

Obstructive Sleep Apnea and its Comorbidities

Clinical References (Consumer)

Obstructive Sleep Apnea (OSA) 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 it is proven to have a significant positive effect on primary diagnosis outcome; and treating OSA as the primary diagnosis can mitigate the likelihood of developing the 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.

The clinical study abstracts contained herein have been edited, replacing complex medical terminology with equally descriptive terms more likely to be understood by non-medical individuals.

Diseases Associated with OSA

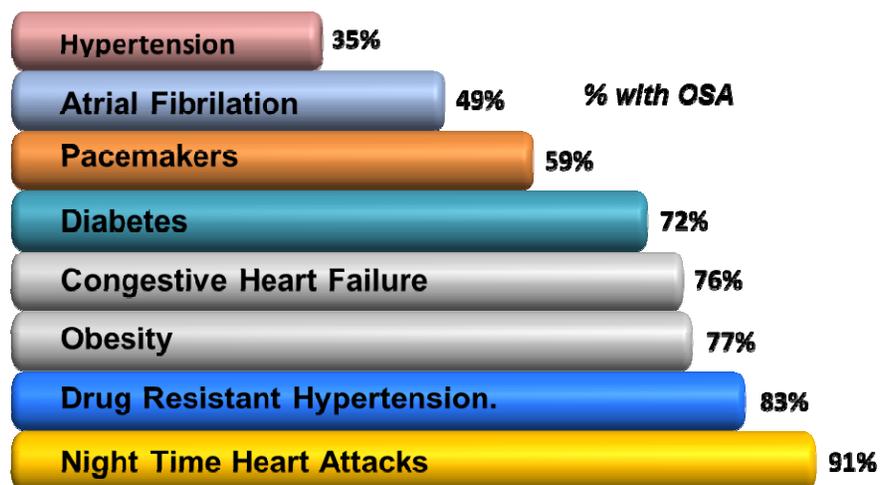


Table of Contents

I. OSA & Cardiovascular Disease	1
A. <i>Sleep-disordered Breathing and Cardiovascular Disease – A Vicious Cycle?</i>	1
B. <i>Oxidative Stress in Obstructive Sleep Apnea (2005)</i>	1
II. OSA & Hypertension	2
A. <i>High Cardiovascular Risk Profile in Patients with Sleep Apnea (2013)</i>	2
B. <i>Resistant Hypertension and Obstructive Sleep Apnea (2013)</i>	2
C. <i>Obstructive Sleep Apnea - A Cardio Metabolic Risk in Obesity and the Metabolic Syndrome</i>	3
D. <i>Obesity, Sleep Apnea and Hypertension (2003)</i>	3
III. OSA & Stroke	4
A. <i>Mechanism of Ischemic Stroke in Patients with Obstructive Sleep Apnea</i>	4
B. <i>Association of Sleep-disordered Breathing and the Occurrence of Stroke</i>	4
C. <i>Cerebrovascular Consequences of Obstructive Sleep Apnea (2012)</i> Journal of the American Heart Association 2012;1:e000091	1
D. <i>Obstructive Sleep Apnea as a Risk Factor for Stroke and Death (2005)</i>	5
E. <i>Basics of Sleep Apnea and Ischemic Stroke (2013)</i>	5
IV. OSA & Heart Attacks	6
A. <i>OSA and the Risk of Sudden Cardiac Death - A Longitudinal Study of 10,701 Adults (2013)</i>	6
B. <i>Benefits of obstructive sleep apnea treatment in coronary artery disease</i>	6
C. <i>Clinical Characteristics of Patients with Acute Coronary Syndrome at High Clinical Suspicion for Obstructive Sleep Apnea Syndrome (2013)</i>	7
D. <i>Sleep Apnea and Cardiovascular Disease - A Bidirectional Relationship (2012)</i>	8
E. <i>Day-Night Pattern of Sudden Death in Obstructive Sleep Apnea (2005)</i>	8
F. <i>Obstructive Sleep Apnea and Cardiovascular Disease (2003)</i>	9
G. <i>Influence of obstructive sleep apnea on mortality in patients with heart failure)</i>	10
V. OSA & Diabetes	11
A. <i>Independent Association Between Obstructive Sleep Apnea Severity and Glycated Hemoglobin in Adults Without Diabetes (2012)</i>	11
B. <i>Associations between Sleep Loss and Increased Risk of Obesity and Diabetes</i>	11
C. <i>Impact of Untreated Obstructive Sleep Apnea on Glucose Control in Type 2 Diabetes (2010)</i>	12
D. <i>Sleep-disordered breathing and type 2 diabetes - International Diabetes Federation (2008)</i>	12
E. <i>High Cardiovascular Risk Profile in Patients with Sleep Apnea (2013)</i>	13
VI. OSA & Obesity	14
A. <i>Obesity and Obstructive Sleep Apnea - Pathogenic Mechanisms and Therapeutic Approaches</i>	14
B. <i>Abdominal Fat and Sleep Apnea - The chicken or the egg? (2008)</i>	14
C. <i>Inadequate Sleep as a Risk Factor for Obesity (2005)</i>	15
D. <i>Obesity Is Associated with the Future Risk of Heavy Truck Crashes among Newly Recruited Commercial Drivers (2012)</i>	16
E. <i>Obstructive sleep apnea in the adult obese patient: implications for airway management</i>	16
VII. OSA & Oxidative Stress	17
A. <i>Oxidative Stress — A Unifying Paradigm in Obstructive Sleep Apnea and Comorbidities</i>	17

I. OSA & Cardiovascular Disease

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

Clinical Advantage 2011; voll; no1

Abstract:

A growing body of evidence suggests that OSA is often associated with the development of various CARDIAC disorders. Untreated OSA is associated with progression of cardiac disease due to the increased pressure against which the heart must work to eject blood and the fact that pulse rates do not drop while sleeping thus causing high blood pressure, enlargement of the left ventricle, stiffening of the artery, coronary artery disease, heart attack and heart failure.

- 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 Obstructive Sleep Apnea (OSA) and the level of arterial wall damage due to the lack of oxygen. OSA is characterized by recurrent night time obstruction of the upper airway. Each episode of airway obstruction is usually followed by a marked decrease of arterial oxygen levels, which rapidly normalizes after breathing resumes. Repeated changes in oxygen levels, (normal to low and back to normal), damage the arterial wall.

Although several mechanisms are involved, this damage is mainly attributed to the production of reactive oxygen when an OSA patient's breathing resumes and is considered to have an important role in the development of cardiovascular disease.

All of these studies have indicated a significant relationship between OSA and the stress put on the body's systems due to lack of oxygen. It is well known that the prevalence of undiagnosed sleep apnea is several times higher than diagnosed sleep apnea. Therefore, stress due to lack of oxygen in persons with sleep apnea 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 high blood pressure 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 high blood pressure, 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:

High Blood Pressure 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 have high blood pressure. .

Large population-based studies have demonstrated that Obstructive Sleep Apnea (OSA) is a risk factor for resistant high blood pressure. The mechanism has been identified as a pattern of intermittent low blood oxygen levels associated with increase retention of salt and water and the increase excretion of potassium by the kidneys thus causing arterial stiffening, vascular constriction and inflammation.

Treating OSA (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 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 people 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 activation of what is often termed the “fight or flight” response of the central nervous system, vascular inflammation, and stiffening of the arterial wall, are significantly increased in obese patients with OSA versus those without OSA.

Intermittent low blood oxygen levels accelerates the negative effects of obesity, causing insulin resistance and nonalcoholic fatty liver disease. In patients with “metabolic syndrome” (high blood pressure, low good cholesterol levels, and an excess of abdominal fat) that increases a person's risk of

heart disease, stroke, and diabetes. The prevalence of moderate to severe OSA is very high (~60% in

this population). OSA is independently associated with increased glucose and triglyceride levels as well as markers of inflammation and arterial stiffness.

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 Body Mass Index (BMI) and systolic/diastolic blood pressure. Incompletely treated OSA was found to be an independent predictor of cardiovascular disease, including high blood pressure.

The evidence supporting the association between OSA and chronic, longstanding high blood pressure is compelling and is demonstrated by several studies. The Framingham Heart Study suggests that 65% of the risk for high blood pressure in women and 78% in men can be related to OSA.

Whereas obesity increases the risk for OSA, sleep apnea may actually contribute to 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 causes people to be hungry, 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 (interrupted blood flow to the brain) within one year after a sleep study to identify OSA.

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 cardiac risk factor. Dangerous irregular heart rates were 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 apnea and prevalent stroke, independent of any other factors.

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

In addition to the evidence presented that sleep apnea contributes to the development of stroke, the presence of sleep apnea after stroke may slow the recovery.

C. Cerebrovascular Consequences of Obstructive Sleep Apnea (2012)Journal of the American Heart Association 2012;1:e000091

Abstract:

Patients presenting with stroke or interrupted blood flow to the brain 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 interrupted blood flow to the brain had an AHI>10 (Moderate OSA).

Published studies have reported an association between OSA and loss of memory in the elderly, with the severity of the loss of memory 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 increases damage produced by a stroke, (3) OSA increases the risk for another stroke, and (4) OSA contributes to brain atrophy and loss of memory 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 high blood pressure and diabetes was higher in the group with Obstructive Sleep Apnea (OSA) than in the comparison group. Patients with OSA also were more obese, as reflected by the higher body-mass index, and had lower blood oxygen levels and a higher arousal index.

There was a significant association with Obstructive Sleep Apnea and stroke or death.

Obstructive sleep apnea significantly increases the risk of stroke or death from any cause, and the increase is independent of other risk factors, including high blood pressure.

- 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 causes strokes.

Sleep apnea may negatively influence the early treatment 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 percent of decline in blood oxygen levels while sleeping.

Notably, the severity of decline in blood oxygen levels while sleeping, common in people with OSA, strongly predicted sleep apnea independent of well-established risk factors.

There is a cascade of conditions linking OSA to Sudden Cardiac Death during the daytime and during sleep. Obstructive apnea causes a drop in blood oxygen, which is sometimes severe and prolonged. These repetitive drops in blood oxygen levels in OSA patients may cause irregular heart beat.

Excessive rapid heartbeat and surges in blood pressure at the end of apneas result in increased heart oxygen demand at a time when blood oxygen levels are at their lowest, a situation that may lead to lack of adequate blood flow to the heart and potentially irregular heart rate. Individuals with OSA also have an increase in clotting during the night which can cause stroke or heart attack.

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 cardiovascular events (death, cerebrovascular events, and heart attack).

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

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

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

The results of our studies confirm the previous finding that over 30% of heart attack patients have OSA. The study strongly reinforces that OSA is common and under-diagnosed among patients with heart attacks.

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

OSA patients had significantly larger left ventricular diameter, a thicker wall, and a higher left ventricular mass index. Patients also had a longer hospitalization duration and higher death rate.

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

This finding calls for physicians to perform routine screening and individual evaluation of heart attack patients for sleep apnea.

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 negative events, 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), lack of oxygen, and negative central nervous system events due to lack of oxygen in susceptible individuals may well lead to heart disease and a decline in cardiac output.

The mechanical, autonomic, and lack of oxygen imposed by sleep apnea when combined with lack of blood flow to the heart can contribute to increased mortality, through the generation of irregular ventricular beats.

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 high blood pressure, Heart failure, irregular heart rate, 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 hormone adjustments and abnormal electrical activity in the heart that may increase the risk of sudden death from cardiac causes, especially during sleep.

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

Sudden death from cardiac causes during the sleeping hours is more likely in people with obstructive sleep apnea. People with sudden death from cardiac causes from midnight to 6 a.m. had a significantly higher apnea-hypopnea index. The degree of severity of OSA correlated directly with the relative risk of sudden death from cardiac causes.

The severity of obstructive sleep apnea correlated directly with the risk of night time sudden death from cardiac causes, such that the relative risk of sudden death from heart 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 OSA is strongly associated with known cardiovascular risk factors, including obesity, and insulin resistance, OSA is an independent risk factor for high blood pressure and has also been implicated in the cause of congestive heart failure, high pulmonary pressure, irregular heart rate, and arterial stiffness.

A recent sleep clinic study reported a direct relationship between high blood pressure and severity of OSA, with each extra apnea per hour increasing the odds of high blood pressure by 1%.

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

Patients with OSA have many features in common with the “metabolic syndrome,” (high blood pressure, low good cholesterol levels, and an excess of abdominal fat) including systemic high blood pressure, central obesity, and insulin resistance. The severity of OSA correlates with Body Mass Index, waist-to-hip ratio, high blood pressure, and diabetes, whereas trends toward lower high-density lipoprotein and elevated triglycerides are reported for OSA subjects.

In OSA, 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 damaging sympathetic nerve activity during sleep causes damaging sympathetic nerve activity at approximately twice the normal levels during the day 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.

Obstructive sleep apnea is common in heart failure patients. The frequency of apnea is highly predictive of mortality, with severe OSA providing prognostic information.

- 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 intra-thoracic pressure during apneas results in diminished cardiac output.

Apnea-related drops in blood oxygen levels also can reduce cardiac output by impairing heart contractility and increasing pulmonary artery pressure. The combination of repetitive apneas, reduction in blood oxygen levels, and arousals due to sleep apnea increases in negative central nervous system activity is greater in patients with sleep apnea.

The resultant surges in blood pressure further increase afterload and increase the need for oxygen. In the face of reduced oxygen supply, this increase in oxygen demand can provoke low blood flow to the heart and irregular heartbeat, and may increase the risk of sudden death during sleep.

Therapy reverses OSA acutely, eliminates apnea related drops in blood oxygen levels, dampens negative intra-thoracic pressure swings, and lowers blood pressure. Treatment of OSA in patients with heart failure reduces irregular heart rate during sleep; lowers blood pressure, heart rate and damaging 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 an elevated number of apneas were also more likely to be older and male and to have higher Body Mass Index, waist size, and fasting glucose and more frequent cardiovascular morbidities.

Our findings that declines in blood oxygen levels due to OSA provide additional evidence that night time reduction in blood oxygen levels is involved in the relationship between OSA and diabetes.

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 consistently demonstrate that lack of sleep increases the risk of diabetes.

Sleep curtailment is also associated with increased appetite, with a reduction of the hormone that curbs hunger, leptin, and an increase in the hunger-promoting hormone, ghrelin.

C. 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 directly tied to 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 Body Mass Index and greater waist size. 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-drug intervention in the management of millions of patients with type 2 diabetes.

D. 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 OSA 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 size, blood pressure, fasting lipids and fasting glucose.

Patients with Type 2 diabetes and the “metabolic syndrome” (high blood pressure, low good cholesterol levels, and an excess of abdominal fat) should be assessed for symptoms of OSA: snoring, observed apnea during sleep and daytime sleepiness/tiredness.

- E. 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 a high risk to develop Type 2 Diabetes.

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, and age, have been associated with an increased prevalence of obstructive sleep apnea in the general population.

Among these, obesity is a potent risk factor for sleep apnea. Obesity accompanied by sleep apnea can increase the probability that the patient loses airway neuromuscular control thus causing the airway to collapse while sleeping.

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 airway size due to fatty tissue within the airway or in its lateral walls, decreased upper airway muscle control due to fatty deposits in the muscle, and reduced upper airway size secondary to the large abdomen on the chest wall.

Conversely, OSA may itself predispose individuals to worsening obesity because of sleep deprivation, daytime sleepiness/tiredness, and disrupted breathing. OSA is associated with increased damaging sympathetic nerve activity, interrupted sleep, poor sleep quality, 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 causing people to gain weight.

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 development 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. 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 obesity is a major cause 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 Body Mass Index is considered the principal risk factor for OSA. Sleep apnea often causes excessive daytime sleepiness (EDS).

- 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 when in surgery. Life-threatening problems can arise when using a breathing tube during surgery, and providing satisfactory postoperative pain control.

The incidence of adult obese patients presenting for anesthesia and surgery with either a sleep study diagnosis of OSA can be expected to increase 5-10 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 night time snoring/snorting/apnea and sleepiness/tiredness.

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 Diseases 2009; Vol51, No4, 303-312

Abstract:

There is an emerging consensus that because OSA causes repeated cycles in blood oxygen levels (normal to low and back to normal) cells degenerate and are not as effective in transporting oxygen throughout the body.

These large swings in blood oxygen levels is the single most common condition linking sleep apnea with the associated conditions and related diseases such as high blood pressure, high cholesterol, type 2 diabetes, and obesity, all resulting in inflammatory pathway activation, arterial wall damage, and eventual stiffening of the arteries.

These converging lines of evidence point at large swings in blood oxygen levels in people with OSA as the most prevalent underlying cause of death due to cardiovascular issues in people with OSA.

The continuous decreases and increases in blood oxygen levels in people with OSA is a major contributor to obesity, high cholesterol, and type 2 diabetes.