

Untreated OSA
can be a Killer

Obstructive Sleep Apnea and its Comorbidities

Clinical References

(Provider)

Obstructive Sleep Apnea is closely associated (comorbid) with a number of diseases, particularly obesity, diabetes, hypertension and cardiovascular disease.

Patients with these diseases are far more likely to have OSA. Treating OSA is proven to have a significant positive effect on primary diagnosis outcome. Treating OSA as the primary diagnosis can mitigate the likelihood of developing comorbid diseases.

This document is intended to summarize just a few of the many clinical reports documenting the extent of the comorbidities and the impact of treatment.

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Diseases Associated with OSA

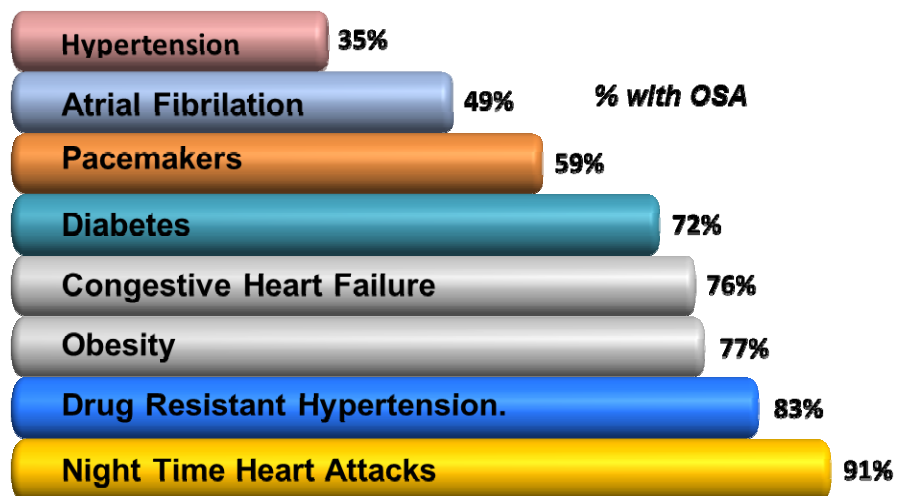


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I. OSA & Cardiovascular Disease

A. Sleep-disordered Breathing and Cardiovascular Disease – A Vicious Cycle?

Clinical Advantage 2011; vol1; no1

Abstract:

A growing body of evidence suggests that OSA is often associated with the development of various CARDIAC disorders. In addition, when non-ischemic or ischemic cardiomyopathy has developed, impaired cardiac function itself may contribute to the development of both obstructive and central SA by inducing ventilator control instability and rostral fluid shift induced upper airway narrowing during sleep.

Untreated OSA is associated with progression of cardiac disease via acute increase of cardiac afterload and non-dipping, hypertension, left ventricular hypertrophy, endothelial dysfunction and atherosclerosis, coronary artery disease, myocardial infarction and heart failure.

Cardiovascular disease also promotes sleep disordered breathing. Participants with incident cardiovascular disease experienced larger increases in both mean obstructive and central apnea indices.

B. Oxidative Stress in Obstructive Sleep Apnea (2005)

Chest Journal - American College of Chest Physicians 2005;127/5

Abstract:

Studies have revealed a relationship between the severity of OSA and the level of oxidative stress. OSA is characterized by recurrent nocturnal obstruction of the upper airway. Each episode of airway obstruction is usually followed by a marked decrease of arterial oxygen saturation, which rapidly normalizes after ventilation resumes.

These repeated changes of oxygen saturation could be considered analogous to recurrent episodes of ischemia-reperfusion injury, which causes damage after the restoration of blood flow to ischemic or hypoxic tissues.

Although several mechanisms are involved, such damage is mainly attributed to the production of reactive oxygen species (ROS) during re-oxygenation. ROS are highly reactive molecules that interact with nucleic acids, lipids, and proteins, and are considered to have an important role in the development of cardiovascular disease.

All of these studies have indicated a significant relationship between OSA and oxidative stress. It is well known that the prevalence of asymptomatic sleep-disordered breathing (SDB) is several times higher than that of recognized SDB. Therefore, oxidative stress in persons with SDB may also be a public health issue.

II. OSA & Hypertension

- A. High Cardiovascular Risk Profile in Patients with Sleep Apnea (2013)
Laryngoscope 2013; DOI: 10.1002/24304

Abstract:

Heart disease and hypertension was highly prevalent in patients with moderate to severe sleep apnea. Severe Sleep Apnea was associated with a 60% increased cardiovascular risk compared with not having Sleep Apnea.

In Sleep Apnea patients without previously diagnosed hypertension, 44% had prehypertension and an additional 45% had significant elevated blood pressure. Only 11% had optimal blood pressure. In participants without previously known heart disease, sleep apnea was found in 72% of the patients.

- B. Resistant Hypertension and Obstructive Sleep Apnea (2013)
International Journal of Hypertension 2013;193010;1-6

Abstract:

Hypertension is a treatable, highly prevalent, risk factor for cardiovascular morbidity and renal dysfunction worldwide and is increasing in incidence. Approximately 68 million (31%) United States adults aged ≥ 18 years had Hypertension.

Large population-based studies have demonstrated that Obstructive Sleep Apnea (OSA) is a risk factor for resistant Hypertension. The mechanism has been identified as a pattern of intermittent hypoxia associated with hyperaldosteronism, increased sympathetic tone, endothelial dysfunction, hypoxic vasoconstriction and inflammation.

Treatment with OSA therapy (PAP, Oral Appliance or Surgery) can lead to improvement in the control of Blood Pressure in patients with resistant Hypertension. While the reduction in blood pressure with is modest, it only requires a small decrease in blood pressure to significantly reduce cardiovascular risk.

C. Obstructive Sleep Apnea - A Cardio Metabolic Risk in Obesity and the Metabolic Syndrome

Journal of the American College of Cardiology 2013;62(7): 569-576

ABSTRACT:

Obesity predisposes to OSA, and the prevalence of OSA is increasing worldwide because of the ongoing epidemic of obesity. Recent evidence has shown that cardiovascular risk, including sympathetic activation, systemic inflammation, and endothelial dysfunction, are significantly increased in obese patients with OSA versus those without OSA.

Intermittent hypoxia exacerbates the metabolic dysfunction of obesity, augmenting insulin resistance and nonalcoholic fatty liver disease. In patients with the metabolic syndrome, the prevalence of moderate to

severe OSA is very high (~60%). In this population, OSA is independently associated with increased

D. Obesity, Sleep Apnea and Hypertension (2003)

Hypertension Journal (American Heart Association) 2003; 42:1067-1074

Abstract:

Obstructive Sleep Apnea (OSA) might be an important mechanism underlying the association between obesity and hypertension. In some populations, an almost linear relation exists between BMI and systolic/diastolic blood pressure. Incompletely treated OSA was found to be an independent predictor of cardiovascular disease, including hypertension.

The evidence supporting the association between OSA and chronic, longstanding hypertension is compelling and is provided by several cross-sectional, longitudinal, and treatment studies. The Framingham Heart Study suggests that 65% of the risk for hypertension in women and 78% in men can be related to obesity.

Whereas obesity increases the risk for OSA, sleep apnea may also actually predispose an individual to weight gain and obesity. Indeed, patients with newly diagnosed OSA have a history of excessive recent weight gain in the period preceding the diagnosis. It appears then that there may be a reciprocal relation between obesity and OSA that triggers a feed-forward mechanism, whereby obesity and OSA mutually enhance their progression and severity.

III. OSA & Stroke

A. Mechanism of Ischemic Stroke in Patients with Obstructive Sleep Apnea

Sleep Journal 2012; vol35 Suppl., Abstract0826

Abstract:

Patients presenting to the Mayo Clinic over a 10 year period were followed for subsequent ischemic stroke within one year after a sleep study to identify OSA.

Cardio embolic strokes were more than twice as common in OSA patients (72%). In addition, the frequency of stroke rose with the severity of OSA.

Among patients with OSA, 84 percent had at least one cardio embolic risk factor, such as dilated cardiomyopathy. Atrial fibrillation was almost twice as common in OSA patients (47%).

B. Association of Sleep-disordered Breathing and the Occurrence of Stroke

American Journal of Respiratory and Critical Care Medicine 2005;172,14471451

Abstract:

The data demonstrates a strong association between moderate to severe sleep-disordered breathing and prevalent stroke, independent of confounding factors.

The data also provides the first prospective evidence that sleep-disordered breathing precedes stroke and may contribute to the development of stroke. Moderate Sleep Apnea (n AHI of at least 20) is associated with a highly increased probability of suffering a stroke within the next 4 yr.

In addition to the evidence presented herein that SDB contributes to the development of stroke, the presence of SDB after stroke may have adverse prognostic implications.

C. Cerebrovascular Consequences of Obstructive Sleep Apnea (2012)

Journal of the American Heart Association 2012; 1:e000091

Abstract:

Patients presenting with stroke or transient ischemic attack were 3 to 4 times more likely to have OSA than were matched control subjects. Regardless of sex, between 60% and 80% of patients with stroke and transient ischemic attack had an AHI>10 (Moderate OSA).

Published studies have reported an association between OSA and dementia in the elderly, with the severity of the dementia being related to the severity of the sleep-disordered breathing.

Strong evidence indicates that (1) OSA is an independent risk factor for stroke, (2) OSA exacerbates damage produced by a stroke, (3) OSA increases the risk for a subsequent stroke, and (4) OSA contributes to brain atrophy and dementia in the elderly.

D. Obstructive Sleep Apnea as a Risk Factor for Stroke and Death (2005)
New England Journal of Medicine 2005; 353, 2034-41

Abstract:

As expected, the prevalence of hypertension and diabetes mellitus was higher in the group with the syndrome than in the comparison group. Patients with the syndrome also were more obese, as reflected by the higher body-mass index, and had lower nadir oxygen saturations and a higher arousal index. Obstructive apnea was the predominant apneic event; central apnea was rare.

The obstructive sleep apnea syndrome retained a statistically significant association with stroke or death.

The obstructive sleep apnea syndrome significantly increases the risk of stroke or death from any cause, and the increase is independent of other risk factors, including hypertension.

E. Basics of Sleep Apnea and Ischemic Stroke (2013)
CardioSource - Sleep Apnea and CV Disease

Abstract:

Sleep apnea is frequent in patients with acute ischemic stroke. While in the general population approximately one in ten adults suffer sleep apnea of various subtypes and degrees, OSA frequency in acute stroke patients appears much higher, reaching almost 70%.

Sleep apnea is a risk factor for acute ischemic stroke. Studies also suggest that sleep apnea constitutes a pre-existing condition rather than a consequence of acute ischemic brain damage.

The pathophysiologic mechanism by which sleep apnea contributes to cerebrovascular complications is supported by a recent observation that the intima media thickness in the carotid arteries, a marker for general atherosclerotic burden.

A variety of mechanisms such as inflammatory processes, endothelial malfunction, enhanced activity of thrombocytes and coagulation factors leading to hypercoagulable state, and progression of atherosclerosis may trigger atherothrombotic and embolic strokes.

Sleep apnea may negatively influence the clinical course in the acute phase of ischemic stroke. More specifically, up to an 8-fold increased risk for early worsening of neurological symptoms within 72 hours from stroke onset has been described.

IV. OSA & Heart Attacks

A. OSA and the Risk of Sudden Cardiac Death - A Longitudinal Study of 10,701 Adults (2013)

Journal of the American College of Cardiology 2013; 62(7): 610-616

Abstract:

10,701 Mayo Clinic patients were followed for up to 15 years. The presence of Obstructive Sleep Apnea after an average of 5 years predicted incident Sudden Cardiac Death, and the magnitude of risk was predicted by the severity of OSA, including the Apnea-Hypopnea Index and the degree of nocturnal oxygen desaturation.

Notably, the severity of nocturnal hypoxemia, an important pathophysiological feature of OSA, strongly predicted SCD independently of well-established risk factors.

There is a cascade of possible pathophysiological mechanisms linking OSA to SCD during the daytime and during sleep. Obstructive apneic events cause systemic hypoxemia, which is sometimes severe and prolonged. These repetitive oxygen desaturations in OSA patients may cause ventricular ectopy. Hypoxemia, with associated hypercapnia, also activates the chemoreflex, which increases vascular sympathetic nerve activity and serum catecholamines.

Tachycardia and surges in blood pressure at the end of apneas result in increased myocardial oxygen demand at a time when oxygen saturation is at its lowest, a situation that may lead to myocardial ischemia and potentially dysrhythmic consequences. Individuals with OSA also have a paradoxical increase in coagulability during the night. Platelet activation and aggregation are increased, fibrinogen levels are increased, and fibrinolytic activity is decreased during sleep in patients with OSA.

B. Benefits of obstructive sleep apnea treatment in coronary artery disease

European Heart Journal 2004; 25,728–734

The aim of this long-term prospective study was to evaluate the effect of treating obstructive sleep apnea (OSA) on the rate of cardiovascular events in coronary artery disease patients.

That OSA is associated with an increased risk of cardiovascular events in CAD patients has been reported previously. Mooe et al.¹⁰ observed a 62% relative increase and a 10.1% absolute increase in a composite endpoint of cardiovascular events (death, cerebrovascular events, and myocardial infarction).

OSA treatment significantly reduced the risk of cardiovascular death, acute coronary syndrome, hospitalization for heart failure, or need for coronary revascularisation. In addition, the time to events was longer in the group of patients who accepted OSA treatment.

C. Clinical Characteristics of Patients with Acute Coronary Syndrome at High Clinical Suspicion for Obstructive Sleep Apnea Syndrome (2013)

Hellenic Journal of Cardiology 2013; 54: 348-354

Abstract:

Acute Coronary Syndrome is an umbrella term for situations where the blood supplied to the heart muscle is suddenly blocked, including heart attack or unstable angina. OSAS significantly increases cardiovascular morbidity and mortality.

The results of our studies confirm the previous finding that over 30% of myocardial infarction patients have OSAS. The study strongly reinforces that OSAS is common and under-diagnosed among patients with myocardial infarction.

Undiagnosed OSA patients had significantly higher systolic and diastolic blood pressure. OSAS is associated with poor blood pressure control, especially during the night hours. OSAS is also associated with elevated levels of plasma C-reactive protein, a well-known marker of inflammation and of cardiovascular risk.

OSAS patients had significantly larger left ventricular diastolic diameter, a thicker interventricular septum, and a higher left ventricular mass index. Patients also had a longer hospitalization duration and more frequent mortality.

One out of every three ACS patients was diagnosed with a high clinical suspicion for OSAS. The prevalence of cardiovascular risk factors among ACS patients at high clinical suspicion for OSAS was high. A high clinical suspicion of OSAS was also associated with an increase in the risk of adverse cardiac events in myocardial infarction patients.

This finding calls for physicians to perform routine screening and individual evaluation of myocardial infarction patients for sleep disorders.

D. Sleep Apnea and Cardiovascular Disease - A Bidirectional Relationship (2012)

Circulation Journal - American Heart Association 2012;126:1495-1510

Abstract:

Repetitive obstructive apneas expose the heart and circulation to a cascade of noxious stimuli that, over time, may initiate or contribute to the progression of most cardiovascular disorders.

Over a period of years, the accumulated impact of recurrent nightly cycles of increased heart wall stress (Left ventricular), hypoxia, and sympathetic activation in susceptible individuals may well lead to Left ventricular hypertrophy, dilatation, and a decline in systolic function.

The mechanical, autonomic, and oxidative stresses imposed by sleep apnea can aggravate myocardial ischemia and contribute to increased mortality, perhaps through the generation of malignant ventricular arrhythmias.

Eighteen-year follow-up data from the Wisconsin Sleep Cohort showed that, in comparison with subjects without sleep apnea, the adjusted mortality risks of those with severe untreated OSA were significantly higher.

Data from epidemiological studies and randomized clinical trials strongly suggest that OSA is a common and treatable risk factor for development of hypertension, HF, arrhythmias, and stroke, especially in men.

E. Day-Night Pattern of Sudden Death in Obstructive Sleep Apnea (2005)

The New England Journal of Medicine 2005; 352:1206-14

Abstract:

Obstructive sleep apnea is highly prevalent and associated with neurohormonal and electrophysiological abnormalities that may increase the risk of sudden death from cardiac causes, especially during sleep.

The risk of sudden death from cardiac-only causes in the general population is significantly greater during the morning hours after waking (i.e., from 6 a.m. to noon).

People with obstructive sleep apnea have a peak in sudden death from cardiac causes during the sleeping hours. People with sudden death from cardiac causes from midnight to 6 a.m. had a significantly higher apnea-hypopnea index. The apnea-hypopnea index correlated directly with the relative risk of sudden death from cardiac causes.

The severity of obstructive sleep apnea correlated directly with the risk of nocturnal sudden death from cardiac causes, such that the relative risk of sudden death from cardiac causes during the sleeping hours was 40 percent higher in persons with severe obstructive sleep apnea (apnea-hypopnea index, ≥ 40) than in those with mild-to-moderate obstructive sleep apnea (apnea-hypopnea index, 5 to 39).

F. Obstructive Sleep Apnea and Cardiovascular Disease (2003)
Journal of the American College of Cardiology 2003:1429–37

Abstract:

As it is strongly associated with known cardiovascular risk factors, including obesity, insulin resistance, and dyslipidemia, OSA is an independent risk factor for hypertension and has also been implicated in the pathogenesis of congestive cardiac failure, pulmonary hypertension, arrhythmias, and atherosclerosis.

A recent sleep clinic study reported a linear relationship between hypertension and severity of OSA, with each extra apneic episode per hour increasing the odds of hypertension by 1%.

The implications of the Wisconsin Sleep Cohort Study are profound, indicating that OSA is a new primary cause of hypertension.

Patients with OSA have many features in common with the “metabolic syndrome,” including systemic hypertension, central obesity, and insulin resistance. The severity of OSA correlates with Body Mass Index, waist-to-hip ratio, hypertension, and diabetes, whereas trends toward lower high-density lipoprotein and elevated triglycerides are reported for OSA subjects.

In OSA, cyclical variations in heart rate and blood pressure are dramatic, more so than many hemodynamic stresses in daily life, and occur during sleep, a time when in normal subjects blood pressure and heart rate are the lowest and least variable.

In OSA, increased peripheral sympathetic nerve activity during sleep persists during wakefulness at approximately twice the normal levels and may affect acute coronary events in the early hours of the day.

OSA is an independent predictor of coronary artery disease. At long-term follow-up, subjects with coronary artery disease whose OSA remained untreated had worse mortality

Both tachyarrhythmias and bradyarrhythmias have been implicated as possible causes of cardiovascular morbidity in OSA patients. The risk of arrhythmia with OSA appears to be related to sleep apnea severity.

G. Influence of obstructive sleep apnea on mortality in patients with heart failure)

Journal of the American College of Cardiology 2007; 49:1625–1631.

Abstract:

Increased mortality rate observed in Heart Failure patients with untreated OSA due to generation of negative intrathoracic pressure during obstructive events causes both an increase in left ventricular afterload and a decrease in left ventricular preload, accompanied by reductions in stroke volume.

Apnea-related hypoxia also can reduce cardiac output by impairing myocardial contractility and increasing pulmonary artery pressure. The combination of repetitive apneas, hypoxia, and arousals from sleep stimulate reflex increases in sympathetic nervous system activity (SNA), which is greater in patients with than in those without Heart Failure. The resultant surges in blood pressure further increase afterload and myocardial O₂ demand. In the face of reduced O₂ supply, this increase in O₂ demand can provoke myocardial ischemia and arrhythmias, and may increase the risk of sudden death during sleep. Moreover, this increase in SNA is sustained into wakefulness.

Therapy reverses OSA acutely, eliminates apnea related hypoxia, dampens negative intrathoracic pressure swings, and lowers blood pressure. Treatment of OSA by CPAP in patients with heart failure reduces ventricular ectopy during sleep; lowers blood pressure, heart rate and sympathetic nervous system activity during both sleep and wakefulness.

Many patients with OSA in our study were not started on CPAP, most likely because they were not self-referred for sleep assessment and lacked subjective sleepiness, which is the usual indication for CPAP. Among the patients who started CPAP but discontinued it before the 3-month follow-up clinic visit, most stopped because they were not sleepy beforehand, and as a consequence, either had no reduction in daytime sleepiness or had difficulties tolerating the CPAP mask.

V. OSA & Diabetes

A. Independent Association Between Obstructive Sleep Apnea Severity and Glycated Hemoglobin in Adults Without Diabetes (2012)

Diabetes Care Journal 2012; 35:1902-1906

Abstract:

Among adults without known diabetes, increasing OSA severity is independently associated with impaired glucose metabolism, which may expose them to higher risks of diabetes and cardiovascular disease.

This multisite study can be assumed to describe a “typical” pattern of patients with OSA, because it included a large sample of patients with a wide range of disease severity.

Patients with elevated AHI were also more likely to be older and male and to have higher BMI, WC, and fasting glucose and more frequent cardiovascular morbidities.

Our findings that indices of sleep-related hypoxemia are independently related to HbA1c provide additional evidence that nocturnal hypoxia is involved in the relationship between OSA and impaired glucose metabolism.

B. Associations between Sleep Loss and Increased Risk of Obesity and Diabetes

New York Academy of Sciences 2008; 1129: 287–304

Abstract:

Evidence is rapidly accumulating to indicate that chronic partial sleep loss may increase the risk of obesity and diabetes.

Insulin sensitivity decreases rapidly and markedly without adequate compensation in beta cell function, resulting in an elevated risk of diabetes. Prospective epidemiologic studies in both children and adults are consistent with a causative role of short sleep in the increased risk of diabetes.

Sleep curtailment is also associated with a dysregulation of the neuroendocrine control of appetite, with a reduction of the satiety factor, leptin, and an increase in the hunger-promoting hormone, ghrelin.

B. Impact of Untreated Obstructive Sleep Apnea on Glucose Control in Type 2 Diabetes (2010)

American Journal of Respiratory and Critical Care Medicine 2010; 181,507–513

Abstract:

OSA has been identified as a highly prevalent comorbidity of type 2 diabetes. In particular, among patients who represent the vast majority of individuals with type 2 diabetes in the United States, the prevalence of OSA has recently been estimated at a staggering 86%.

Increasing severity of OSA was associated with poorer glucose control, increasing BMI and greater waist circumference. Patients without OSA had fewer diabetic complications than those with OSA.

There is a relentless increase in type 2 diabetes worldwide. Diligent control of glucose levels is needed to prevent or delay the development of life-threatening complications. Most patients are treated with multiple drugs, and a substantial proportion requires insulin injections.

Our findings have important clinical implications, as they support the hypothesis that reducing the severity of OSA may improve glycemic control. Thus, effective treatment of OSA may represent a novel non-pharmacologic intervention in the management of millions of patients with type 2 diabetes.

C. Sleep-disordered breathing and type 2 diabetes - International Diabetes Federation (2008)

Diabetes Research and Clinical Practice 2008;81,2-12

Abstract:

International Diabetes Federation Taskforce on Epidemiology and Prevention strongly recommends that health professionals working in both type 2 diabetes and SDB adopt clinical practices to ensure that a patient presenting with one condition is considered for the other.

OSA patients should be routinely screened for markers of metabolic disturbance and cardiovascular risk. Minimum testing should include measurement of, waist circumference, blood pressure, fasting lipids, fasting glucose.

Patients with Type 2 diabetes and the metabolic syndrome should be assessed for symptoms of OSA: snoring, observed apnea during sleep and daytime somnolence.

D. High Cardiovascular Risk Profile in Patients with Sleep Apnea (2013)

Laryngoscope 2013; DOI: 10.1002/24304

Abstract:

We found 51% of patients without known diabetes to have an impaired glucose metabolism, which puts them at a high risk to develop Type 2 Diabetes.

Among patients with moderate to severe sleep apnea, 57% had pathological glucose disposal.

VI. OSA & Obesity

A. Obesity and Obstructive Sleep Apnea - Pathogenic Mechanisms and Therapeutic Approaches

Proceedings of the American Thoracic Society 2008; Vol5, 185–192

Abstract:

Obesity is one of the strongest sleep apnea risk factors. Mild to moderate obesity has been associated with markedly increased sleep apnea prevalence. In severe obesity the prevalence of sleep apnea was estimated to vary between 40 and 90%. A 10% change in body weight was associated with a parallel change of approximately 30% in the apnea–hypopnea index (AHI), the major index of sleep apnea severity. Concerns about the health impact of sleep apnea have been increasing in light of the growing epidemic of obesity in Western society and worldwide.

Several risk factors, including obesity, male sex, age, and heritable factors, have been associated with an increased prevalence of obstructive sleep apnea in the general population.

Among these, obesity and particularly central adiposity are potent risk factors for sleep apnea. They can increase pharyngeal collapsibility through mechanical effects on pharyngeal soft tissues and lung volume, and through central nervous system–acting signaling proteins (adipokines) that may affect airway neuromuscular control.

B. Abdominal Fat and Sleep Apnea - The chicken or the egg? (2008)

Diabetes Care 2008; 31(Supp2), S303–S309

Abstract:

Obesity is probably the most important risk factor for the development of OSA. Some 60–90% of adults with OSA are overweight.

There are several mechanisms responsible for the increased risk of OSA with obesity. These include reduced pharyngeal lumen size due to fatty tissue within the airway or in its lateral walls, decreased upper airway muscle protective force due to fatty deposits in the muscle, and reduced upper airway size secondary to mass effect of the large abdomen on the chest wall and tracheal traction.

Conversely, OSA may itself predispose individuals to worsening obesity because of sleep deprivation, daytime somnolence, and disrupted metabolism. OSA is associated with increased sympathetic activation, sleep fragmentation, ineffective sleep, and insulin resistance, potentially leading to diabetes and aggravation of obesity. Furthermore, OSA may be associated with changes in leptin, ghrelin, and orexin levels; increased appetite and caloric intake; and again exacerbating obesity.

Thus, it appears that obesity and OSA form a vicious cycle where each results in worsening of the other.

C. Inadequate Sleep as a Risk Factor for Obesity (2005)

Sleep Journal 2005;28(10),1289-1296

Abstract:

Modern humans are experiencing two parallel trends, increasing Body Mass Index (BMI) and a decline in average sleeping time. Sleep duration has been associated with obesity in a large longitudinally monitored United States sample. The results from this study suggest that sleep deprivation could play a significant role in the etiology of obesity in some individuals.

Women who slept less than 7 hours per night were progressively more likely to be obese as their sleep durations decreased. Men who slept 6 or fewer hours per night were more likely to be obese than those who slept 7 hours per night.

Subjects who reported getting 4 or fewer hours of sleep per night at baseline continued to be significantly more likely than those who reported getting 7 hours per night to be obese.

The average BMI for subjects who slept 2 to 4, 5, and 6 hours per night was higher than the average BMI of subjects who slept 7 hours per night. Subjects with 2- to 4-hour sleep durations had the highest average BMI, while those with 5- and 6-hour sleep durations had the second and third highest average BMI.

Those with sleep durations less than 7 hours were more likely to be obese and had higher average BMIs among those with sleep durations less than 7 hours. As their sleep durations decreased, their likelihoods of being obese progressively increased. Subjects who got 2 to 4 hours of sleep per night at baseline gained the most weight over the follow-up period, while subjects who got 10 or more hours of sleep gained the least weight.

Inadequate sleep could also influence body weight by making it more difficult to maintain a healthy lifestyle. In results from the National Sleep Foundation's 2002 "Sleep in America" Poll, not getting enough sleep was associated with irritability, impatience, pessimism, and feeling tired and stressed.² It would seem that these feelings and emotional states would function to lessen one's resolve and willpower to follow a diet or exercise routine.

D. Obesity Is Associated with the Future Risk of Heavy Truck Crashes among Newly Recruited Commercial Drivers (2012)

Institute for the Study of Labor 2012; No26408

Abstract:

Accumulating evidence in the field supports the notion that through inflammatory pathways and mechanisms, visceral adiposity, insulin resistance and neuro-hormonal signaling, obesity plays a major role in the pathogenesis of sleep apnea as well as excessive daytime sleepiness.

Using a variety of statistical approaches we find consistent evidence that commercial truck drivers with a BMI ≥ 35 have increased crash risk.

Obstructive sleep apnea (OSA) is strongly associated with obesity and what is more, increased BMI is considered the principal risk factor for OSA. Sleep apnea often causes excessive daytime sleepiness (EDS). Moreover, excessive daytime sleepiness is a frequent complaint of obese patients even if they do not have sleep apnea which may be attributable to metabolic and circadian abnormalities related to obesity.

E. Obstructive sleep apnea in the adult obese patient: implications for airway management

Anesthesiology Clinics of North America 2002; 20,789– 811

Abstract:

Adult obese patients with suspected or sleep test confirmed OSA present a formidable challenge throughout the perioperative period. Life-threatening problems can arise with respect to tracheal intubation, tracheal extubation, and providing satisfactory postoperative analgesia.

The incidence of adult obese patients presenting for anesthesia and surgery with either a presumptive clinical and/or a sleep study diagnosis of OSA can be expected to increase five- to ten-fold in the next decade.

Since a firm diagnosis of OSA will likely impact on anesthetic management, it is reasonable to suggest that all adult obese patients (or those who observe them while asleep) be routinely asked about nocturnal snoring/snorting/apnea and diurnal sleepiness.

If the anesthesiologist is the first care-giver to diagnose OSA, then it may sometimes be prudent to postpone the surgery and refer the patient to an appropriate physician and perhaps a formal sleep study obtained to quantify the severity of OSA.

VII. OSA & Oxidative Stress

A. Oxidative Stress — A Unifying Paradigm in Obstructive Sleep Apnea and Comorbidities

Progress in Cardiovascular

Abstract:

There is an emerging consensus that OSA is an oxidative stress disorder. Accumulated evidence implicates the apnea-related multiple cycles of hypoxia/re-oxygenation in promoting the formation of reactive oxygen species and inducing oxidative stress.

Oxidative stress is the common unifying paradigm in sleep apnea and in the associated conditions and comorbidities such as hypertension, hyperlipidemia, type 2 diabetes mellitus, and obesity, all resulting in inflammatory pathway activation, endothelial dysfunction, and consequent atherosclerosis.

These converging lines of evidence point at oxidative stress as the unifying paradigm underlying the fundamental mechanisms in the pathophysiology of cardiovascular morbidity in OSA, and very likely also in promoting the metabolic disorders associated with OSA.

Oxidative stress is a crucial component of obesity and metabolic disorders such as dyslipidemia and type 2 diabetes mellitus/insulin resistances, which cluster with OSA and involve inflammatory pathways as well.