Magnetic Resonance Imaging of the Upper Airway Structure of Children with Obstructive Sleep Apnea Syndrome

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The anatomical relationships between lymphoid, bony, and other tissues affecting the shape of the upper airway in children with obstructive sleep apnea syndrome (OSAS) have not been established. We therefore compared the upper airway structure in 18 young children with OSAS (age 4.8 ± 2.1 yr; 12 males and 6 females) and an apnea index of 4.3 ± 3.9, with 18 matched control subjects (age, 4.9 ± 2.0 yr; 12 males and 6 females). All subjects underwent magnetic resonance imaging under sedation. Axial and sagittal T1- and T2-weighted sequences were obtained. Images were analyzed with image-processing software to obtain linear, area, and volumetric measurements of the upper airway and the tissues comprising the airway. The volume of the upper airway was smaller in subjects with OSAS in comparison with control subjects (1.5 ± 0.8 versus 2.5 ± 1.2 cm³; p < 0.005) and the adenoid and tonsils were larger (9.9 ± 3.9 and 9.1 ± 2.9 cm³ versus 6.4 ± 2.3 and 5.8 ± 2.2 cm³; p < 0.005 and p < 0.0005, respectively). Volumes of the mandible and tongue were similar in both groups; however, the soft palate was larger in subjects with OSAS (3.5 ± 1.1 versus 2.7 ± 1.2 cm³; p < 0.05). We conclude that in children with moderate OSAS, the upper airway is restricted both by the adenoid and tonsils; however, the soft palate is also larger in this group, adding further restriction.

Keywords: obstructive sleep apnea syndrome (OSAS); magnetic resonance imaging (MRI)

Obstructive sleep apnea syndrome (OSAS) is estimated to affect 2% of children (1). The disorder most commonly occurs between 2 and 6 yr of age and correlates with lymphoid hyperplasia during childhood (2, 3). Other important factors promoting OSAS in children include craniofacial anomalies and neuromuscular disorders that could affect the size, shape, and collapsibility of the upper airway during sleep. Traditional methods used in children to assess the upper airway and tissues surrounding the airway include lateral neck radiographs and cephalometry measurements (2–6). However, these methods are essentially two-dimensional and provide little information about lateral structures of the nasopharyngeal and oropharyngeal regions. Newer techniques such as acoustic reflection, ultrafast computed tomography, and magnetic resonance imaging (MRI) are readily available, and are used in adults for more detailed analysis of the upper airway structure (7–14). Of the above-cited methods, MRI provides superior resolution of tissues composing the upper airway; it is accurate, reproducible, and free of ionizing radiation. However, MRI has not been used in the past to systematically evaluate the upper airway in children with OSAS.

We hypothesized that the upper airway as assessed by MRI in children with OSAS is smaller because of adenoid and/or tonsillar overgrowth in comparison with control subjects. To this end we quantified total upper airway volume and cross-sectional area at expected sites of upper airway restriction in the nasopharyngeal and oropharyngeal regions. In addition, we measured the sizes of soft tissues and skeletal structures that define the upper airway. Finally, we validated our methods by examining the accuracy and reliability of these measurements.

METHODS

Subjects with OSAS

Eighteen children were recruited from the pool of patients evaluated for sleep-disordered breathing at the Children’s Hospital of Philadelphia (Philadelphia, PA). After OSAS was confirmed by polysomnography, patients were allowed to undergo MRI of the upper airway under sedation. The study was approved by the Institutional Review Board of the Children’s Hospital of Philadelphia. Informed consent was obtained from parents of the subjects.

Control Subjects

Eighteen children with normal growth and development were matched to subjects with OSAS by age, sex, ethnicity, weight, and height. Control subjects were selected from patients who underwent head MRI at the Children’s Hospital of Philadelphia for other medical indications. Exclusion criteria included (1) subjects with scores ≥ –1 (as assessed by a standard questionnaire, see below), (2) evidence of a brain tumor or a seizure disorder requiring therapy, (3) genetic disorders associated with any craniofacial anomaly, and (4) chronic respiratory disease such as asthma or bronchopulmonary dysplasia.

Overnight Polysomnography

For subjects with OSAS, polysomnography was performed 0–4 wk before MRI. Subjects were studied in the Sleep Disorders Center at the Children’s Hospital of Philadelphia. Scoring of respiratory variables was performed on the basis of standards set by the American Thoracic Society and previous published data about children (15, 16; details in online data supplement). Sleep stages were determined by the criteria of Rechtschaffen and Kales (17).

Sleep Questionnaire

A questionnaire regarding symptoms of sleep-disordered breathing, based on the questionnaire developed by Brouillette and coworkers (18), was used to assess the likelihood of OSAS in control subjects and subjects with OSAS. On the basis of the questionnaire no subject with a score < –1 would be expected to have OSAS; a score between –1 and 3.5 is considered indeterminate, and a score > 3.5 is considered highly predictive of obstructive sleep apnea.

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This article has an online data supplement, which is accessible from this issue’s table of contents online at www.atsjournals.org


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Magnetic Resonance Imaging

MRI studies were performed in the Department of Radiology at the Children’s Hospital of Philadelphia. All studies were performed under sedation with intravenous pentobarbital (2–6 mg/kg), administered in increments until sleep was achieved; a maximum of 200 mg was administered. All subjects were monitored continuously by pulse oximetry and observed by a critical care physician until recovery (~1 h).

MRI was performed with a 1.5T Siemens (Iselin, NJ) Vision system. Images were acquired with a commercially available head coil. The patient’s head was positioned supine in the soft tissue Frankfort plane. Axial and sagittal sequential T1-weighted (TR [repetition time], 650 ms; TE [echo time], 14 ms) and T2-weighted (TR, 6,000 ms; TE, 90 ms) images with 3-mm slice thickness and 1 NEX (number of excitations) were obtained from the orbital cavity to the larynx and from the midline bilaterally and sagittally.

Image Processing and Anatomic Measurements

Measurements from MR images were made with image processing software (Volumetric Image Display and Analysis [VIDA]; Department of Radiology, University of Iowa, Ames, IA) (9, 10, 13). Airway, soft tissue, and bony structure segmentation was performed by manual tracing.

Axial Measurements

From an axial T1-weighted image at the level of the maximal tonsillar cross-sectional area (Figure 1A), we determined the cross-sectional area of the oropharyngeal airway, tonsils, pterygoids, and parapharyngeal fat pads. The oropharyngeal airway was defined radiologically as being bounded anteriorly by the soft palate or tongue, laterally by the tonsils, and posteriorly by the pharyngeal constrictor muscle. At this level we also performed a series of linear measurements along a transverse line crossing the center of the tonsils (e.g., intertonsillar width, bilateral tonsillar width, bilateral fat pad width, bilateral pterygoid width, and intermandibular distance). In addition, we measured at other axial levels the largest adenoid cross-sectional area, maxilla width, and the internal distance between mandibular heads.

Sagittal Measurements

From a midsagittal T1-weighted image (Figure 1B), we determined the cross-sectional area of the nasopharyngeal airway, adenoid, soft palate, tongue, mandible, and hard palate. The nasopharyngeal airway was defined radiologically as being bounded anteriorly by the vomer, posteriorly by the adenoid, and inferiorly by a horizontal line above the hard and soft palate. In addition, we obtained a series of linear measurements along an oblique line connecting the mental spine, the center of the soft palate, and the clivus (i.e., tongue oblique, soft palate oblique, airway oblique, adenoid oblique, and mental spine-clivus oblique). We measured the length of the hard palate, defined from anterior nasal spine to end of the palatine bone.

Volumetric Measurements

Adjacent axial slices were used to determine the volumes of the following: combined upper airway (nasopharynx and oropharynx), adenoid, tonsils, tongue, soft palate, and mandible. Volumetric measurements (except tonsils and adenoid) were made from axial T1-weighted slices spanning from the base of the orbital cavities to the epiglottis. For measurements of adenoid and tonsils we used T2-weighted images because of their better resolution of lymphoid tissue. Tonsillar volume is the combined volume of right and left tonsils.

Validation Studies

(See online data supplement.) Accuracy of measurements was determined by using a set of commercial phantoms for lengths, areas, and volumes spanning the measurements used in the study. Intraclass correlation coefficient (ICC) was computed to assess the reliability of MRI measurements (19, 20).

Data Analysis

We hypothesized that children with OSA have a smaller upper airway in comparison with matched control subjects. Therefore, the primary outcome variable set was defined as (1) axial oropharyngeal cross-sectional airway area at the level of the maximal tonsillar cross-sectional area, (2) midsagittal nasopharyngeal cross-sectional airway area, and (3) upper airway volume. Secondary outcome measures included lengths, areas, and volumes of the tissues surrounding the upper airway and were considered hypothesis generating.

Means and standard deviations were used to summarize continuous variables. For comparisons between the groups for MRI data, demographics, and questionnaire data, we used a two-tailed unpaired t test, the Wilcoxon rank test, or χ² test as appropriate. The Pearson correlation was used to assess the linear correlation of volume percent difference of each OSAS–control pair and the corresponding apnea–hypopnea index. A p value < 0.05 was considered significant.

RESULTS

We studied 18 children with OSAS, (mean age, 4.8 ± 2.1 yr; range, 1.9–9.3 yr) and 18 control subjects (mean age, 4.9 ± 2.1 yr; range, 1.8–8.7 yr). Children with OSAS were not significantly different from control subjects with respect to age, sex, ethnicity, height, or weight (Table 1). All controls had normal development and cognitive function, intact tonsils and adenoid, and no respiratory disorders or craniofacial anomalies. The primary indications for head MRI in control subjects were as follows: single seizure/febrile convulsion (10 subjects), migraine/headache (4 subjects), head concussion (2 subjects), torticollis (1 subject), and eye injury (1 subject). Thus, none of these clinical indications would be expected to affect the upper airway anatomy.

Polysomnography

For subjects with OSA the mean total sleep time during polysomnography was 7.3 ± 1.0 h. The mean respiratory variable values during this period were as follows: apnea index, 4.3 ± 3.9; apnea–hypopnea index, 11.2 ± 6.8; baseline arterial oxy-
gen saturation (\(Sa_O_2\)), 95 ± 1%; and \(Sa_O_2\) nadir: 80 ± 10%. Thus, these data suggest moderate OSAS in this group.

Sleep Questionnaire
All controls had an apnea score < 1, indicating absence of obstructive sleep apnea in this group (18), and as a group had a mean apnea score of 2.8 ± 0.8. This score was significantly lower than the apnea score noted in the OSAS group, of 3.2 ± 1.0 (\(p < 0.0001\)).

Magnetic Resonance Imaging
The amount of sedation given before MRI was similar to both groups. A mean of 3.8 ± 1.1 and 4.0 ± 1.2 mg of pentobarbital per kilogram was given to subjects with OSAS and control subjects, respectively. Representative midsagittal and axial images of a control subject and a subject with OSAS are presented in Figure 2. The MRI measurements of the various tissues forming the upper airway of control subjects and children with OSAS are presented graphically in Figures 3–5.

**Airway.** The upper airway volume of children with OSAS was significantly smaller in comparison with the control group, 1.5 ± 0.8 versus 2.5 ± 1.2 cm\(^3\) (\(p < 0.005\)). Similarly, midsagittal nasopharyngeal airway cross-sectional area was smaller in the children with OSAS, 0.6 ± 0.3 versus 1.1 ± 0.5 cm\(^2\) (\(p < 0.005\)), as was the axial oropharyngeal cross-sectional airway area at the level of maximal tonsillar cross-sectional area, 0.4 ± 0.3 versus 0.7 ± 0.5 cm\(^2\) (\(p < 0.02\)).

**Soft tissues.** The cross-sectional areas of the pterygoids, parapharyngeal fat pads, tongue, and soft palate obtained from the axial and midsagittal images are presented along with the volumetric measurements of the tongue and soft palate in Figure 3. The axial and sagittal cross-sectional areas of the soft tissues were similar in both groups, as was the volume of the tongue. However, we noted a significantly larger soft palate volume in the OSAS group, 3.5 ± 1.1 versus 2.7 ± 1.2 cm\(^3\) (\(p < 0.05\)).

**Adenoid and tonsils.** As can be noted from all the measurements obtained in Figure 4, both the adenoid and tonsils were significantly larger in children with OSAS. The mean adenoid volume in children with OSAS was 9.9 ± 3.9 cm\(^3\) in comparison with 6.4 ± 2.3 cm\(^3\) in control subjects (\(p < 0.005\)) and mean tonsillar volume in children with OSAS was 9.1 ± 2.9 versus 5.8 ± 2.2 cm\(^3\) in control subjects (\(p < 0.0005\)).

**Facial skeletal structure.** Figure 5 demonstrates the skeletal findings of our study. The mandible width, length (as implied by mental spine–clivus distance), and volume were similar in both groups. Similarly, maxilla width, hard palate length, and sagittal cross-sectional area did not differ between groups. Thus, the similar skeletal findings in this set of measurements do not suggest a primary skeletal difference between subjects with OSAS and control subjects.

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**TABLE 1. DEMOGRAPHICS**

<table>
<thead>
<tr>
<th></th>
<th>Subjects with OSAS (n = 18)</th>
<th>Control Subjects (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>4.8 ± 2.1</td>
<td>4.9 ± 2.1</td>
</tr>
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<td>Sex, male/female</td>
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<td>12/6</td>
</tr>
<tr>
<td>Ethnicity, black/white</td>
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<td>10/8</td>
</tr>
<tr>
<td>Height, cm</td>
<td>107 ± 15</td>
<td>108 ± 16</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>20.2 ± 9.6</td>
<td>19.9 ± 7.1</td>
</tr>
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* Values represent means ± SD.
Validation of Methods

Analysis of data obtained from phantom MRI measurements indicated, in general, that accuracy increases with the size of the object measured. The ICC values for 13 representative parameters obtained include 1 measurement with a value of 0.78, indicating substantial reliability, and 12 with values greater than 0.88, indicating almost perfect reliability (20).

DISCUSSION

We used MRI to study the upper airway and surrounding tissues as well as the lower face skeletal structure in young children with OSAS. This is the first study of children with OSAS to use MRI to delineate the airway in detail, the tissues surrounding the airway, and the three-dimensional relationships of these tissues. Our volumetric measurements indicate that the adenoid and tonsils as well as the soft palate are significantly larger in children with OSAS concomitant with significantly smaller upper airway volume.

OSAS is common in children, with a prevalence of about 2% (1). OSAS may occur in all age groups. However, the peak incidence occurs between 2 and 6 yr of age, concomitant with rapid growth of the lymphoid tissue during these years (3). Diagnosis and management of OSAS are important because untreated OSAS may lead to altered neurodevelopmental performance (21–23), growth retardation (21, 24), pulmonary hypertension (25), and cor pulmonale (21, 26).

Our validation studies show that MRI provides both highly accurate and reliable measurements of the various tissues composing the upper airway. However, a disadvantage of MRI compared with ultra-fast computed tomography (CT) scan is its relatively long acquisition time (e.g., 2 min versus 10 s for each sequence) and therefore its sensitivity to motion artifact. To minimize movement during MR scanning, light sedation is given routinely to all children in our institution younger than 8 yr of age. We are aware that sedation could have reduced muscle tone impacting on airway measurements in our subjects. We assume that because the same sedation protocol was
used for both groups, airway measurements would be affected in a similar fashion. Sedation should not have affected the volumetric measurements of muscle, lymphoid, and bone tissues.

To obtain the most reliable comparison, we performed a case control study and matched subjects by age, height, weight, sex, and ethnicity. All of these may influence the anatomy of the structures studied, especially in respect to skeletal growth (3). On the basis of volumetric measurements of the upper airway and cross-sectional area measurements of the midsagittal and axial images, we conclude that the upper airway in children with moderate OSAS is significantly restricted in both the nasopharyngeal and oropharyngeal regions. The main factors contributing to this restriction are oversized adenoid and tonsils, which were noted to be 55 and 58% larger in volume, respectively, in comparison with control subjects.

Moreover, the positive correlation between the percent difference of the combined tonsil and adenoid volume and the apnea–hypopnea index found in the present study suggests that volumetric measurements of these tissues may be a useful way to predict severity of OSAS in these subjects. We found, however, no correlation of percent difference in airway volume alone with severity of OSAS. It is possible that airway shape, rather than simply volume, is a stronger predictor in determining airway resistance and airway collapsibility.

We also noted the volume of the soft palate to be about 30% larger in subjects with OSAS, adding additional restriction to the airway. This finding, not previously reported in children, has been observed in adults with OSAS (27–29). Histological evaluation of the soft palate of adults who underwent uvulopalatopharyngoplasty for OSAS indicated significant inflammatory changes and edema (27, 28). In another study, adults treated for OSAS with continuous positive airway pressure showed significant reduction in soft palate volume measured by MRI after several weeks of therapeutic use (29). Increased volume of the soft palate, hypothesized to be caused by chronic vibratory injury due to snoring and leading to edema and inflammation in adults, may be true in children as well.

Other soft tissues (excluding the tonsils) contributing to the width of the lateral pharyngeal wall, such as the pterygoid muscles, pharyngeal constrictor muscles, and parapharyngeal fat pads, were similar in size in both groups studied. These tissues did not contribute to airway restriction by thickening the lateral pharyngeal wall as reported in adults with OSAS (13). It is possible that these structures develop as risk factors later in life and contribute to the adult form of OSAS.

Several studies applying cephalometry to children with OSAS reported various facial skeleton differences, including retroposed mandible and maxilla, low positioned hyoid bone, and alterations in face length and width (30–33). On the basis of these, it has been suggested that OSAS may be caused by a combination of both adenotonsillar hypertrophy and abnormalities in the development of the lower face skeleton (32, 33). However, another prospective study showed that most cephalometric differences found in children reversed soon after adenotonsillectomy, suggesting that some of these differences detected by cephalometry may be secondary or compensatory and not a primary cause of OSAS (34).

Our set of skeletal measurements of children with no apparent craniofacial anomaly does not suggest a primary skeletal difference between our OSAS and control groups. The reason we did not find such a difference in our subjects can only be speculated at this time. We used different techniques and made measurements different from those performed in cephalometry, including lateral measurements obtained by axial images. Our subjects were sedated and in the supine position during imaging, compared with the upright awake subject studied by cephalometry. It is conceivable that an altered mandibular–skull or hyoid–tongue orientation detected in subjects in the upright position by cephalometry is positional in nature and could not be confirmed in our study of children in the supine position. Finally, differences in skeletal measurements may be related to subject-control matching criteria. It would be helpful in future to analyze cephalometric and MR images simultaneously to draw more definite conclusions.

In summary, we used MRI to study the upper airway in normal children and in children with moderate OSAS. We noted no significant lower face skeletal differences between these groups. The upper airway was restricted in children with OSAS by overgrowth of the adenoid and tonsils as well as a larger soft palate. Our data suggest a positive correlation between the percent difference in adenoid and tonsil volumes (OSAS to control) and the apnea–hypopnea index. Because OSAS represents a spectrum of disorders with a range of severity it will be essential in future to determine more precisely the relationships between these structures and the risk for, and severity of, OSAS at a given age.

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