Insights into the Management of SDB Utilizing Upper Airway Imaging

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What is the Best Upper Airway Imaging Modality?

- Morphometric examination/digital photography
- Cephalometrics
- Nasopharyngoscopy
- Acoustic Reflectance
- Optical Coherence Tomography
- Computed Tomography
- Magnetic Resonance Imaging

Insights into the Management of SDB Utilizing Upper Airway Imaging

- Upper airway imaging modalities
- Phenotyping the pharynx
  - Anatomic risk factors/three dimensional MRI
- Treatment of sleep apnea
  - CPAP
  - Weight loss
  - Oral appliances
  - Upper airway surgery
- Clinical utility of upper airway imaging

Normal Upper Airway
Physical Examination and Sleep Apnea
(Schellenberg AJRCCM 162:740-748, 2000)

- Enlarged Uvula
- Lateral Narrowing

Physical Examination and Sleep Apnea
(Schellenberg AJRCCM 162:740-748, 2000)

- Macroglossia
- Tongue ridging

Digital Morphometrics with Laser Ruler
Digital Morphometrics with Laser Ruler

Airway

Hyoid

Three Dimensional CT Reconstruction

Mandible

Airway

Optical Coherence Tomography


Subcutaneous Fat

Normal Subject (Mid-Sagittal View)


Endoscopic optical technique that allows macroscopic images of the airway in order to accurately determine shape and size of the upper airway

Soft Palate

Tongue

Airway

Mandible

Subcutaneous Fat

Retropalatal

Retroglossal
**Anatomic Risk Factors for Sleep Apnea**

- Are the upper airway soft tissue structures truly enlarged in patients with sleep apnea?
  - Remember it is the "donut" itself rather than the "hole of the donut" that is important
- If so, why are they enlarged?
Axial Upper Airway MR Images

Anatomic Risk Factors for Sleep Apnea
(Schwab et al, AJRCCM 168; 522-530, 2003)

Case-Control Study

Analysis 1

48 Probands
(Apneics)

48 Neighborhood Controls
matched by gender & race

Analysis 3

Hertability

48 Proband Sibs
same gender

Analysis 2

Familial aggregation study

48 Controls Sibs
same gender

Cases (N=48)/Controls (N=48) Demographics
(Schwab et al, AJRCCM 168; 522-530, 2003)

<table>
<thead>
<tr>
<th></th>
<th>Age (years)</th>
<th>BMI (kg/m²)</th>
<th>AHI (events/hour)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>45.3 ± 9.7</td>
<td>36.2 ± 8.8</td>
<td>43.8 ± 25.4</td>
</tr>
<tr>
<td>Controls</td>
<td>41.1 ± 10.5</td>
<td>25.9 ± 4.8</td>
<td>20 ± 1.6</td>
</tr>
<tr>
<td>P-Value</td>
<td>0.054</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

MRI Airway Reconstructions

Airway

Retropalatal

Retroglossal

Normal

Apneic
Volumetric Anatomic Risk Factors for Sleep Apnea (Cases/Controls: N = 96)
(Schwab et al, AJRCCM 168; 522-530, 2003)

Adjusted§ Odds Ratio (OR) for Sleep Apnea:

<table>
<thead>
<tr>
<th>Soft Tissue Volume</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat pads</td>
<td>1.64</td>
<td>1.00 - 2.81</td>
</tr>
<tr>
<td>Lateral Walls</td>
<td>6.01*</td>
<td>2.62 - 17.14</td>
</tr>
<tr>
<td>Soft Palate</td>
<td>1.66</td>
<td>0.99 - 3.18</td>
</tr>
<tr>
<td>Tongue</td>
<td>6.55*</td>
<td>2.81 - 19.42</td>
</tr>
<tr>
<td>Total Soft Tissue</td>
<td>6.95*</td>
<td>3.08 - 19.11</td>
</tr>
</tbody>
</table>

§Adjusted for gender, ethnicity, age, craniofacial size and visceral neck fat
* = Significant

Why are Upper Airway Soft Tissue Structures Enlarged in Apneics?

- Edema from negative pressure
- Weight gain/obesity
- Primary muscle disorder/injury
- Changes in blood flow
- Trauma from apneic events/snoring
- Gender
- Genetic factors
Examination of Heritability for Sleep Apnea
(Schwab et al, AJRCCM 173: 453-463, 2006)

Case-Control Study
- 55 Probands (Apneics)
- 55 Neighborhood Controls matched by gender & race

Analysis 1
- Probands-Sibs
- Controls-Sibs

Analysis 3
- Familial aggregation study

Heritability

Demographics (N = 220; 50% Men)

- Significant group differences in age (ANOVA: p = 0.022); however, no differences between probands and controls (t-test: p = 0.08) and probands and pro-sibs (t-test: p = 0.64)
- Significant group differences in BMI (ANOVA: p < 0.0001)
- Apneics had a significantly higher AHI (p < 0.0001)

Total Pharyngeal Lateral Wall Volume
(Schwab et al, AJRCCM 173: 453-463, 2006)

* ANOVA: p < 0.0001 Controlling for Age, Sex, Race, Craniofacial Size, and Visceral Neck Fat (N = 220; ± SD)

Paired contrasts between groups
- pro v pro-s <0.0363
- pro v con <0.0001
- pro-s v con <0.0001
- pro-s v con-s <0.0001
- con v con-s 0.1784

- Significant differences between family and no differences within controls

Heritability Indices* for Upper Airway Soft Tissue Volumes (N = 220)
(Schwab et al, AJRCCM 173: 453-463, 2006)

<table>
<thead>
<tr>
<th>Soft Tissue Volume</th>
<th>h²</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat pads</td>
<td>16.5%</td>
<td>0.063</td>
</tr>
<tr>
<td>Lateral Walls</td>
<td>36.8%</td>
<td>0.001</td>
</tr>
<tr>
<td>Soft Palate</td>
<td>9.3%</td>
<td>0.218</td>
</tr>
<tr>
<td>Tongue</td>
<td>36.5%</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total Soft Tissue</td>
<td>37.5%</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

*Adjusted for gender, ethnicity, age, craniofacial size and visceral neck fat

<table>
<thead>
<tr>
<th>Soft Tissue Volume</th>
<th>Pro/Sib ICC</th>
<th>Con/Sib ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat pads</td>
<td>0.05</td>
<td>0.45</td>
</tr>
<tr>
<td>Lateral Walls</td>
<td>0.21</td>
<td>0.28</td>
</tr>
<tr>
<td>Soft Palate</td>
<td>0.06</td>
<td>0.11</td>
</tr>
<tr>
<td>Tongue</td>
<td>0.07</td>
<td>0.42</td>
</tr>
<tr>
<td>Total Soft Tissue</td>
<td>0.07</td>
<td>0.44</td>
</tr>
</tbody>
</table>

*Adjusted for gender, ethnicity, age, craniofacial size and visceral neck fat

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**Understanding the Heritability of Upper Airway Structures: A Sib Pair Approach**

- These upper airway soft tissue structures demonstrated strong heritability independent of age, gender, race, craniofacial size and obesity
  - These data provide compelling evidence that genetic factors are important in determining the size of the upper airway structures
- Future studies should examine for the presence of candidate genes for these intermediate traits
  - Study in Iceland to examine candidate genes using MRI and a genealogy database

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**Effect of CPAP on Upper Airway Geometry?**

- Airway size increases with application of CPAP in both normals and apneics
  - CT: Kuna et al. ARRD 1988; 138:969-975
  - MRI: Abbey et al. ARRD 1989; 140:717-723
- CPAP originally thought to push tongue and soft palate forward
  - AP or lateral airway changes?

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**CPAP - Airway 3D Volumes**

(Schwab et al, AJRCCM 154:1106-1116, 1996)
Obesity and Obstructive Sleep Apnea

- Obesity reaching epidemic proportions in United States; approximately 55% population overweight
- Major phenotypic risk factor for OSA in adults appears to be obesity
- Weight loss in over 15 clinical studies decreases severity of OSA and decreases collapsibility of airway (increased Pcrit)
  - Why??
Neck Size and Obstructive Sleep Apnea

- What type of obesity is important?
  - BMI is not necessarily a gold standard
- Upper body obesity, rather than a more generalized distribution of body fat may be important for development of sleep apnea
- Increased neck size in several population studies good predictor of sleep apnea

Effect of Obesity on Upper Airway Tissues

- Increased volume of adipose tissue (several studies have demonstrated this)
  - In parapharyngeal fat pads
  - Within tongue
  - Fat under mandible and subcutaneous
- Increased muscular tissue with weight gain
  - Increase in size of lateral walls, tongue, soft palate

“Thank you for calling the Weight Loss Hotline. If you’d like to lose a half pound right now, press ‘1’ 18,000 times"
Weight Loss and Sleep Apnea

- How much weight loss results in clinical improvement?
  - Weight loss of 5 - 10% may be effective
- Does size of parapharyngeal fat pads decrease with weight loss?
- Does size of lateral pharyngeal walls, soft palate and tongue decrease with weight loss?
  - Weight loss is associated with reductions in both fat (75%) and fat-free mass (25%)

Effect of Weight Loss on UA Structures
(Welch et al, Sleep 25; 532-542, 2002)

- MRI in 12 normal women (AHI <1) before and after 17% weight loss - volumetric analysis
- Upper airway volume significantly increased with weight loss
- Volume of parapharyngeal fat pads and lateral pharyngeal walls decreased significantly with weight loss - why?
- Tongue and soft palate volume did not decrease significantly with weight loss - why?
Apneic Pre- and Post-Weight Loss:
(AHI 56.1 → 4.7)

**Oral Appliances**

- Mandibular repositioning devices are an effective alternative to CPAP in patients with mild to moderate OSA
- Mandibular repositioning devices clasp on upper and lower teeth pulling mandible forward and downward
- To determine most effective oral appliance we need to understand each appliance's mechanism of action

**How do Oral Appliances Change Upper Airway Geometry?**

- Do oral appliances simply pull mandible and tongue forward?
- How important is vertical bite opening?
- Studies indicate airway caliber increases in lateral dimension with oral appliances
- Structures lateral to airway may be important in understanding how oral devices maintain upper airway patency
Is Upper Airway Surgery Effective?

- Why is uvulopalatopharyngoplasty (UPPP) only effective in 50% of patients?
- Patients with retropalatal obstruction have a better surgical outcome than patients who manifest retroglossal obstruction.
- Should upper airway surgery be more directed at the lateral pharyngeal walls or tongue than the soft palate?

Upper Airway Surgery and Lateral Pharyngeal Walls

- UA surgery that affects lateral pharyngeal walls directly or indirectly (hyoid bone repositioning) has been shown to be effective:
  - Hyoid advancement/rotation
  - Lateral pharyngoplasty
    - Cahali et al, Sleep 27; 942-950, 2004
    - Lateral pharyngoplasty (15 cases; AHI 42 pre, 16 post) was shown to be more effective than UPPP (12 cases; AHI 35 pre, 30 post)
  - Tonsillectomy
Anterior suture of the superior pharyngeal constrictor muscle (lateral flap) to the palatoglossus muscle

Palatine flap, section of the palatopharyngeus muscle

Z-plasty covering the superior part of the tonsillar fossa, (A) palatine flap, (B) upper part of the palatopharyngeus muscle. Incision to remove part of the uvula (dashed line).

Elevation and section of the left superior pharyngeal constrictor muscle

Final aspect of the lateral pharyngoplasty.

Why is UPPP Surgery Not More Effective?

- Soft palate a strut for lateral pharyngeal walls?
  - Palatopharyngeus muscles arise from soft palate and make up a portion of lateral walls
- Proximal (nonresected) soft palate may be a problem
- Surgery primarily directed at AP tissues
- No effect on tongue
- Scarring from UPPP may result in traction and stiffing of lateral walls
  - Over time scarring may “soften” and apnea could return? (UPPP outcomes worsen with time)
Clinical Indications for Upper Airway Imaging in Apneics

- Upper airway imaging not indicated in patients successfully treated with CPAP
- Patients undergoing upper airway surgery may benefit from upper airway imaging
  - MRI and nasopharyngoscopy
- Success rate in patients undergoing UPPP related to site of obstruction
  - Better results with retropalatal compared to retroglossal obstruction

Imaging of the Upper Airway - "Take Home Message"

- Increased volume of upper airway soft tissue structures is an important risk factor for sleep apnea
- Upper airway soft tissue structures demonstrate heritability
- Lateral pharyngeal walls in addition to tongue and soft palate are important
  - CPAP, oral appliances, weight loss, decrease thickness of lateral walls
  - Thicken during sleep, expiration, Müller maneuver

Clinical Indications for Upper Airway Imaging in Apneics

- Nasopharyngoscopy with a Müller maneuver to determine if collapse occurs in retropalatal or retroglossal regions prior to UPPP
- If MRI or nasopharyngoscopy demonstrates significant retroglossal collapse surgery directed at advancing tongue should be considered
- CT scan or MRI prior to maxillomandibular surgery should be considered

Thank you for your attention!!!
Upper Airway Surgery and Lateral Pharyngeal Walls

- Scarring from UPPP may result in traction on lateral walls resulting in a reduction in thickness and collapsibility of these walls
  - Over time scarring may soften and apnea returns

Upper Airway Fat Deposition (Mortimore, Am J Resp Crit Care Med 157; 1998)

- Comparison of controls (BMI 25), nonobese apneics (BMI 26, AHI 33) and obese apneics (BMI 42, AHI 34)
- Total neck tissue volume obese apneics > nonobese apneics > controls
- Total neck fat volume obese apneics > nonobese apneics > controls
- Minimum cross sectional area controls > nonobese apneics > obese apneics

Imaging of the Upper Airway - "New Horizons"

- Ultrafast MRI to evaluate apneas dynamically
- Examine volumetric upper airway soft tissue changes with various treatment modalities (surgery, oral appliance, weight loss)
- Use upper airway imaging to study genetics (phenotypic risk factors) for sleep apnea
- Develop an biomechanical model to understand airway closure during sleep

Morphometric Measurements (Schellenberg AJRCCM 162;740-748, 2000)

- Macroglossia: tongue being above level of mandibular occlusal plane
- Uvula enlargement: > 1.5 cm in length or > 1.0 cm in width
- Enlargement of lateral pillars: > 25% impingement pharyngeal space by peritonsillar tissues
- Tonsillar enlargement: > 50% lateral impingement of posterior pharyngeal airspace
Physical Examination and Sleep Apnea
(Schellenberg AJRCCM 162:740-748, 2000)

Adjusted Odds Ratio (OR) for Sleep Apnea:

<table>
<thead>
<tr>
<th>Physical Finding</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral Narrowing</td>
<td>2.6*</td>
<td>1.7 - 4.1</td>
</tr>
<tr>
<td>Tonsillar hypertrophy</td>
<td>2.1*</td>
<td>1.1 - 4.2</td>
</tr>
<tr>
<td>Macroglossia</td>
<td>2.0</td>
<td>1.1 - 3.6</td>
</tr>
<tr>
<td>Enlarged soft palate</td>
<td>1.9</td>
<td>1.2 - 2.9</td>
</tr>
<tr>
<td>Retrognathia</td>
<td>1.3</td>
<td>0.8 - 2.1</td>
</tr>
</tbody>
</table>

*Maintained significance after adjusting for BMI/neck size
Upper Airway Soft Tissue Changes

Müller Maneuver - Retropalatal Region
Normal
Sitting - Baseline
Sitting - Maximum Effort

Müller Maneuver - Retropalatal Region
Apneic
Sitting - Baseline
Sitting - Maximum Effort

Müller Maneuver - Retropalatal Region
Normal
Baseline (Quiet Respiration)
10 cm H2O
20 cm H2O
30 cm H2O
40 cm H2O

Pharyngeal Wall Width
Fat Pad Width
Fat Pad Distance

mm
0
10
20
30
40
50
60

Normal
Snorer
Apneic

* *
Müller Maneuver - Retropalatal Region

Apneic

Baseline - Quiet Breathing

10 cm H₂O  20 cm H₂O  30 cm H₂O  40 cm H₂O

Respiratory Related Changes in Upper Airway

Upper Airway Area

Tidal Volume

Normal Respiratory-Related Dimensional Changes in the RP Region

1. Early Inspiration
2. Mid Inspiration
3. End Inspiration
4. Maximum Expiration
5. End Expiration
Apneic Respiratory-Related Dimensional Changes in the RP Region

1. Early Inspiration  
2. Mid Inspiration  
3. End Inspiration  
4. Maximum Expiration  
5. End Expiration

State Dependent Changes in UA Area and Soft Tissues in Normals

AHI = 0
- Wakefulness
- Sleep

State Dependent Changes in UA Area and Soft Tissues in Apneics

AHI >100
- Wakefulness
- Sleep

Pathogenesis of Sleep Apnea

- **Neural hypothesis:**
  - Sleep induces a decrease in pharyngeal muscle activity and this decrease is greater in apneics than normals
- **Anatomic hypothesis:**
  - Abnormal upper airway soft tissue and craniofacial structures during wakefulness
  - Decrease in upper airway muscle tone during sleep against the background of an abnormally narrowed pharynx
Anatomic Hypothesis

Pro/Con Editorial

Pro: Sleep Apnea Is an Anatomic Disorder
Richard J. Schwab, M.D.

Con: Sleep Apnea is not an Anatomic Disorder
Kingman P. Strohl, M.D.

UA Changes in Normals and Apneics

- Apneic airway is narrowed in lateral dimension
  - Predisposition to airway closure during sleep because of airway geometry?
- Thickness of lateral pharyngeal muscular walls caused airway narrowing
- Soft palate enlargement, secondary to increased vertical length, was greater in apneics
- However, volume of tongue, lateral walls and soft palate were not measured and may be more important for the development of apnea

State-Dependent Change
3D Airway Volumes in Normals

Pharyngeal Lateral Wall Volume Difference
* ANOVA: p < 0.0001 Controlling for Age, Sex, Race, Craniofacial Size, and Visceral Neck Fat (N = 220; ± SD)

- Significant differences between family; no differences in controls
**Lateral Upper Airway Dilatation with CPAP**

- Increase in airway size with CPAP is largely in lateral dimension
  - Kuna et al. ARRD 1988; 138:969-975
  - 8 - 16% increase in lateral airway dimensions
  - 2 - 4% increase in A-P dimensions
- Structures lateral to airway must be important in mediating these effects of CPAP

**Upper Airway Fat Deposition and Obstructive Sleep Apnea**

- If upper body obesity is a primary risk factor for sleep apnea than fat deposition around upper airway should be greater in apneics
- Imaging studies have demonstrated increased size of lateral parapharyngeal fat pads in obese patients with apnea