Impact of Heart Disease

- Cardiovascular disease (CVD) accounts for nearly 801,000 deaths in the US (1/3 of all deaths)
- 2,200 Americans die of CVD each day (1 death every 40 seconds)
- CVD claims more lives each year than all forms of cancer and Chronic Lower Respiratory Disease combined.
- About 92.1 million American adults are living with some form of CVD or the after-effects of stroke.
- Direct and indirect costs of CVD and stroke are estimated to total more than $316 billion.
- By 2030, total direct medical costs of CVD are projected to increase to about $920 billion.

Heart and Stroke Statistics-2017; Circulation 2017

OUTLINE

- Overview of physiology of the cardiovascular system during sleep
- Mechanism of cardiovascular disease in Sleep Disordered Breathing (SDB)
- Management of SDB in heart disease

Physiologic Changes in Cardiovascular Parameters during Sleep

<table>
<thead>
<tr>
<th>NREM</th>
<th>Tonic REM vs. NREM</th>
<th>Phasic REM vs. Tonic REM and NREM</th>
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<tbody>
<tr>
<td>HR</td>
<td>HR</td>
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<td>CO</td>
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<td>BP</td>
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<td>SVR</td>
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National Sleep Foundation 2011 Sleep in America Poll

- 63% say their sleep needs are not being met during the week (Most need about 7 1/2 hours of sleep to feel their best, but get 6:55 sleep on weeknights).
- 60% experience a sleep problem every night (snoring, waking in the night, waking up too early, or non-refreshed sleep).
- 63% say their sleep needs are not being met during the week (Most need about 7 1/2 hours of sleep to feel their best, but get 6:55 sleep on weeknights).
- 15% of adults say they sleep less than 6 hours on weeknights.

Voluntary Sleep Loss: a risk factor for insulin resistance and Type 2 DM


ABSTRACT: Sleep is increasingly recognized as an important lifestyle contributor to health. However, this has not always been the case, and an increasing number of Americans choose to curtail sleep in favor of other social, leisure, or work-related activities. This has resulted in a decline in average sleep duration over time. Sleep duration, mostly short sleep, and sleep disorders have emerged as being related to adverse cardiometabolic risk, including obesity, hypertension, type 2 diabetes mellitus, and cardiovascular disease. Here, we review the evidence relating sleep duration and sleep disorders to cardiometabolic risk and call for health organizations to include evidence-based sleep recommendations in their guidelines for optimal health.
Prevalence of OSA

• In 1993, OSA (defined as AHI > 5 events/hour of sleep) is present in:
  – 24% men and 9% women 30-60 years
  – 31% men and 16% women 50-60 years
  » Wisconsin Sleep Cohort NEJM 1993
• Increased age and weight are the most important risk factors for OSA
• In individuals with CVD, the prevalence of OSA exceeds 50%
OSA and Metabolic Dysfunction

• OSA is an independent risk factor for the metabolic syndrome (Coughlin et al. Eur Heart J. 2004)
• OSA is associated with increased peroxidation of lipids, endothelial dysfunction and atherosclerosis
• Treatment of OSA reverses the metabolic syndrome in OSA
• CPAP improves insulin sensitivity in some patients with OSA

Obstructive sleep apnea (OSA)

Hypoxia is the Critical Stimulus BP and Sympathetic Surge in Both Central and Obstructive Apneas

Immediate Consequences of an apnea

• Hypoxia
• Arousal
• Increased sympathetic activity
• Surge in blood pressure

Nocturnal Blood Pressure Response to SDB


Varadharaj et al. Respir Physiol Neurobiol 2015


OSA is associated with Oxidant Mediated Vascular Endothelial Dysfunction
**Cardiovascular Disease Risk in OSA Patients**

<table>
<thead>
<tr>
<th>Arteriolar superoxide production</th>
<th>Arteriolar nitric oxide availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Graph](Varadharaj et al Respir Physiol Neurobiol 2015)</td>
<td>![Graph](Varadharaj et al Respir Physiol Neurobiol 2015)</td>
</tr>
</tbody>
</table>

**OSA and CVD**

- OSA is a cause of hypertension
- OSA patients have endothelial dysfunction and oxidative stress even in the absence of measurable CVD
- OSA is associated with CAD, stroke, and heart failure

**OSA and Arrhythmia**

- Increased atrial and ventricular ectopy during the night in patients with OSA
  - Mehra et al 2006
- Increased firing of defibrillators in patients with heart failure and both OSA and CSA
  - Oldenburg Eu Heart J 2015

**OSA and Atrial Fibrillation**

- Increased prevalence of OSA in patients with AF
- Increased rate of recurrence of AF in patients with untreated OSA
- Increased rate of failure of anti-arrhythmic medication in AF patients who have untreated OSA
- Increased likelihood of failure of first and second ablation procedure if OSA is untreated


Varadharaj et al Respir Physiol Neurobiol 2015
Cerebrovascular Accidents (CVA)

- High prevalence of SDB in stroke/TIA patients
  - Meta analysis demonstrated frequency of AHI > 5 was 72%, and AHI > 20 was 38%
  - Wisconsin Sleep Cohort Study showed AHI > 20 associated with 4 fold increase risk of having CVA
- Several potential mechanisms
  - Hypertension, diabetes, inflammation effects
  - Atrial fibrillation association with stroke and SDB
  - Intracranial hemodynamic changes as a result of blood pressure surges, transient hypoxia and resulting drop in cerebral perfusion


Pathways of Cardiovascular Disease in Sleep Apnea

- Patients referred to sleep lab compared to controls
  - AHI > 30 or between 5-30 with daytime somnolence offered CPAP

If OSA is a Cardiovascular Risk Factors, Why are the RCTs negative?

- Is CPAP an effective treatment for OSA?
- Dose of CPAP in the RCTs was not adequate
- Power and duration of follow up are not adequate
- Outcomes measured are not representative
- Populations studied are not appropriate

Treatment options

- Mandibular advancement devices
- Surgery
  - UPPP
  - Jaw advancement surgeries
  - Bariatric procedures
  - Tracheostomy
- Neurostimulation: Inspire®
- Positional therapy
- Weight loss

Treatment of OSA in Patients with Cardiovascular Disease

- CPAP remains the mainstay of treatment
- CPAP has the most available data on safety and efficacy
- Improvement in blood pressure, atrial fibrillation control and endothelial dysfunction are reported only with CPAP
- Tolerance of CPAP is likely increased with improved technology of device and interface

Evaluation for OSA

- Patients at high risk for OSA should be evaluated for OSA symptoms
  - Obesity (BMI > 35)
  - Congestive heart failure
  - Atrial fibrillation
  - Refractory hypertension
  - Type II diabetes
  - Nocturnal dysrhythmias
  - Stroke
  - Pulmonary hypertension
  - High risk driving populations
  - Preoperative evaluation

Epstein et al. JCSM Vol 5, No 3; 2009
### OSA symptoms that should be evaluated during a comprehensive sleep evaluation

- Witnessed apneas
- Snoring
- Gasping/choking at night
- Excessive sleepiness
- Nonrefreshing sleep
- Total sleep amount
- Sleep fragmentation
- Nocturia
- Morning headaches
- Decreased concentration
- Memory loss
- Decreased libido
- Irritability

- CPAP is effective in improving symptoms of SDB
  - Sleepiness; insomnia; cognitive; mood; and functional parameters
- CPAP must be viewed as a highly personalized intervention:
  - Exposure time
  - Sleep time
  - Residual AHI
- Traditional CVD biomarkers may not reflect actual CPAP effects
- Subpopulations of OSA patients who benefit most from CPAP need to be identified.