Sleep-disordered breathing, glucose intolerance, and insulin resistance

Rationale: Clinic-based studies suggest that sleep-disordered breathing (SDB) is associated with glucose intolerance and insulin resistance. However, in the available studies, researchers have not rigorously controlled for confounding variables to assess the independent relation between SDB and impaired glucose metabolism.

Objectives: The purpose of this study was to determine whether SDB was associated with glucose intolerance and insulin resistance among community-dwelling subjects (n = 2,656) participating in the Sleep Heart Health Study (1994–1999). SDB was characterized with the respiratory disturbance index and measurements of oxygen saturation during sleep. Fasting and two-hour glucose levels measured during an oral glucose tolerance test were used to assess glycemic status.

Measurements and main results: Relative to subjects with a respiratory disturbance index of less than 5.0 events/hour (the reference category), subjects with mild SDB (5.0–14.9 events/hour) and moderate to severe SDB (≥15 events/hour) had adjusted odds ratios of 1.27 (95% confidence interval: 0.98, 1.64) and 1.46 (95% confidence interval: 1.09, 1.97), respectively, for fasting glucose intolerance (p for trend < 0.01). Sleep-related hypoxemia was also associated with glucose intolerance independently of age, gender, body mass index, and waist circumference.

Conclusions: The results of this study suggest that SDB is independently associated with glucose intolerance and insulin resistance and may lead to type 2 diabetes mellitus.
Risk factors for Obstructive Sleep Apnea in adults
Young, T., Skatrud, J., Peppard, P.E.

Obstructive Sleep Apnea (OSA) is a sleep disorder characterized by intermittent complete and partial airway collapse, resulting in frequent episodes of apnea and hypopnea. The breathing pauses cause acute adverse effects, including oxyhemoglobin desaturations, fluctuations in blood pressure and heart rate, increased sympathetic activity, cortical arousal, and sleep fragmentation. The condition has received increasing attention during the past three decades. Until 1981, the only effective treatment for OSA was tracheostomy. The advent of continuous positive air pressure therapy, an effective noninvasive treatment, was a turning point, and clinical interest began to increase in tandem with the accumulation of research linking OSA to cognitive, behavioral, cardiovascular, and cerebrovascular morbidities (Figure).

Findings from large population studies in different countries during the last decade have contributed to a better understanding of the epidemiology of OSA. In most population studies, OSA status has been indicated by the frequency of apnea and hypopnea events per hour of sleep (apnea-hypopnea index) as determined by polysomnography (a continuous overnight recording of sleep, breathing, and cardiac parameters). The apnea-hypopnea index cutpoints of 5, 15, and 30 (with or without daytime sleepiness) are commonly used to indicate mild, moderate, and severe OSA, respectively. These studies have demonstrated that OSA is highly prevalent in adults. Approximately one in five adults has at least mild OSA and one in 15 adults has OSA of moderate or worse severity.

In the United States, 75% to 80% of OSA cases that could benefit from treatment remain undiagnosed. Associations of OSA with serious morbidity have raised concern that untreated OSA is a substantial but underappreciated public health threat. Primary care physicians are currently being encouraged to be alert to OSA symptoms of disruptive snoring, breathing pauses, and excessive daytime sleepiness in their patients. It is important that physicians also recognize that not all OSA patients are “Pickwickian” (i.e., male, obese, sleepy, snoring, and middle-aged), a stereotype that emerged from clinical observations of the highly selective patient populations observed in earlier years.

Figure. Risk factors, symptoms, outcomes, and comorbid conditions of Obstructive Sleep Apnea (OSA) in adults

### Demographic correlates of increased OSA prevalence
- Male sex
- Age 40-70 years
- Familial aggregation

### Risk factors
**Established**
- Body habitus
  - Overweight and obesity
  - Central body fat distribution
  - Large neck girth
  - Craniofacial and upper airway abnormalities

**Suspected**
- Genetics
- Smoking
- Menopause
- Alcohol use before sleep
- Nighttime nasal congestion

### OSA Symptoms
- Habitual, loud snoring
- Nocturnal breathing pauses, choking, gasping
- Excessive daytime sleepiness

### Outcomes and/or comorbid conditions
- Problems with daytime functioning
  - Daytime sleepiness
  - Motor vehicle crashes
  - Psychological problems
  - Decreased cognitive function
  - Reduced quality of life
- Cardiovascular and cerebrovascular disease
  - Hypertension
  - Coronary artery disease
  - Myocardial infarction
  - Congestive heart failure
  - Stroke
- Diabetes and the metabolic syndrome

*These conditions are associated with OSA. The associations may be due, in part, to common risk factors; they may also reflect a role of OSA in their etiology.

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Association of sleep apnea and type II diabetes: A population-based study
Reichmuth, K.J., Austin, D., Skatrud, J.B., Young, T.
Am J Respir Crit Care Med 2005:172:1590-1595

Rationale: Cross-sectional association has been reported between sleep-disordered breathing (SDB) and insulin resistance, but no prospective studies have been performed to determine whether SDB is causal in the development of diabetes.

Objectives: The purpose of our study was to investigate the prevalence and incidence of type II diabetes in subjects with SDB and whether an independent relationship exists between them.

Methods: A cross-sectional and longitudinal analysis was performed in 1,387 participants of the Wisconsin Sleep Cohort. Full polysomnography was used to characterize SDB. Diabetes was defined in two ways: (1) physician-diagnosis alone or (2) for those with glucose measurements, either fasting glucose ≥ 126 mg/dl or physician diagnosis.

Measurements and main results: There was a greater prevalence of diabetes in subjects with increasing levels of SDB. A total of 14.7% of subjects with an apnea–hypopnea index (AHI) of 15 or more had a diagnosis of diabetes compared with 2.8% of subjects with an AHI of less than five. The odds ratio for having a physician diagnoses of diabetes mellitus with an AHI of 15 or greater versus an AHI of less than five was 2.30 (95% confidence interval, 1.28–4.11; p = 0.005) after adjustment for age, sex, and body habitus. The odds ratio for developing diabetes mellitus within four years with an AHI of 15 or more compared with an AHI of less than five was 1.62 (95% confidence interval, 0.67–3.65; p = 0.24) when adjusting for age, sex, and body habitus.

Conclusions: Diabetes is more prevalent in patients with SDB and this relationship is independent of other risk factors. However, it is not clear that SDB is causal in the development of diabetes.

Table 3: Odds ratio for prevalent, physician-diagnosed diabetes for two levels of sleep-disordered breathing

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p Value</th>
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</thead>
<tbody>
<tr>
<td>Adjusted for sex and age</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>AHI 5-15 vs. AHI &lt;5</td>
<td>1.83</td>
<td>1.07-3.11</td>
<td>0.026</td>
</tr>
<tr>
<td>AHI ≥15 vs. AHI &lt;5</td>
<td>4.75</td>
<td>2.62-8.63</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Adjusted for sex, age, and body habitus*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI 5-15 vs. AHI &lt;5</td>
<td>1.25</td>
<td>0.75-2.07</td>
<td>0.40</td>
</tr>
<tr>
<td>AHI &gt;15 vs. AHI &lt;5</td>
<td>2.30</td>
<td>1.28-4.11</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Definition of abbreviation: AHI = apnea-hypopnea index.

*Body habitus measures: waist girth and waist girth x sex interaction.

Table 4: Odds ratio for 4-yr incidence of physician-diagnosed diabetes for two levels of sleep-disordered breathing

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted for sex and age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI 5-15 vs. AHI &lt;5</td>
<td>2.81</td>
<td>1.51-5.23</td>
<td>0.001</td>
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<tr>
<td>AHI ≥15 vs. AHI &lt;5</td>
<td>4.06</td>
<td>1.86-8.85</td>
<td>0.0004</td>
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<tr>
<td>Adjusted for sex, age, and body habitus*</td>
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<tr>
<td>AHI 5-15 vs. AHI &lt;5</td>
<td>1.56</td>
<td>0.80-3.02</td>
<td>0.19</td>
</tr>
<tr>
<td>AHI &gt;15 vs. AHI &lt;5</td>
<td>1.62</td>
<td>0.67-3.65</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Definition of abbreviation: AHI = apnea-hypopnea index.

*Body habitus measures: waist girth.

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