SLEEP DISORDERED BREATHING

Anatomic and Physiologic Predictors of Apnea Severity in Morbidly Obese Subjects

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Study Objectives: While obesity is the most common risk factor for the development of obstructive sleep apnea, the correlation between measures of obesity and apnea severity is only moderate. We thus attempted to identify anatomic and physiologic predictors of apnea severity.

Design: We combined a careful assessment of upper airway anatomy, upper airway physiology, and ventilatory control in a group of obese individuals to identify predictors of apnea severity.

Setting: Tertiary care academic medical center.

Patients: 14 morbidly obese subjects being evaluated for weight-reduction surgery.

Interventions: N/A

Measurement and Results: We found no relationship between obesity (weight or body mass index) and apnea severity (respiratory disturbance index, RDI). However, those with severe apnea (RDI > 30) were found to have higher peak genioglossus EMG (GGEMG) (23.5 +/- 1.9 vs. 14.1 +/- 3.7 %max, p = 0.05) and greater airway collapsibility during pulses of negative pressure (7.6 +/- 0.9 vs. 4.4 +/- 0.7 cmH2O, p = 0.02). Airway collapsibility was significantly associated with RDI (r = 0.62, p < 0.01) as was peak GGEMG (r = 0.55, p < 0.05). Of the anatomic variables airway shape (A-P/lateral ratio) and volume change of the pharyngeal airway between total lung capacity and residual volume were different between those with and without severe apnea. Both correlated with RDI (A-P/lateral ratio: r = 0.70, p < 0.01 and volume change: r = 0.77, p < 0.01).

Conclusions: We believe these findings suggest that specific anatomic and physiologic properties of the airway interact with obesity to predispose to the development of airway collapse during sleep.

Key Words: obesity, upper airway, genioglossus, airway collapse


INTRODUCTION

OBSTRUCTIVE SLEEP APNEA (OSA) IS A COMMON DISORDER WITH IMPORTANT CLINICAL CONSEQUENCES FOR AFFECTED INDIVIDUALS.1 This disorder is characterized by repetitive collapse of the pharyngeal airway during sleep yielding hypoxia and hypercapnia, with arousal being required to reestablish airway patency.2 The associated consequences include daytime sleepiness,3 decreased cognitive performance, decreased quality of life,4 an increased risk of automobile accidents5,6 and potentially adverse cardiovascular consequences such as hypertension,7,8 myocardial infarction9 and stroke.10 Numerous studies have confirmed that obesity is the strongest risk factor for the development of OSA. A body mass index (BMI) > 28 kg/m2 is found in 60% to 90% of patients diagnosed with apnea,11 with the relative risk of sleep apnea from obesity (BMI > 29 kg/m2) being as great as 10 to 14.12-14 In the Wisconsin Sleep Study, a 1 standard deviation increase in BMI was associated with a 4.5 fold increased risk of OSA.1 In several investigations have also suggested that upper body or truncal obesity may be a better predictor of sleep apnea than BMI, perhaps by signifying greater fat deposition in the pharynx.15 Recently, neck circumference and waist-hip ratio (WHR) have been suggested by some (but not all) studies to be better predictors of sleep apnea than previous measures and may be especially useful in predicting risk in thin subjects.15,16

However, the relationship between measures of obesity and severity of OSA is only moderate. In fact, several studies of morbidly obese subjects have shown that the severity of apnea varies widely in these subjects. In a group of 250 morbidly obese men and women (mean BMI 45 kg/m2) Vgontzas found that only 50% of the men and 8.5% of the women had more than 30 apneas plus hypopneas over the course of the night (an apnea-hypopnea index, AHI > 5). There was no difference in mean BMI in the group with and without apnea.17 Similarly, Rajala found no difference in mean BMI or neck circumference in a group of morbidly obese subjects (BMI = 50 kg/m2) with and without sleep-disordered breathing.18 Finally, in a large population of patients referred to a sleep laboratory in Israel, the correlation between BMI and AHI, while significant, was found to be only moderate (r2 = 0.23) and weakened when the group was restricted to individuals who were overweight (r2 = 0.17).19 Taken together, these data suggest that other factors must interact with obesity in the development of OSA. Such features might include variability in upper airway anatomy (fat deposition), specific tissue characteristics of the upper airway, neuromuscular control of pharyngeal dilator muscles, lung volume, or ventilatory control mechanisms.

We are currently in the process of studying obese subjects before and up to 1 year after bariatric surgery to determine the effects of weight loss on apnea frequency, upper airway anatomy, and pharyngeal dilator muscle function. In this study, we noted that prior to weight reduction surgery, our subjects had a wide range of apnea severity (respiratory disturbance index, RDI 4.6-132 events/hour) despite the fact that all were morbidly obese (BMI > 40 kg/m2). Furthermore, there was no correlation between apnea severity and the degree of obesity in this patient population. We hypothesized that by combining a careful assessment of airway anatomy in conjunction with measurement of pharyngeal dilator muscle function, airway mechanics, and ventilatory control, we would be better able to identify predictors of apnea severity in this group of morbidly obese subjects.
METHODS

Subjects

Fourteen morbidly obese subjects (BMI ≥ 40 kg/m²) were studied. These participants were recruited from a group of patients electing to undergo weight reduction surgery at the Brigham and Women’s Hospital. All subjects being evaluated for bariatric surgery were given a flyer regarding the study, and those who called were provided with more information and screened for eligibility. Subjects were recruited consecutively and were not asked any questions about sleep prior to entering the study. None were on medications known to affect the upper airway or sleep. Specific medications excluded were all sedative medications, calcium channel blockers, and all antidepressants (as they might affect central serotonin or norepinephrine levels and upper airway muscle tone). Informed consent was obtained from each participant, with the protocol having the prior approval of the Human Subjects Committee of the Brigham and Women’s Hospital.

Equipment and Techniques

All subjects underwent each of the following tests:

Polysomnography: Polysomnography was performed according to standard laboratory protocol. Data recorded included electroencephalography (EEG) (central and occipital), electrooculography, submental electromyography (EMG), arterial oxygen saturation, nasal-oral airflow (thermistor), nasal pressure, electrocardiography, chest and abdominal wall motion, bilateral anterior tibialis EMG, snoring, and body position. All signals were simultaneously recorded and stored using the ALICE 3™ digital polysomnography system (Respironics, Inc., Murraysville, PA). All subjects were recorded for greater than 8 hours in bed in an attempt to record sleep for ≥ 7 hours in each subject/patient. All of the polysomnographic records were scored by one of the authors (SDP). Sleep was staged according to standard criteria.19 Arousals were defined according to American Academy of Sleep Medicine (AASM) guidelines.20 Respiratory events were scored according to the recently published AASM guidelines for measurement in clinical research.21 Specifically, apnea was defined as a complete cessation in airflow of ≥ 10 seconds. They were classified as central if there was no associated effort and obstructive if respiratory effort was present. Hypopneas were scored as a clear reduction in amplitude in the nasal pressure signal for ≥ 10 seconds that was associated with either an oxygen desaturation of >3%, EEG arousal, or both. The AHI was calculated as the number of apneas plus hypopneas divided by the number of hours of sleep. Subjects were classified as having severe OSA if the AHI was > 30, as defined by recent AASM guidelines, and all others were defined as being in the mild-moderate group.21

Pulmonary Function Testing: Spirometry was performed according to American Thoracic Society guidelines22 and using published predicted values.23 Lung volume determinations were made via plethysmography and are reported as percent predicted as well.

Upper Airway Physiology: All studies were performed during wakefulness in the supine posture. Inspiratory flow was determined with a calibrated pneumotachometer (Fleish, Inc., Lausanne, Switzerland) and differential pressure transducer (Validyne Corp., Northridge, CA). The standard techniques of our laboratory were used to measure end-tidal carbon dioxide (ETCO₂), mask leak, mask pressure, choanal pressure, epiglottic pressure, and intramuscular genioglossus EMG (GGEMG, as a percent of maximum activity).24,25 To assess genioglossal responsiveness and airway collapsibility, negative airway pressure stimuli were applied during early inspiration using a partially evacuated 50-liter canister and a solenoid valve, as described previously.26 Each negative pressure application (NPA) had a rapid onset and offset for a total duration of < 0.5 sec. Each NPA generated –13 to –17 cm H₂O pressure at the choanae, with a goal of –15 cm H₂O. An index of airway collapsibility was assessed during NPA as previously described.27 This collapsibility index was taken as the pressure difference between the choanae and the epiglottis during NPA.

All signals were recorded on a 16-channel Grass model 78 polygraph (Grass Instruments, Quincy, Ma.). Certain signals (GGEMG MTA, airway pressures, ETCO₂, and inspiratory flow) were also recorded onto the computer using signal-averaging software (SPIKE 2; Cambridge Electronic Design, LTD, Cambridge, UK). During basal breathing and NPA, all breaths were signal averaged, yielding a single calibrated waveform of each variable for subsequent data analysis. During tidal breathing, peak phasic and tonic GGEMG were determined for each subject. Airflow resistance was determined both at 0.2 l/s inspiratory flow and at peak inspiratory flow. Pharyngeal resistance was determined between the choanae and the epiglottis, nasal resistance between the mask and the choanae, and supraglottic resistance between the mask and the epiglottis. During negative pressure pulses, the peak GGEMG response and its latency were also determined from the signal-averaged waveform of many breaths. The GGEMG response to negative pressure was quantified as the increase in GGEMG from time zero to its maximum during the negative pressure stimulus.

Hypercapnic Ventilatory Responsiveness: The hyperoxic hypercapnic ventilatory response (HCVR) was determined by Read’s rebreathing technique. 

Figure 1—An example of an axial computed tomographic scan image in one subject at the level of the minimal cross-sectional area of the pharyngeal airway. It is at this level that 2-dimensional measurements were made for each subject. The airway is outlined in yellow and the parapharyngeal fat pad on the right in green. Labeled are other anatomic structures used as landmarks for measurements.

Figure 2—An example of 3-dimensional reconstruction of the pharyngeal airway (between the hard palate and the hyoid bone) and the parapharyngeal fatpads. A combination of semi-automated and manual editing techniques was used to define these structures in each subject.
method.\textsuperscript{28} At least 3 trials of rebreathing were performed on each subject, with at least 10 minutes between each trial. Linear regression was used to determine the slope of the HCVR, and the average value of the 3 trials is reported.

**Upper Airway Imaging:** All images were obtained on the same spiral computed tomography (CT) scanner. Subjects were studied in the supine posture with the head secured in the neutral anatomic position (Frankfort plane). Using a single breath hold, scans were obtained of the upper airway (from the nasopharynx to epiglottis) in approximately 10 seconds. We obtained images at 3 separate lung volumes: functional residual capacity (FRC, end of normal expiration), total lung capacity (TLC, end of maximal inspiration), and residual volume (RV, end of maximal expiration). Images were repeated if there was evidence of respiratory motion during the study. Once imaging was complete, the images were then transferred to a UNIX-based SUN Station (Sun Microsystems, Mountain View, CA) where they were processed, analyzed, and interpreted.\textsuperscript{29} The data were segmented by using advanced multiplane image analysis software (3D Slicer) developed by the MIT Artificial Intelligence Laboratory (www.slicer.org) in collaboration with the Surgical Planning Laboratory of the Brigham and Women’s Hospital. Editing can be applied to the data on a 3D or slice-by-slice basis. The output of the segmentation process is a set of label maps, where pixels take on values corresponding to tissue type. The bounding surfaces of the label maps (the airway, fat pads, etc.) are extracted and represented as a collection of triangles using marching cubes. Volumes were computed by multiplying the number of volume elements (voxels) enclosed by the segmented 3D volume, by the voxel volume, which is the product of the pixel area and slice thickness.\textsuperscript{30,31} This technique has been widely applied by our laboratory\textsuperscript{29,32-34} and has been shown to have excellent reproducibility.\textsuperscript{35} All 2-dimensional measurements listed below were made on the image acquired at FRC. The measurements made were based on Schwab, et al with minor modifications.\textsuperscript{36-38}

**Two-Dimensional Determinations:**
- Minimal axial airway image (Figure 1): Airway cross-sectional area, anterior-posterior (AP) and lateral (LAT) widths of the airway, thickness of the lateral pharyngeal walls, intramandibular width, pterygoid muscle thickness, and area of the parapharyngeal fat pads
- Sagittal anatomy: Soft palate area, soft palate length, pharyngeal length (measured from the hard palate to the base of the epiglottis)
- Volumetric Measurements — (Figure 2) Volume of the pharyngeal airway between the hard palate and hyoid bone and the volume of the parapharyngeal fat pads. In addition, pharyngeal airway volume was quantified at TLC and RV, along with the percent decrease in airway volume between TLC and RV

### Table 1—Patient Characteristics

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>Sex</th>
<th>BMI (kg/m\textsuperscript{2})</th>
<th>AHI</th>
<th>FEV\textsubscript{1} (% predicted)</th>
<th>FVC (% predicted)</th>
<th>FRC (% predicted)</th>
<th>ERV (% predicted)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>21</td>
<td>F</td>
<td>68.4 ± 5.1</td>
<td>121</td>
<td>117</td>
<td>66</td>
<td>35</td>
<td></td>
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<tr>
<td>2</td>
<td>46</td>
<td>F</td>
<td>70.5 ± 10.0</td>
<td>81</td>
<td>78</td>
<td>76.3</td>
<td>38</td>
<td></td>
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<tr>
<td>3</td>
<td>27</td>
<td>F</td>
<td>74.6 ± 13.2</td>
<td>72</td>
<td>71</td>
<td>53</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>55</td>
<td>F</td>
<td>51.6 ± 46.6</td>
<td>71</td>
<td>75</td>
<td>85</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>29</td>
<td>M</td>
<td>49.7 ± 28.6</td>
<td>87</td>
<td>89</td>
<td>71</td>
<td>48</td>
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<tr>
<td>6</td>
<td>41</td>
<td>F</td>
<td>46.3 ± 80.8</td>
<td>85</td>
<td>81</td>
<td>72</td>
<td>34</td>
<td></td>
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<td>7</td>
<td>37</td>
<td>M</td>
<td>64.5 ± 132</td>
<td>87</td>
<td>86</td>
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<td>25</td>
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<td>8</td>
<td>57</td>
<td>F</td>
<td>55.0 ± 68.8</td>
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<td>104</td>
<td>78</td>
<td>69</td>
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<td>9</td>
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<td>F</td>
<td>58.0 ± 11.8</td>
<td>90</td>
<td>98</td>
<td>77</td>
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<tr>
<td>10</td>
<td>43</td>
<td>F</td>
<td>52.2 ± 89.01</td>
<td>86</td>
<td>86</td>
<td>66</td>
<td>34</td>
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<td>11</td>
<td>40</td>
<td>F</td>
<td>47.8 ± 4.6</td>
<td>80</td>
<td>92</td>
<td>75</td>
<td>52</td>
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<tr>
<td>12</td>
<td>30</td>
<td>F</td>
<td>41.7 ± 12.4</td>
<td>88</td>
<td>90</td>
<td>58</td>
<td>41</td>
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<tr>
<td>13</td>
<td>50</td>
<td>F</td>
<td>46.2 ± 41.4</td>
<td>109</td>
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<td>120</td>
<td>35</td>
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<tr>
<td>14</td>
<td>42</td>
<td>F</td>
<td>59.0 ± 12.8</td>
<td>97</td>
<td>106</td>
<td>110</td>
<td>109</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td>56.1 (SD 48.9)</td>
<td>91.2</td>
<td>91.5</td>
<td>78.2</td>
<td>51.1</td>
<td></td>
</tr>
</tbody>
</table>

**BML body mass index; AHI, apnea hypopnea index; FEV\textsubscript{1}, forced expiratory volume in 1 second; FVC, forced vital capacity; FRC, functional residual capacity; ERV, expiratory reserve volume**

### Table 2—Airway Physiology and Ventilatory Responsiveness

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Mild-Moderate</th>
<th>Severe</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tonic GEGMG (% maximum)</td>
<td>8.51 (6.3)</td>
<td>11.52 (2.9)</td>
<td>0.26</td>
</tr>
<tr>
<td>Peak GEGMG (% maximum)</td>
<td>14.13 (8.5)</td>
<td>23.51 (5.5)</td>
<td>0.04</td>
</tr>
<tr>
<td>Pharyngeal Resistance (cmH\textsubscript{2}O/l/s)</td>
<td>4.26 (3.2)</td>
<td>4.94 (1.5)</td>
<td>0.60</td>
</tr>
<tr>
<td>Supraglottic Resistance (cmH\textsubscript{2}O/l/s)</td>
<td>5.30 (3.5)</td>
<td>7.70 (2.3)</td>
<td>0.38</td>
</tr>
<tr>
<td>Response to Negative Pressure (% increase)</td>
<td>76.65 (25.5)</td>
<td>53.90 (38.8)</td>
<td>0.24</td>
</tr>
<tr>
<td>Airway Collapsibility (cm H\textsubscript{2}O)</td>
<td>4.44 (1.7)</td>
<td>7.60 (2.5)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>HCVR (l/min/mmHg)</td>
<td>2.18 (0.4)</td>
<td>1.55 (0.5)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

**GEGMG: genioglossal electromyogram; HCVR, hypercapnic ventilatory responsiveness**

### Statistical Analysis

Given the small sample size, nonparametric methods were used to compare anatomic and physiologic differences between the group with and without severe apnea. Correlation analyses were performed with AHI as the dependent variable using standard least squares linear regression techniques for single variables after log transformation of AHI to approximate normality. Data are presented as the mean +/- SD. For all analyses, two-tailed significance was set as \( \alpha < 0.05 \).

### RESULTS

Table 1 shows the demographic, apnea severity, and pulmonary function data for the individuals in this study. The study population included 12 women and 2 men, reflecting the make-up of patients who typically seek treatment in this weight reduction center. Three of the women were postmenopausal (subjects 4, 8, and 13), and two were on hormonal replacement therapy. As can be seen in Table 1, the subjects were moderately obese (BMI = 56.1 +/- 10.1 kg/m\textsuperscript{2}) and tended to be slightly younger (mean age 38.1 +/- 11.3 years, range 21 to 57) than most patients with OSA. While the mean AHI was in the range of moderately severe disease, (48.9 +/- 38.9) the entire spectrum of sleep-disordered breathing was seen, as AHI varied from 4.6 to 132 events per hour. Using the predefined cutoff of 30 events/hour, 8/14 subjects had severe OSA. The mean RDI was 72 in the severe group and 14 in the group with mild to moderate apnea. Pulmonary function testing revealed that no subject had evidence of obstructive lung disease, and the findings showed the typical physiology associated with morbid obesity (reduction in FRC and expiratory reserve volume, along with normal forced expiratory volume in 1 second and forced vital capacity, Table 1). While arterial blood gas analysis was not performed, no subject had an elevated ETCO\textsubscript{2} measurement (> 45 mm Hg) suggestive of obesity-hyperventilation syndrome.

In comparing the group with and without severe OSA, no significant difference was found in commonly used measures of obesity such as BMI (56.8 +/- 9.1 vs. 55.1 +/- 11.5 kg/m\textsuperscript{2}, p = 0.77) or neck circumference (45.7 +/- 4.1 cm vs. 43.2 +/- 7.43, cm, p = 0.45) or of central obesity such as waist-hip ratio (0.84 +/- 0.09 vs. 0.85 +/- 0.08, p = 0.83). Furthermore, there was no correlation between any of these measures, and the severity of apnea (all r values less than 0.30, p = n.s.). The only demographic difference between the 2 groups that approached significance was a trend for those with severe apnea to be older (43.8 +/- 11.4 vs. 32.5 +/- 6.7 years, p = 0.054).

Upper airway physiology data are presented for the group in Table 2. While there was a trend for those with more severe apnea to have higher tonic GGEMG plus pharyngeal and supraglottic resistances, none of these differences reached statistical significance. However, peak GEGMG was higher in the group with severe compared to those with mild OSA (23.5 +/- 5.5 vs. 14.1 +/- 8.5 % maximum, p = 0.05). While there was no difference in genioglossal response to negative pressure, airflow collapsibility was greater in those with severe apnea (7.7 +/- 2.5 vs. 4.3 +/- 1.7 cmH\textsubscript{2}O, p = 0.02). Figure 3 shows an example of airway collapse during NPA in one subject with mild and one with severe OSA. Regression analysis revealed that both airway collapsibility (Figure 4, r
DISCUSSION

The primary finding of the present study was that in a group of morbidly obese subjects several physiologic and anatomic variables were able to distinguish between those with and without severe apnea, whereas BMI and other measures of obesity were not.

First, airway collapsibility during pulses of negative pressure was greater in those with severe apnea than in those with mild to moderate apnea. These data are consistent with the hypothesis that the airway of the patient with OSA is more compliant and with previous data from our laboratory showing increased collapsibility in subjects with severe OSA compared with controls.

The present study extends those findings by showing that the degree of collapsibility correlated with the severity of apnea. Associated with this increased collapsibility was an increased peak phasic GGEMG (during basal breathing) in those with severe apnea, likely reflecting neuromuscular compensation for this more collapsible airway.

If the pharyngeal airway of those with severe apnea was less patent at baseline, superimposition of a negative pressure pulse would likely lead to increased collapsibility on this basis alone. However, our data do not support the idea that the airway of those with severe OSA was less patent during wakefulness. Airway volume at FRC was not significantly less in this group (data not shown), nor was pharyngeal resistance significantly greater.

Second, several anatomic variables were found to be different in those with severe apnea. The shape of the pharyngeal airway was found to be oriented more in the AP than in the LAT dimension in those with severe apnea. These data are consistent with previous findings by Schwab and colleagues comparing those with OSA to mild snorers and controls.

Leiter has suggested that this orientation of the airway may place pharyngeal dilator muscles (such as the genioglossus) at a relative mechanical disadvantage, such that they are less effective at maintaining pharyngeal airway patency. This hypothesis has not been tested but is supported by the data in this study. Finally, we found that there was a much greater reduction in pharyngeal airway volume at RV compared to TLC in those with severe apnea. Bradley et al used acoustic reflection to show that airway area decreased more in patients with OSA when going from TLC to RV than in those without apnea, suggesting that airway area was more dependent on higher lung volumes in these patients.

In addition, using cine-CT during tidal breathing, both Schwab and Shepard have shown that in the patient with OSA there is a marked reduction in airway area at end-expiration (when lung volume is lowest) whereas there was no such reduction in airway area during tidal breathing in normal controls. We also found that the degree of lung-volume dependence of the pharyngeal airway correlated with the severity of apnea in these patients.

Taken together, these findings add to our knowledge regarding the pathophysiology of airway collapse in OSA. We hypothesize that airway collapsibility during negative pressure reflects the intrinsic properties of airway tissues (such as edema, local fat deposition, muscle fiber type) but may also be affected by airway shape. It could be argued that the ability of muscles such as the genioglossus to protect airway patency is compromised in the patient with an AP-oriented airway.
The relationship between lung volume dependence of pharyngeal volume and apnea severity is also of considerable interest. It is been previously shown in dogs that increases in thoracic volume can lead to decreases in upper airway resistance. Studies in humans as well confirm this effect, with Begle et al showing a decrease in pharyngeal resistance during sleep with increased end-expiratory lung volume (EELV) produced by a negative pressure ventilator. Preliminary data from our laboratory also suggests that in normal individuals, airway collapsibility during NPA is reduced during non-rapid eye movement when EELV is mechanically increased (Stanchina, unpublished observations). This “tracheal tug” effect may work by causing pharyngeal unfolding or decreased pharyngeal compliance by stretching upper airway tissues or may stabilize the upper airway by changing the position of structures such as the hyoid. Changing lung volume could effect pharyngeal muscle function as well. The greater dependence on higher lung volumes in those with severe OSA is also consistent with previous observations, and suggests that these patients may maintain higher lung volume awake in the supine posture, thus protecting airway patency. Such a compensatory mechanism would not likely be preserved during sleep. While it is well known that lung volume decreases at sleep onset, whether this decrease is greater in the obese apnea patient has not been previously tested.

Our study has a number of limitations that must be recognized. First, the subjects included in these studies represented only a small proportion of those who were being evaluated for weight reduction surgery. This is likely due to the invasive nature of the protocol but raises the possibility that those who chose to do the study “self-selected” in some way and thus are not representative of obese subjects in general. We think this is unlikely as the subjects were not specifically asked questions regarding sleep before agreeing to participate in the study. Secondly, subjects with a wide range of OSA severity were studied, as would be expected in a general population of obese subjects. In addition, the number of subjects studied was relatively small. However, the findings were robust, despite the use of multiple comparisons.

Second, CT scanning was used rather than magnetic resonance imaging (MRI) for imaging the upper airway. While MRI is clearly superior for delineating upper airway soft tissues, CT was performed due to table size restrictions based on our subjects’ weight. It is for this reason that certain soft tissue structures such as the soft palate and tongue were not 3-dimensional reconstructed, as this would be quite difficult using CT data. However, air-tissue interfaces are extremely well defined by CT and, thus, analysis of the pharyngeal airway should be excellent using this technology. Furthermore, the rapid acquisition speed of spiral CT (seconds, rather than minutes via MRI) allowed us to image the entire pharyngeal airway at different lung volumes, which would not have been possible by MRI. While some manual image analysis was required to develop the 3-dimensional models, all such analysis was performed blinded to the results of polysomnography by one author for consistency(GD). Our previous experience has shown excellent reproducibility using these techniques.

Third, our subject group comprised primarily morbidly obese females, while the majority of subjects with OSA are male and only moderately overweight. Whether these anatomic and physiologic predictors found in this group can be generalized to less obese subjects is unknown but deserves further study.

Fourth, all of our anatomic and physiologic measurements were performed during wakefulness, while, by definition, OSA is a sleep-dependent phenomenon. Studying patients with OSA is difficult, as they often do not achieve stable periods of sleep but, rather, have periods of alternating sleep-disordered breathing and arousal. In addition, our goal was to identify potential variables that, during wakefulness, correlated with the abnormality during sleep, as this may provide information that further our understanding of state-dependent control of the pharyngeal airway.

Finally, our methods for defining muscle activity (percentage of maximum) and airway collapsibility could be faulted due to variable needle electrode placement, subject effort, etc. However, we have extensive experience making such measurements in humans and have shown them to be stable over time.

In conclusion, we found that in a group of morbidly obese subjects, measures of airway collapsibility, the shape of the pharyngeal airway, and the lung volume dependence of the upper airway were the best predictors of apnea severity, as there was no relationship between standard measures of obesity and apnea severity in this group. Hopefully these data will lead to future hypotheses and experiments aimed at understanding how each of these variables influences airway patency.

Figure 5—An example of lung-volume dependent changes in 3-dimensional pharyngeal airway volume in one subject with mild (top) and one with severe (bottom) obstructive sleep apnea. Note the minimal change in airway volume in the first subject and the large reduction in airway size in the second subject at residual volume (RV), with complete collapse of the retropalatal airway.

Figure 6—The relationship between lung volume dependence of the pharyngeal airway (% collapse at residual volume compared to total lung capacity) and the severity of obstructive sleep apnea (lnRDI, respiratory disturbance index). Those with more severe apnea showed greater reduction in airway volume with changes in lung volume.
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