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Research Paper

Anatomic measures of upper airway structures in obstructive sleep apnea☆

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Abstract *Objective:* Determine if anatomic dimensions of airway structures are associated with airway obstruction in obstructive sleep apnea (OSA) patients.
Methods: Twenty-eight subjects with ($n = 14$) and without ($n = 14$) OSA as determined by clinical symptoms and sleep studies; volunteer sample. Skeletal and soft tissue dimensions were measured from radiocephalometry and magnetic resonance imaging. The soft palate thickness, mandibular plane-hyoid (MP-H) distance, posterior airway space (PAS) diameters and area, and tongue volume were calculated.
Results: Compared to controls, the OSA group demonstrated a significantly longer MP-H distance ($P = 0.009$) and shorter nasal PAS diameter ($P = 0.02$). The PAS area was smaller ($P = 0.002$) and tongue volume larger in the OSA group ($P = 0.004$). The MP-H distance, PAS measurements, and tongue volume are of clinical relevance in OSA patients.
Conclusions: A long MP-H distance, and small PAS diameters and area are significant anatomic measures in OSA; however the most substantial parameter found was a large tongue volume.

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Introduction

Craniofacial anatomical skeletal or soft tissue dimensions of the upper airway as measured from radiologic images in patients with obstructive sleep apnea (OSA) have been the focus of various studies for the last 25 years. However, the precise site of obstruction in OSA patients is still a matter of debate because different radiological methods have been used and none have been standardized.

In many institutions, radiocephalometry is the standard diagnostic approach used by otolaryngologists and sleep specialists to assess the site of obstruction in patients with OSA and ultimately, to plan surgical treatment. It is a simple, low-cost and easily available tool to assess skeletal morphology, especially maxillofacial abnormalities. It is widely used to measure the length, width and cross-sectional area of soft tissue susceptible to impinge on the posterior airway space.[1] Various cephalometric parameters correlate fairly well with the presence of OSA and its severity.[1,2] However, radiocephalometry is of limited potential when used for prognostic purposes regarding intervention.[3,4]

Radiocephalometry itself has several limitations. One important limitation is that the landmarks used to evaluate soft tissues or spaces are not very precise and therefore prone to analysis bias. Another limitation is that cephalometry gives only a two-dimensional representation that limits accurate representation of the three-dimensional structures of interest.

Three-dimensional information likely would be of tremendous value. Several 3-D imaging techniques have been developed, including computed tomography (CT), conebeam CT and magnetic resonance imaging (MRI).[4–7] Dynamic information also likely would be of great value. Several dynamic imaging techniques have been developed including cine-CT (cine fluoroscopy), electron beam computed tomography (EBCT), cine and real-time MRI.[3,8,9] The MRI methods have several advantages over radiocephalometry and CT by offering superior soft tissue contrast without exposure to ionizing radiation. None of these methods have been used specifically for airway measures in OSA patients though MRI has been used by Stuck et al[3] to assess anatomic dimensions of upper airway soft tissue morphology in subjects without OSA. Scarce information is found in the literature regarding anatomic sites of obstruction using MRI with simultaneous measures of respiratory events and function for subjects with sleep disordered breathing.

The purpose of our study was to determine what anatomic dimensions correlate with obstruction in adult sleep apnea compared to control subjects. Specifically, our study addresses the following questions: (1) What airway dimensions can be reliably ascertained from 2D and 3D imaging?; (2) Which skeletal and soft tissue dimensions of the upper airway structures are consistent with obstruction in patients with OSA?; (3) Do airway dimensions in OSA patients differ in comparison with non-OSA subjects?

Methods

Study design

A prospective, non-randomized case control series included 28 subjects (non-OSA = 14 and OSA = 14) recruited from, evaluated, and followed by the Department of Otolaryngology-Head and Neck Surgery, Stanford University, California. The study protocol was approved by the Institutional Review Board and written informed consent was obtained from all subjects.

Subjects

Inclusion criteria were (1) 18—70 years of age; (2) No evidence of claustrophobia; (3) No evidence of sleepiness or functional abnormality as determined by Epworth Sleepiness Score (ESS) and Functional Outcomes Sleepiness Questionnaire (FOSQ) for control subjects, and evidence of sleepiness or functional derangement in OSA subjects; (4) AHI $<$ 15 events/h in control subjects and an AHI $>$ 15 events/h for OSA subjects. We excluded patients who were pregnant, those with a body mass index (BMI) greater than 40 kg/m^2 and those with contraindications to MRI.

OSA was defined by conventional OSA sleep studies including an apnea-hypopnea index (AHI) and lowest oxyhemoglobin saturation score (LSAT), Fujita classification, FOSQ score, and ESS. All OSA subjects and three control subjects were evaluated using an attended overnight polysomnogram. Due to cost constraints, an alternative, unattended overnight assessment using a portable device (Watch-Pat 100, Itamar Inc., Israel) was used in the remaining 11 control subjects.

Cephalometry protocol

Lateral cephalometry was performed in 10 patients (control, $n = 5$; OSA, $n = 5$) with subjects awake and in a sitting position using a standardized technique described previously (C-Dental X-Ray, Inc, Palo Alto, CA).[1,10] During evaluation, the subjects were advised not to swallow and not to move.

From the lateral images (Fig. 1), the skeletal structures measured were the angle from sella to nasion to point A (SNA), angle from sella to nasion to point B (SNB), difference between SNA and SNB (ANB), and the distance from the mandibular plane to the hyoid (MP-H). The soft tissue structures measured were the length of the soft palate, and the posterior airway space (PAS) diameter at the mandibular plane. For cephalometric PAS, point B to gonion marked the reference plane.

Magnetic resonance imaging protocol

MRI investigations were performed in 28 patients (control, $n = 14$; OSA, $n = 14$) with the subject in the supine position in a 0.5 T MRI scanner (GE Medical Systems, Waukesha,

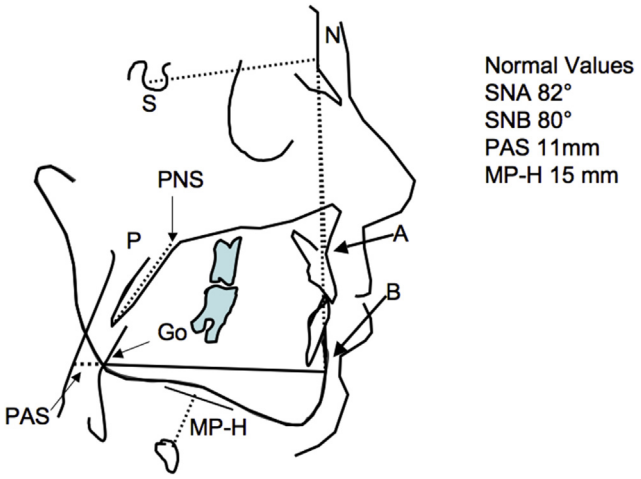

Fig. 1 Cephalometric analysis. S: sella; N: nasion; A: subspinale; B: supramentale; PNS: posterior nasal spie; Go: gonion; PAS: posterior airway space; MP-H: mandibular plane-hyoid distance.

WI, USA) using a multiplanar T1 localizing sequence (GE Turbo-Spin-Echo Sequence) in sagittal and coronal orientation. The subjects were advised not to swallow and not to move.

From the MRI scans the following distances, areas, and volumes were measured: maximum thickness of the soft palate, maximum length of the soft palate, PAS diameters at the nasal, occlusal and mandibular plane (measured on a line joining point B to gonion), PAS cross-sectional area (retrolingual space between nasal and mandibular planes) and tongue volume.

Analysis

The analysis of the 2D images was performed using imaging software (OsiriX Medical Imaging Software) that allows measures of distance and cross-sectional area after manually segmenting the structures of interest. Soft palate length (posterior nasal spine to tip of soft palate) and maximum thickness were estimated using two orthogonal lines. The PAS was then measured as the airway diameter along three parallel planes at the hard palate (nasal plane), the occlusal surface (incisive plane), and the mandible (mandibular plane) using the same reference points as Stuck et al[3] (Fig. 2A). For both imaging modalities, there was no significant difference between the measure for PAS at point B and that of the mandibular PAS, therefore, only mandibular PAS was reported.

PAS area was measured as the airway cross-sectional area from the nasal plane to the mandibular plane (Fig. 2B).

For tongue volume measures, a 3D image analysis application (Dextroscope, Volume Interactions, Singapore) was used. The tongue was defined as all its intrinsic muscles and the genioglossus, geniohyoid and mylohyoid muscles (Fig. 3) because, as Stuck et al[3] reported, the distinctions among them were not sufficiently and consistently clear from one image to the other or from one patient to the other. The *t*-test for normal continuous variables was used to test the null hypothesis that differences between groups were equal to zero. All results of continuous variables are expressed as mean $\pm$ standard deviation (SD) as per Kazis et al.[11]

Results

Subject demographics and sleep apnea outcome measures are shown in Table 1. The gender ratio was slightly asymmetrical but not statistically different ($P = 0.68$), with 5 of 14 female patients in the control group, compared to 3 of 14 female patients in the OSA group. BMI as expected was greater in the OSA group ($P = 0.015$). Further, OSA subjects reported significantly higher levels of functional disturbance than the control subjects, including a higher ESS score ($P = 0.01$) and a lower global FOSQ score ($P = 0.01$). While OSA patients had lower scores than controls in each of the five FOSQ sub-categories as defined by Weaver et al,[12] only the differences in scores for General Productivity and Social Outcome were statistically significant ($P < 0.05$) (Table 1).

Outcome measures of skeletal and soft tissue structures as determined by radiocephalometry and by MRI are

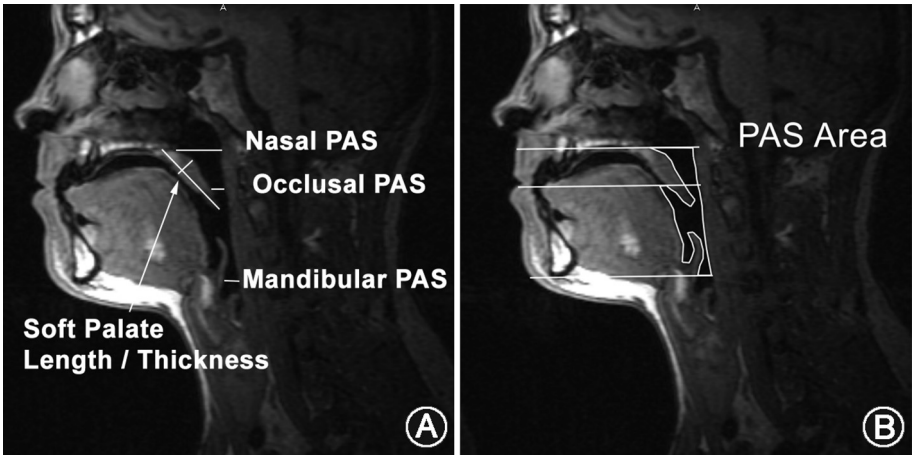

Fig. 2 A: Maximum length and thickness of the soft palate, and PAS diameter shown for nasal, occlusal, and mandibular planes; B: PAS area.

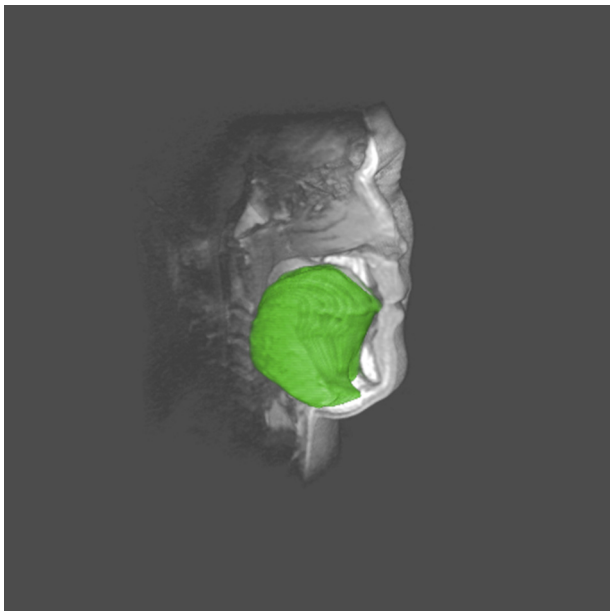

Fig. 3 Tongue volume from an OSA subject.

detailed in Table 2. The OSA group had normal SNA and SNB angles, according to current normal standard data.[1,2] However, SNA and SNB were significantly smaller than the values obtained among our control group, mean SNA = 91.5; mean SNB = 85.5. The mean cephalometric determined soft palate length of OSA subjects showed no difference compared to controls; however, a significant difference was shown in mandibular PAS and MP-H distance (Fig. 4).

Using both imaging modalities, the soft palate length did not differ between the OSA and non-OSA patients. However, compared to controls, the MP-H distance was significantly longer in the OSA group as measured with either type of imaging. Mandibular PAS diameter, while significantly shorter in the OSA group as measured by radiocephalometry, was not found to differ significantly between control and OSA subjects when assessed by MRI. Both imaging modalities showed that the PAS cross-sectional area was smaller in the OSA group compared to controls ($P = 0.002$).

The nasal and occlusal PAS diameters were measurable only with 3-D MRI, which demonstrated a significantly shorter nasal PAS diameter in the OSA group ($P = 0.02$), but no significant difference in occlusal PAS between control and OSA subjects (Fig. 5). Soft palate thickness, as assessed by MRI, also did not differ significantly between the two groups.

Tongue volume reached a mean of 124.02 cm^3 among the OSA patients compared to 97.43 cm^3 among the controls ($P = 0.0004$), as measured from the tomographic MRI (Fig. 6).

Table 1 Sleep apnea outcome measures for control and OSA subjects (Means ± SD).

Characteristics	Control	OSA	*P*
Number	5	5	
Male/Female	3/2	4/1	
Age (years)	31.0 ± 3.8	33.0 ± 4.8	
BMI (kg/m^2)	21.0 ± 2.7	28.0 ± 5.3	
ESS	5.0 ± 1.9	8.8 ± 4.8	0.07
FOSQ	3.85 ± 0.05	3.25 ± 0.59	<0.05
AHI (events/h)	8.26 ± 3.40	60.5 ± 36.1	<0.05
LSAT (%)	94.6 ± 2.3	87.7 ± 7.1	<0.05

BMI: Body mass index; ESS: Epworth Sleepiness Score; FOSQ: Functional Outcomes Sleep Questionnaire; AHI: Apnea-Hypopnea Index; LSAT: Lowest O_2 Saturation.

Discussion

In the literature, there are only a few publications dealing with the evaluation of soft tissue and skeletal anatomy using MRI and lateral cephalometry with both control and OSA subjects. These studies utilized dynamic or ultrafast MRI sequences and cephalometric measures, but did not discriminate OSA from control subjects by sleep study or validated questionnaires as shown in our study.

The soft tissue landmarks in cephalometry are influenced by the superposition of all the structures present in the same plane, which makes some of the landmarks difficult to accurately and reliably identify. Also, cephalometry provides a static assessment of the upper airway in a non-supine subject, with exposure to ionizing radiation. Several authors have looked for an imaging modality that would provide improved airway assessment in OSA.[4–9]

MRI provides unparalleled definition of soft tissue structures and their relationships in the upper airway, without exposing patients to ionizing radiation. However, MRI offers less precise bony contour definition. The bony landmarks could be harder to identify while analyzing the images, although this has not been a significant caveat encountered in our study. Contraindications for MRI imaging have to be taken into account (e.g., cardiac pacemakers, metallic implants). The usual concerns about claustrophobia have not been encountered during our evaluations secondary to using an open magnet MRI. Nevertheless, the measurements described earlier in this study can be performed on almost every commercially available MRI scanner.

In our study, radiocephalometry and MRI produced similar results for measures of soft palate length and MP-H distance. Because the enhanced soft tissue resolution of MRI affords greater measurement accuracy and allows for the determination of additional airway measures, which cannot be achieved through cephalometry (e.g., tongue volume, PAS area), we believe that MRI is superior to radiocephalometry for assessment of anatomic measures in OSA patients. For this reason, MRI was used as the primary imaging modality in this study and performed in all 28 of the study subjects, whereas radiocephalometry was only used to evaluate a subset of the subjects ($n = 10$). Although mandibular PAS diameter was found to be significantly shorter in OSA subjects by cephalometry, but not by MRI, this is likely due to small sample size in the cephalometry group and/or inaccuracy of cephalometric measurements.

The statistical analysis of the measured values obtained from MRI shows no significant difference in the linear dimensions of the soft palate (length and thickness of the soft

Table 2 Radiocephalometry and MRI images for control and OSA subjects (Means ± SD).

Measures	Radiocephalometry			MRI		
	Control	OSA	*P*	Control	OSA	*P*
Skeletal dimensions						
SNA angle (°)	91.5 ± 1.3	83.5 ± 3.0	0.001	–	–	–
SNB angle (°)	85.5 ± 3.7	80.8 ± 3.3	0.03	–	–	–
ANB angle (°)	6.0 ± 3.9	2.7 ± 1.4	0.07	–	–	–
MP-H distance (mm)	10.9 ± 5.8	24.2 ± 5.8	0.003	10.9 ± 5.8	24.2 ± 5.8	0.003
Soft tissue dimensions						
Soft palate length (mm)	39.8 ± 4.3	39.0 ± 4.9	0.39	34.4 ± 3.7	36.7 ± 3.8	0.17
Soft palate thickness (mm)	–	–	–	9.2 ± 2.4	9.8 ± 2.0	0.35
Airway dimensions						
Nasal PAS diameter (mm)	–	–	–	26.55 ± 7.49	15.38 ± 8.54	0.03
Occlusal PAS diameter (mm)	–	–	–	7.98 ± 2.58	6.23 ± 4.20	0.23
Mandibular PAS diameter (mm)	8.1 ± 3.7	2.0	0.01	12.54 ± 2.78	7.16 ± 4.01	0.02
PAS cross-sectional area (cm^2)	–	–	–	7.78 ± 1.86	5.11 ± 1.44	0.02
Organ dimension						
Tongue volume (cm^3)	–	–	–	90.01 ± 11.87	135.95 ± 13.71	0.0002

PAS: posterior airway space; MP-H: mandibular plane-hyoid.

palate) and the PAS occlusal distance. These findings are consistent with other studies.[13] The PAS diameter at the nasal plane, which corresponds to the traditional Fujita classification for palate obstruction, is significantly shorter in OSA patients compared to controls.

Studies using static MRI in patients to distinguish differences in the pharyngeal cross-sectional areas and volumes among OSA and normal subjects have shown mixed results. Three of these studies showed no difference, while three did show a difference in pharyngeal volumes and cross-sectional areas.[14–16] Our study shows significant difference in both nasal and mandibular PAS distance and PAS area. In addition we found MP-H distance to be greater in OSA patients compared to controls, even if our patients were not matched for BMI. Despite not controlling for BMI, we believe our finding is a genuine association compared to Brander et al[17] who showed no difference in MP-H distances between obese and non-obese patients with OSA. Our study agrees with these findings in that anatomic parameters for MP-H and PAS dimensions correlate with clinical outcome measures and show statistical and clinical significance compared to controls.

The tongue volumes of patients with OSA were significantly larger compared to the control group and the most substantial parameter in our study ($P = 0.0004$). Lowe et al[7] has measured the tongue volumes of 25 control subjects and 80 patients with OSA and found similar results, although the overall tongue volumes were somewhat different from ours because they did not include muscles of

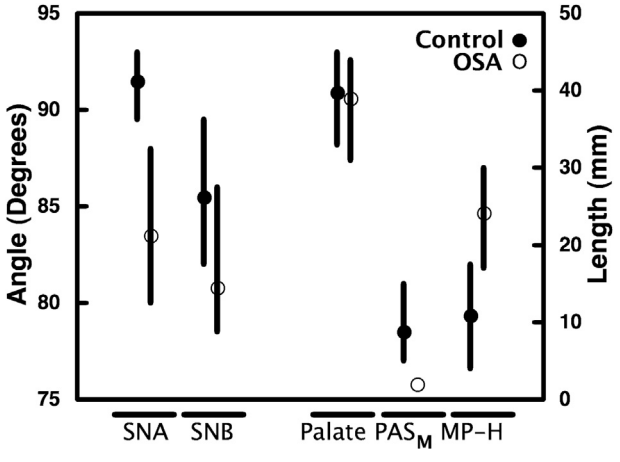

Fig. 4 Airway structure dimensions (mean and range) measured from cephalometry for control and obstructive sleep apnea (OSA) subjects: Sella to nasion to point A angle (SNA) and sella to nasion to point B angle (SNB) in degrees (left axis) and soft palate length (Palate), posterior airway space diameter at the mandibular plane (PASm) and mandibular plane to hyoid distance (MP-H) in millimeters (right axis).

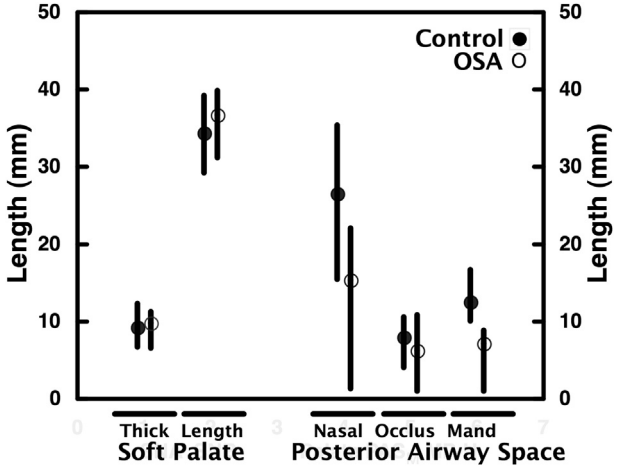

Fig. 5 Airway structure dimensions (mean and range) measured from MRI images for control and obstructive sleep apnea (OSA) subjects. Soft palate thickness and length, posterior airway space diameter at the nasal, occlusal and mandibular planes in millimeters.

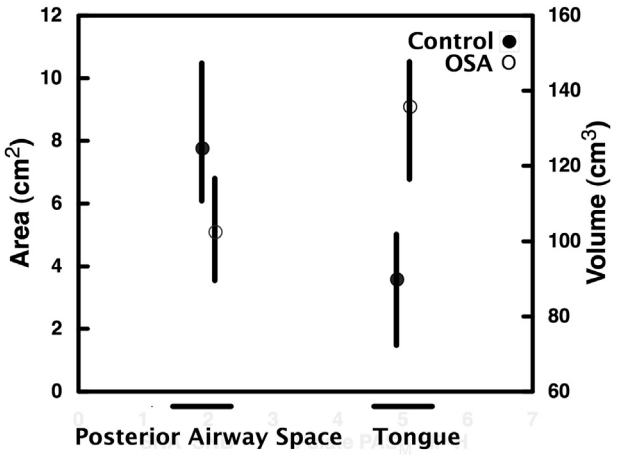

Fig. 6 Airway structure dimensions (mean and range) measured from MRI images for control and obstructive sleep apnea (OSA) subjects. Posterior airway space cross-sectional area in squared centimeters (left axis) and tongue volume in cubic centimeters (right axis).

the floor of mouth. They also described a relation between tongue and soft palate volumes and body mass index ($r = 0.28$, $P < 0.005$) and hypothesized that it could explain the differences in tongue and soft palate volumes between control subjects and OSA patients.[7] The high statistical significance of the difference in tongue volume seen in this study, with an associated power of 98%, suggests that tongue volume is the strongest clinical predictor of OSA among anatomic measures.

Limitations of this study include the moderate sample size of both the control and OSA group, as well as the racial heterogeneity among the groups. Subject size was limited due to the cost of scanning time. However, a power analysis demonstrates that the sample size in the current study was sufficient to generate a power of 80% or greater for the effect size seen in MP-H, PAS area, and tongue volume. To further evaluate if some of our parameters were independently associated with OSA, a multivariate analysis would have been required. Considering the relatively small number of subjects and controls, such an analysis was not valid. Future directions may include a larger focused study evaluating the significant MRI measures found (i.e., MP-H, nasal PAS, PAS area, and tongue volume) in order to elucidate the clinical application of MRI in OSA subjects.

Our study population included subjects from different racial origins, gender and BMI. Although statistically significant, differences in cephalometric measurements likely represent skeletal-facial and morphologic differences found in obese and non-obese patients,[18] male and female subjects[19] and amongst different racial groups. Data are conflicting in the various studies reviewed. Liu et al[20] have matched Caucasian and Chinese patients with OSA for age and BMI and have not found statistically significant differences according to hyoid bone positioning or maxillary bone differences. Future research on these anatomic variables should consider these known differences in race and gender.

Conclusion

Our study shows that anatomic parameters including a small PAS diameter at the nasal plane, a smaller PAS area, a long MP-H distance, and a large tongue volume hold statistical and clinical relevance in patients with OSA. The most substantial measurement was tongue volume. Tomographic MRI is an accurate and informative imaging study for the assessment of anatomic airway measures, and these data may be complemented by outcome measures in order to evaluate patients with OSA and to possibly guide surgical planning.

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