and difficult to access, especially in underdeveloped countries, expensive, and requires

expert technical services [13]. Therefore, a simpler and less costly method is required as a screening method for OSAHS. The present study analyzed various anthropometric indices and ultrasonic parameters (anatomical and dynamic) and their associations with the presence, as well as the severity

of OSA, and to determine their possible cutoff values for predicting patients at risk for OSA, outcome, and severity. A total of 80 adult patients with at least one of the major OSA symptoms who had undergone

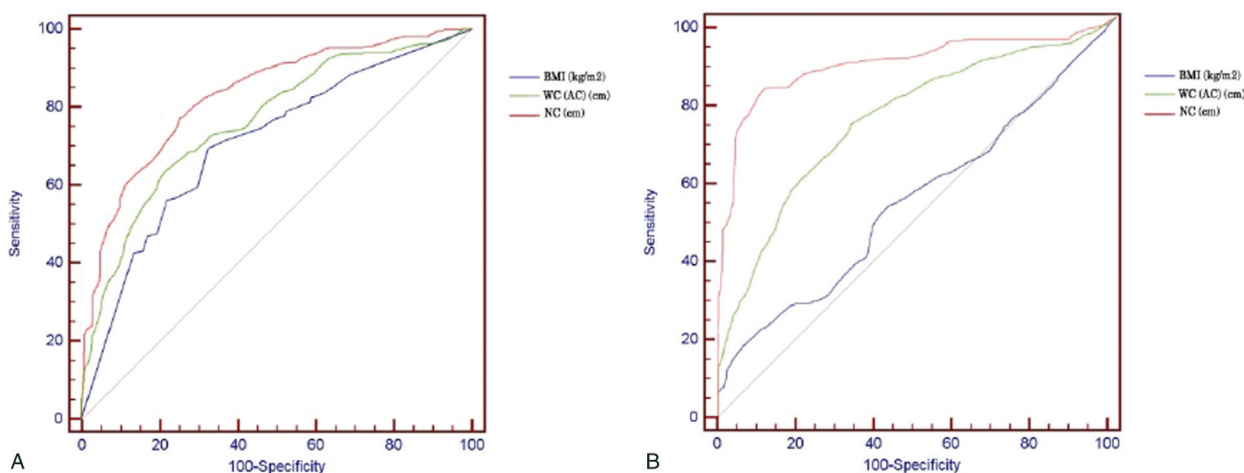
anthropometric measures, including AC, HC, and NC, PSG, and submental ultrasound, were included in this study. In the present study, there was a highly significant statistical increase in NC, WC, HC, and WHR in patients with confirmed OSA than in those without, and among male patients than among females. Despite being younger, the severity of OSA was significantly higher in men compared with women as they had significantly higher AHI compared with female patients. There was a nonsignificant statistical increase in BMI among male patients than among female patients. Age was significantly higher among female patients than among male patients. This is in accordance with the studies by Wang *et al.* [6], who have reported that women with OSA had lesser respiratory disturbances compared with male patients, despite their higher age, and the severity of OSA was significantly higher among male patients. The mechanisms that potentially explain this difference may include the following: significant variation in body fat distribution, dimensions, diameters, and collapsibility of the upper airways, hormonal status, and variability in ventilation

**Table 9 Accuracy, sensitivity, and specificity of the possible optimal cutoff values of the individual anatomical and dynamic ultrasonography indices for diagnosis of obstructive sleep apnea**

US parameters	Cutoff values	Sensitivity (%)	Specificity (%)
Resting tongue base thickness (mm)			
Male	40	64	59
Female	38	62	61
DLA (mm)			
Male	30	70	64
Female	29	72	62
RPD			
Muller maneuver (mm)			
Male	25	80	82
Female	24	82	83
Change at Muller maneuver (%)			
Male	20	79	80
Female	19	77	81

DLA, distance between lingual arteries; RPD, retropalatal diameter; US, ultrasonography.

**Fig. 2**



Receiver operating characteristic (ROC) analysis to determine the optimal cutoff values of the individual anatomical and dynamic ultrasonography (US) indices for predicting obstructive sleep apnea (OSA) in (a) male and in (b) female patients

**Table 10 Multivariate analyses probability for diagnosing and screening for obstructive sleep apnea and severity**

Variables	Presence of OSA (univariate analysis)		P value	Presence of OSA (multivariate analysis)		P value
	Odd ratio	Confidence interval (95% CI)		Odd ratio	Confidence interval (95% CI)	
NC (cm)	1.312	1.22–1.82	<0.001	1.201	1.024–2.34	<0.001
DLA (mm)	1.321	1.117–1.602	<0.001			
RPD						
Muller maneuver (mm)	0.854	0.805–0.987	<0.001	1.301	1.015–1.659	<0.001
Change at Muller maneuver (%)	1.431	1.011–1.726	<0.001			

AHI, apnea–hypopnea index; CI, confidence interval; DLA, distance between lingual arteries; NC, neck circumference; OSA, obstructive sleep apnea; RPD, retropalatal diameter.



control. In particular, sex hormone variability is a well-known recognized risk factor for OSA in women. There was a highly significant statistical increase in NC, significant statistical increase in age, BMI, and WC (AC), but a nonsignificant statistical increase as regards HC and WHR with increased severity of OSA (with increased AHI). These are in accordance with the study performed by Hyeon *et al.* [14] in which NC was considered as a more potent significant predictor for the presence and diagnosis of OSA and its severity compared with other anthropometric variables such as WC and BMI. They concluded that NC reflected upper body obesity and was considered to be a better and more valuable marker compared with BMI, WC, or HC for OSA. They also found that BMI was not significantly different between the groups. These were also in agreement with previous studies performed by Hoffstein and Mateika [13], Ogretmenoglu *et al.* [15], and Young *et al.* [16], who have reported that there was a great association between obesity and OSA, and they also found that patients with OSA had a significantly higher age, BMI, WC, and NC compared with patients without OSA. Yamagishi *et al.* [17], Jeong *et al.* [18], and Eun *et al.* [19] also supported the present study results, as they found that the risk for OSA further increases in individuals with upper body obesity. This may be attributed to the fact that obese OSA patients have a bigger tongue and a narrower upper airway passage. As regards the efficacy of BMI as a predictor of OSA, wide variations in the cutoff values were found among different populations in several studies, thus supporting the present study results that rendered BMI as a less significant and less sensitive index for screening and diagnosing OSA and its severity compared with NC and WC; this may be attributed to the fact that Asians were found to have a higher percentage of body fat compared with White of the same age, sex, and BMI [20]. For this reason, a proportion of the Asian population with a high risk for developing OSA might have BMIs below the existing BMI cutoff value of 25 kg/m<sup>2</sup>, and hence different phenotypic features may contribute differently to the development of OSA. Medeiros *et al.* [21] and Simpson *et al.* [22] also agreed with the present study results and stated that NC is considered a significant marker for central obesity and has been associated not only with OSA but also with increased cardiovascular risk and insulin levels in OSA patients, and because NC is an easily obtainable measurable index with the use of only a tape measure, it is a useful valuable measure in clinical practice. In the present study, highest significant correlation was found between NC and the

diagnosis of OSA. Lesser significance was found between BMI and HC and OSA diagnosis. However, no significant correlation was found between HC or WHR and the presence of OSA. Moreover, the optimal cutoff value for male patients were as follows: 39.5 cm for NC (sensitivity of 80% and specificity of 77%) showing the most predictive value for both the presence and the severity of OSA, followed by 94.4 cm for WC (sensitivity of 69% and specificity of 75%), and 26.98 kg/m<sup>2</sup> for BMI as the least predictive diagnostic index and for severity as well (sensitivity of 67% and specificity of 66%). However, the values of 37.3 cm for NC (sensitivity of 83% and specificity of 84%), followed by 88.9 cm for WC (sensitivity of 74% and specificity of 65%) and 25.23 kg/m<sup>2</sup> for BMI, which had the least predictive value for diagnosis and severity of OSA (sensitivity of 58% and specificity of 59%), were optimal for female patients. These were supported by Ogretmenoglu *et al.* [15], Zhou *et al.* [23], and Hızlı *et al.* [10], who reported that NC has a greater value compared with WC as regards an association with OSA in adult patients. They suggested that the optimal cutoff values of NC for predicting OSA were 35.5 cm in female patients and 39 cm in male patients. Soylu *et al.* [9] from Brazil and Onat *et al.* [4] from the USA showed a similar trend in the present study and found that cutoff value for NC was 40 cm for male patients and 36 cm for female patients. In light of these results and conclusions, NC might be a more useful independent predictor for OSA that is less influenced by ethnicity differences all over the world compared with the other anthropometric indices. In addition, the sex differences in the optimal cutoff values of NC, which was ~4 cm, were also almost similar, and this was similar to the results of these and the present studies. The present study results are in accordance with Soylu *et al.* [9], who found that the cutoff value for WC that has been demonstrated as a risk factor of OSA was over 94 cm in male patients and more than 85 cm in female patients. In a study by Ogretmenoglu *et al.* [15], the cutoff value of WC was not in accordance with the present study indices as well, as it was found to be 105 cm in male patients and 101 cm in female patients in a Turkish population. Onat and colleagues [4] did not confirm the present study results as they found that WC correlates most significantly with AHI for both men and women unlike the present study, and a WC value over 89.01 cm for male patients and over 75.95 cm for female patients determined the risk for OSA (lower than that in the present study). This may be attributed to variable fat distribution according to different races and ethnic variability among different population all over the world.

Despite suffering from a similar grade of OSA severity, Asian patients were found to be less obese compared with White patients, suggesting that ethnicity and race may differentially and variably contribute to OSA with higher probability in some populations compared with others from different countries and races; this may be attributed to the difference in fat distribution and craniofacial variables among populations in different countries [24]. Moreover, the present study results were against those found by Subramanian *et al.* [25], who concluded that BMI was the most influential factor that affects AHI, and weight, NC, WC, and HC are less significantly correlated with AHI. These discrepancies may be attributed to race/ethnic variability and different fat distribution and configuration among different populations of individuals all over the world, because body fat distribution and obesity severity depend on a complex interaction of different genetic and environmental factors. Lee *et al.* [24] evaluated the value of the differences in craniofacial structure and obesity in 150 adults with OSA (74 White and 76 Chinese) and found that Chinese patients with the same degree of obesity as Whites had more severe form of OSA and more craniofacial bony restriction, explaining such discrepancies; therefore, genetic and or craniofacial structural factors might contribute significantly to the risk for OSA beyond obesity could do. Sharma *et al.* [26] have reported that a BMI of 30 kg/m<sup>2</sup> in both sexes was associated with the occurrence of OSA and found that the cutoff value of BMI for obesity in the White population was 30 kg/m<sup>2</sup> but some Asian populations have redefined obesity at a lower BMI of 25 kg/m<sup>2</sup>. In a study that was performed by Young *et al.* [27], they found that most of the Far East Asian men with OSA were not obese and large NC was highly associated with OSA than with obesity, and this result was consistent with a previous study that was conducted by Kawaguchi *et al.* [28]. A possible explanation for this finding is that localized adipose tissue distribution around the neck could be more associated with OSA than with general obesity, and OSA may be more vulnerable and related to the change in NC than other anthropometric indices. This conclusion may be confirmed by the fact that Asians have shorter and steeper anterior cranial bases with smaller and more posteriorly positioned mandibles compared with White, and they have craniofacial characteristics that render the upper airways more narrow and thus more prone and liable to collapse. Thus, NC may be a more effective fixed factor in determining the presence and severity of OSA among different population of patients all over the world [29]. Most of the studies did not perform

anatomic evaluation for different factors such as enlarged tonsils, oropharyngeal crowding, elongated and or redundant uvula, and soft palate, which might greatly and significantly influence the incidence and severity of OSA, and thus could not determine the effects of anatomic factors on OSA. To overcome such limitation submental US was used in the present study to assess anatomical and dynamic upper airway dimensions with possible predictive or confirmatory indices along with anthropometric parameters for both screening and predicting the severity of OSA. As regards US findings in the present study, anatomical parameters showed a highly statistically significant increase in both resting tongue base thickness and DLA among OSA patients and with increased OSA severity. Moreover, there was a highly significant statistical decrease or shortening in the RPD as regards resting measure and MM in the OSA group and with increased OSA severity along with shortening of the RGD (as regards resting measure and mm) in OSA patients, but in a nonsignificant manner. As regards dynamic US parameters, changes in RPD at %MM showed a highly statistically significant increased percentage of shortening and narrowing among patients with OSA than those without (32 vs. 25%, respectively) ( $P < 0.001$ ). RGD showed increased percentage of shortening and narrowing as well among OSA group patients and with increased severity, but in a nonsignificant manner. Moreover, the present study showed highest significant correlation between all RPD indices (mostly on MM and also the change at %MM and the least was the measures at resting position) and DLA and the diagnosis or screening for the presence of OSA. Lesser significance was found between resting tongue base thickness and OSA diagnosis. However, no significant correlation was found between all RGD indices and the presence of OSA. In the present study, the cutoff value of 25 mm for RPD at MM (sensitivity of 80% and specificity of 82%) showed the most predictive value for both the presence and the severity of OSA, followed by cutoff value of 20% change at %MM (sensitivity of 79% and specificity of 80%), 30 mm cutoff value for the distance between lingual arteries (DLA) (sensitivity of 70% and specificity of 64%), and the least predictive index was that for resting tongue base thickness with a cutoff value of 40 mm with a sensitivity of 64% and specificity of 59% for screening of OSA and its severity. The studies by Li *et al.* [30] and Cheng *et al.* [31] are in disagreement with the present results, because they found that the RPD and reduced proportion of Muller's RPD were not different for these two groups (OSA and non-OSA). This may be

attributed to technical difficulties as a drawback in their study, as they stated that the images of retropharyngeal space were difficult to capture with the currently used US probe in their study and also the number of their recruited patients was limited, whereas the tongue base thickness at rest and under MM was the most predictive and significant index for severity of OSA. The present study results were supported by Shu *et al.* [32], who reported that a change in Muller's RPD was a highly significant independent predictor for both OSA diagnosis and severity, and they proposed a prediction model combined with NC and a decreased proportion of Muller's RPD to improve accuracy, sensitivity, and specificity of these two combined indices for evaluating OSA severity as concluded in the present study. Moreover, the present study was in agreement with Lahav *et al.* [33], who used US to determine the width of the tongue base as a predictor for sleep disorder breathing patients and concluded that, when DLA exceeded 30 mm, the risk for OSA was significantly increased and showed that, with that cutoff point of 30 mm for DLA, the sensitivity, specificity, and accuracy for screening and diagnosis of OSA were 71.3, 66.7, and 63.6%, respectively, and stated that the lingual arteries are superficial to the RPS and they are easier to assess. The present study results were also in accordance with Chin-Chung *et al.* [34], who found that, among the different included measurable indices, NC was found to have the highest predictive value followed by RPD on MM %RP shortening on MM for both OSA diagnosis and severity, with 80% sensitivity and 84% specificity by RPD with a cutoff value of about 23.9 mm and 75% sensitivity and 65% specificity as regards DLA. However, unlike the present study, RGD on forced inspiration and MM, were found to be strongly correlated with AHI; this may be attributed to a certain limitation that was mentioned in their literature as they stated that, although all enrolled included patients cooperated, its effect on MM might not be the same for all patients indicating a possible technical defect in their study along with a limited number of patients in their study. Yonatan *et al.* [35] strongly confirmed the present study results as they concluded that the DLA was the single measurable parameter that was shown to strongly correlate with the studied variables and the other US measurements failed to demonstrate any similarly significant relationship. They also stated that the width of the lower tongue base, measured as the DLA, was found to be associated with the existence of and severity of OSA as well and their study also revealed that the distances of 30 mm between the lingual arteries can be considered as a point above

which patients have a higher risk for OSA, representing the most accurate and sensitive predictive cutoff value. The sensitivity and specificity of this indicator were found to be 74 and 67%, respectively (which were very close to the present study results). Furthermore, the lack of a correlation between the BMI and the AHI in their study ( $P=0.094$ ) made the DLA a more significant factor or index compared with the BMI in predicting the presence and severity of OSA in this group of suspected patients.

## Conclusion

Concomitant submental US and NC may be a promising tool for screening of OSA and its severity for possible early intervention.

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## Conflicts of interest

There are no conflicts of interest.

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