Gender Differences in the Expression of Sleep-Disordered Breathing*
Role of Upper Airway Dimensions
Vahid Mohsenin, MD

Study objectives: Obstructive sleep apnea (OSA) is a common disorder that is characterized by repetitive episodes of upper airway narrowing and collapse. Obesity is a major risk factor for OSA. Compared with men, women have greater total body fat and are more obese, and yet the prevalence of OSA is much higher in men. The airway size and compliance and pharyngeal muscle tone are important determinants of upper airway patency during sleep. The discrepancy between greater frequency of obesity and lower prevalence of OSA in women has not been explained and suggests a different pathogenetic mechanism underlying this condition. Most clinical studies in OSA have either combined the sexes or have described results from men only. The object of this study was twofold: (1) to examine the effect of obesity on pharyngeal size in both men and women, and (2) to determine the role of upper airway dimensions in the expression of sleep-disordered breathing (SDB) and its relationship to gender.

Design: Prospective study of subjects referred for evaluation of SDB.

Setting: University-based sleep center.

Subjects: Seventy-eight male patients (mean ± SE age, 49.2 ± 1.5 years) and 52 female patients (mean age, 47.4 ± 1.5 years).

Measurements and results: All subjects underwent in-laboratory polysomnography with measurement of upper airway size using the acoustic reflectance method. Although the two groups were similar in age, the female patients were slightly heavier than the male patients (body mass index [BMI], 36.0 ± 1.7 kg/m² vs 33.3 ± 0.8 kg/m², respectively; p < 0.0001). Despite similar clinical presentation of snoring and excessive daytime sleepiness, women had mild OSA (respiratory disturbance index [RDI], 9.2 ± 2.7 events per hour) or increased upper airway resistance syndrome compared with men with more severe OSA (RDI, 28.0 ± 3.5 events per hour; p < 0.0001). In contrast, women had a significantly smaller oropharyngeal junction and pharynx than men (p < 0.02). Upper airway size correlated significantly with the severity of sleep apnea in men only. There was no correlation between BMI and pharyngeal size in either gender.

Conclusions: This study demonstrates that the static properties of upper airway in awake men but not women correlate with the severity of sleep apnea. This suggests inherent structural and functional differences in upper airway during sleep between men and women with more favorable airway mechanics in women.

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Key words: acoustic reflectance; sleep apnea; upper airways

Abbreviations: BMI = body mass index; OPJ = oropharyngeal junction; OSA = obstructive sleep apnea; RDI = respiratory disturbance index; SDB = sleep-disordered breathing; UARS = upper airway resistance syndrome

Sleep apnea is defined as repetitive cessation of airflow associated with arousals and hypoxemia. Obstructive sleep apnea (OSA) is the most common variety, and it is due to complete or partial occlusion of the upper airway. Upper airway patency depends on the relative influence of upper airway dimensions,
recognized as a common condition and an important health problem with high morbidity and possibly high risk of mortality. In the United States alone, the prevalence of SDB, defined as five or more apneas or hypopneas per hour of sleep, is 15% in men and 9% in women between the ages of 30 years and 60 years and is significantly higher in people ≥ 65 years old. The risk of OSA tends to increase with obesity and increasing neck size (as a surrogate marker of airway narrowing) in both male and female patients. Obesity is thought to affect airway size through deposition of fat in the neck and perhaps by changing resistive loading on the upper airway to promote airway collapsibility. However, previous studies have shown that women have less severe OSA than men of similar age and despite greater weight. This gender difference in the prevalence of SDB has not been adequately explained and suggests that the risk factors and the mechanism for the development of OSA may differ between men and women. A recent study by Pillar and colleagues showed no gender difference in the activation of upper airway dilator muscles or respiratory drive during sleep in response to resistive loading. These investigators speculated that the collapsibility of the pharynx in response to load application is likely due to three factors: (1) the inherent characteristics of pharyngeal tissue, (2) the anatomic structure of the pharynx, and (3) the size of the upper airway lumen prior to load application. Previous studies have demonstrated differences in upper airway size between normal men and women and between obese women with or without OSA. However, to my knowledge, there have been no studies to compare the upper airway size in obese male and female patients and its role in the development of obstructive apnea. In view of these considerations, we undertook this study to examine and compare the effect of pharyngeal size and gender on the expression of SDB. We found that the obese women had significantly smaller pharyngeal airways than men, but the severity of OSA was influenced by the size of the pharynx in men only.

MATERIALS AND METHODS

Subjects

One hundred fifty-two consecutive patients who were referred to the university sleep center for evaluation of SDB were prospectively enrolled in the study. Twenty-two patients were excluded because of diagnoses other than SDB or having prior uvulopalatopharyngoplasty or clinically evident maxillofacial abnormalities in the form of retrognathia or micrognathia. Menopausal state was determined by lack of menses for at least 1 year. Subjective excessive daytime sleepiness was assessed using the Epworth Sleepiness Scale.

Sleep Study

Polysonmography was performed between 9 PM and 7 AM as previously described. Briefly, sleep state was recorded with two channels of EEG (C3/A2 or C4/A1, O2/A1 or O1/A2), two channels of electro-oculogram, and one channel submental electromyogram. Breathing was assessed by monitoring chest wall and abdominal movements using strain-gauge pneumographs, and nasal and oral flows using pneumotachometers. Arterial oxygen saturation was measured using a pulse oximeter. Leg movements were monitored with two channels of electromyogram, and an ECG was recorded continuously. All variables were recorded simultaneously and continuously on either a 16-channel Grass polygraph (model 8–20E; Astro-Med; West Warwick, RI) or SensorMedics sleep data acquisition system (SensorMedics Corporation; Yorba Linda, CA). Sleep recordings were scored in 30-s epochs and staged according to standard criteria. Apnea was defined as at least an 80% reduction in airflow for > 10 s. Obstructive apnea was defined when respiratory efforts were present, and central apnea was defined when respiratory efforts were absent. Mixed apnea was defined as an event beginning with a central component followed by an obstructive component. Hypopneas were scored when there was a 50 to 80% decrease in the airflow signal with a ≥ 4% decrease in arterial oxygen saturation. The respiratory disturbance index (RDI) was defined as the sum of apneas plus hypopneas divided by the total sleep time in hours. OSA was diagnosed when the RDI was five or more events per hour. Respiratory event-related arousal was defined when there was out-of-phase or paradoxical breathing during at least four respiratory cycles terminating with arousal. Increased upper airway resistance syndrome (UARS) was defined when there was subjective report of hypersomnia (score > 8 on the Epworth Sleepiness Scale) and > 15 episodes of respiratory-associated arousals per hour of sleep.

Acoustic Reflection Method

The acoustic reflection technique yields an accurate estimate of cross-sectional area of the upper airways. The equipment, signal processing, and filtering techniques for acoustic reflectance measurements have been described by Brooks et al. Briefly, the apparatus consisted of a 24.1-cm-long tube with a wave-tube diameter of 1.94 cm, a 12-W loud speaker with a bandwidth of 250 Hz to 3.5 KHz with a peak energy of 1.25 to 1.5 KHz, and a pair of piezo-resistive microphones to measure the incident and reflected acoustic waves. We measured 10 to 20 cross-sectional areas vs distance functions of the airway at a rate of three times per second, with the subjects in seated position and breathing ambient air via a rubber mouthpiece without a nose clip. We acquired the acoustic reflectance signals while the subjects breathed ambient air rather than a gas mixture containing helium used in the original studies. In a study by Huang et al., no significant difference was found in the measurement of upper airways between these two methods. The cross-sectional areas vs distance traces were examined for the presence of standard curve of oral cavity peak, oropharyngeal valley, pharyngeal peak, and laryngeal valley. The oropharyngeal junction (OPJ) is the cross-sectional area between the oral cavity and the pharynx (Fig 1). Pharyngeal area was the mean cross-sectional area from the OPJ to the glottis.

Statistical Analysis

Data are presented as mean ± SE. The data were analyzed using unpaired Student’s t test or Mann-Whitney U test for gender differences in anthropometric measurements, upper airway dimensions, and respiratory events during sleep. Linear and nonlinear regression analysis was employed to examine the relationship between variables; p ≤ 0.05 was considered significant.
RESULTS

The demographic characteristics, RDIs, and arousal indexes of apneic and nonapneic patients are shown in Table 1. There were 78 men (mean age, 49.2 ± 1.5 years) and 52 women (mean age, 47.4 ± 1.5 years; p = 0.30). In the male group, patients with OSA were older than those with increased UARS with no significant difference in body mass index (BMI) or Epworth Sleepiness Scale scores. There was no significant difference in age and BMI between increased UARS and OSA in the female patients. Men had more severe OSA with significantly higher RDIs and arousal indexes than women. Both groups reported similar degrees of excessive daytime sleepiness as determined by Epworth Sleepiness Scale. Female patients had significantly smaller upper airway size at the level of the OPJ and pharynx than men (Fig 2). However, there was no difference in upper airway measures between increased UARS and OSA within each gender group.

Adjustment of upper airway dimensions by dividing the area by height did not eliminate the gender difference. There was a significant inverse correlation between pharyngeal cross-sectional area and severity of sleep apnea in male patients (Fig 3). A curvilinear function (Y = 1/−0.023 + 0.029 X; r = 0.43; p = 0.001) best fitted the data with a threshold for pharyngeal caliber (approximately 3.2 cm²), below which the RDI increased in a nonlinear fashion. In order to estimate the significance of this threshold value for the development of OSA, we calculated the odds ratios. The positive likelihood ratio was 1.48 with a negative likelihood ratio of 0.57 yielding an odds ratio of 2.60. This indicates that it is 2.6 times more likely to have OSA with an RDI of five or more events per hour with a pharyngeal size < 3.2 cm² in male patients presenting with symptomatology of OSA. Despite the large size of the cohort, there were few male subjects who had OSA and a pharyngeal size > 3.2 cm². Additionally, we

Table 1—Demographic Characteristics, RDIs, and Arousal Indexes in Male and Female Patients With SDB*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Male Patients</th>
<th>Female Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UARS (n = 21)</td>
<td>OSA (n = 57)</td>
</tr>
<tr>
<td>Age, yr</td>
<td>43.5 ± 3.4</td>
<td>51.3 ± 1.6†</td>
</tr>
<tr>
<td>Height, cm</td>
<td>177.5 ± 2.3</td>
<td>179.6 ± 1.0</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>30.8 ± 1.8</td>
<td>34.2 ± 0.8</td>
</tr>
<tr>
<td>Epworth Sleepiness</td>
<td>14 ± 3</td>
<td>14 ± 4</td>
</tr>
<tr>
<td>Scale</td>
<td>1.8 ± 0.3</td>
<td>62 ± 5.6†</td>
</tr>
<tr>
<td>RDI, events/h</td>
<td>20 ± 3</td>
<td>70 ± 5†</td>
</tr>
<tr>
<td>Arousal index, arousals/h</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SE.
†p < 0.05 when compared with UARS within-gender group.
‡p < 0.02 when compared with male patients with UARS.
§p < 0.05 when compared with male patients with OSA.

Figure 1. Typical distance-area function of the upper airway; 95% confidence lines are drawn around the mean.

Figure 2. The differences in OPJ and mean pharyngeal cross-sectional (pharynx) area in male and female patients with UARS and OSA showing smaller upper airway dimensions in female patients with UARS or OSA than in male patients. *p < 0.05.
have studied large number of normal subjects with no evidence of SDB and found very few with pharyngeal size less than this value. The addition of normal male subjects to the analysis would have only strengthened the association rather than weakening it. In contrast to male patients, there was no relationship between oropharyngeal or mean pharyngeal caliber and the severity of sleep apnea in female patients (Fig 4). In both genders, BMI correlated positively with the severity of OSA but not with pharyngeal cross-sectional area. There was no significant difference in BMI, upper airway dimensions, or RDI between premenopausal (n = 9) and postmenopausal (n = 10; 2 receiving hormonal replacement therapy) female patients with OSA.

**Discussion**

The present study demonstrates a significant gender effect on the upper airway dimensions and expression of sleep-related breathing disorders in a large group of markedly obese male and female subjects. We found that obese female patients presenting with excessive daytime sleepiness and snoring had mild OSA compared with their male counterparts who had severe OSA. In female patients, both OPJ and pharyngeal cross-sectional areas were significantly smaller than male patients for a comparable BMI. One possible explanation is that the smaller airway size in women could be related to body size or differential fat deposition in the neck and around the upper airways. However, Whittle et al. using MRI in normal men and women, demonstrated increased volume of soft tissue in the necks of male patients but with no significant gender differences in fat deposition in the regions prone to collapse during sleep. Likewise, we found no correlation between BMI and pharyngeal size in either gender. However, there was a positive correlation between BMI and RDI in both men (r^2 = 0.10; p = 0.004) and women (r^2 = 0.12; p = 0.016). Studies on awake normal men have shown greater reductions in pharyngeal caliber from seated to supine position (29% decrease) than normal women (21% decrease). Huang and colleagues found normal men had larger pharyngeal areas than normal women, but this difference disappeared in the supine position. This suggests that men have greater tendency for airway collapse than women even while awake. The decrease in airway caliber appears to be related, in part, to the reduction of lung volume in supine position. In addition to these positional changes in upper airway size, there is progressive increase in upper airway resistance from wakefulness to nonrapid eye movement sleep in both genders but to a much greater extent in men. In a recent study of normal men and women exposed to varying inspiratory resistive loads during sleep, Pillar and coworkers found that men had a much higher pharyngeal resistance than women with no significant difference in activation of pharyngeal dilator muscles or ventilatory drive between the sexes. They concluded that the factors underlying collapse of the upper airway must be due to gender differences in airway compliance and tissue characteristics. Our findings extend their observation by showing the dependence of OSA on critical minimal airway size in men below which there is high probability for sleep apnea. Our data and those of Pillar et al. suggest that the mechanism of airway collapse in women differs from those of men and relates mainly to inherent differences in local anatomy and tissue laxity between the genders. In our study, BMI correlated with RDI but not with upper airway dimensions. In a study by Schwab and associates, no significant difference was found in the fat pad size on MRI at the level of minimum airway between normal and apneic subjects. These observations suggest that obesity may not exert its influence on

![Figure 3](http://publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21969/)

**Figure 3.** The relationship between the pharyngeal cross-sectional area and RDI in male patients with OSA showing that the smaller the pharyngeal area the more severe the sleep apnea.

![Figure 4](http://publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21969/)

**Figure 4.** The relationship between the pharyngeal cross-sectional area and RDI in female patients with OSA showing lack of effect of pharyngeal size on RDI.
OSA solely through excess fat deposition around the upper airway. Our data on male and female patients with UARS or OSA show similar BMIs, supporting the hypothesis that obesity may have differential effects on structure and function of the upper airway. Obesity may predispose to upper airway obstruction through mass loading and alteration of tissue characteristic in addition to fat deposition. Histologic studies\(^{25,26}\) have shown an increase in the amount of muscular tissue, thickness of lamina propria, and fibrosis in the uvulas of patients with OSA as compared with normal subjects. The fact that pharyngeal size in women bears no relationship with the severity of sleep apnea suggests that sleep apnea in women is less associated with pharyngeal anatomic size and more with the alterations in airway tone and tissue laxity.

The combination of gender-specific tissue characteristics, and positional and sleep-related narrowing of the upper airway in men can create an unstable segment promoting total collapse. We propose the following sequence of events explaining the gender difference in the propensity for sleep apnea. Measurement of pressure/flow relationship during sleep has shown that men generate almost twice as much pressure as women to achieve similar peak flow rates.\(^{23}\) The flow limitation observed in men can be explained on the basis of (1) more compliant upper airways, (2) more pronounced reduction in the pharyngeal caliber in supine position, and (3) greater inspiratory pressure during sleep.\(^{19}\) These conditions create “orifice flow” aeromechanics promoting total collapse of the upper airway resulting in OSA. The transition from narrowed upper airway to total collapse can be explained on the basis of wave velocity mechanics.\(^{27}\) As the inspiratory flow increases with increasing respiratory effort, the pharyngeal airway pressure decreases because of an increase in kinetic energy at the narrowed segment. In a compliant upper airway, the decrease in luminal pressure will, in turn, decrease cross-sectional area leading to further increase in kinetic energy and subsequent collapse of the most compliant segment.\(^{28,29}\) In female patients, upper airway resistance changes little during sleep with no significant decrease in inspiratory intraluminal pressure, hence maintaining airflow and airway patency.

There are some potential limitations to this study. One limitation of this study was that we measured the upper airway dimensions in awake subjects. The effect of sleep and recumbency on the control of upper airway caliber is known to be significant in the pathogenesis of OSA, which may not be appreciated from measurements in awake individuals. However, the object of this study was to determine the influence of gender and obesity on airway size and the development of sleep apnea in a large cohort of patients with SDB, which would not have been practical to assess during sleep. Another limitation of our study is the unequal sample size between women and men that may have skewed the results in women, potentially obscuring the relationship between airway size and RDI. However, in support of our observation, Shellenberg and colleagues\(^{13}\) also failed to demonstrate a relationship between measures of upper airway anatomic narrowing and severity of sleep apnea in a large group of female patients with OSA.

In summary, airway size is significantly smaller in female patients than in male patients with SDB. The pharyngeal size is an important determinant of OSA in men but not women. Increasing obesity correlated with severity of OSA but not with airway dimensions in either gender. There is evidence to suggest that the gender difference in the expression of SDB is in large part due to upper airway tissue characteristics rather than central control of airway muscles. We found no evidence to suggest the role of menopausal state in the development of SDB in female patients. Measurement of upper airway size in male patients being evaluated for SDB may allow better risk stratification of these patients. Further study is needed to investigate the determinants of OSA in female patients.

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