Sleep Disorders and Cardiac Consequences

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Recommended Citation
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Educational Objectives:
1. Review the clear relationship between obstructive sleep apnea and hypertension.
2. Discuss the cardiac consequences of sleep apnea, including coronary heart disease, heart failure, and different dysrhythmias.
3. Understand that sleep disorders beyond obstructive sleep apnea, such as insufficient sleep itself, may have an impact on the cardiovascular system.
4. Appreciate the potential benefits of identifying and treating sleep disorders for our health.

Background

Primary care clinicians, cardiologists, and sleep clinicians are increasingly aware of the association between sleep disordered breathing and a number of different cardiovascular disorders. The Sleep Heart Health Study and other investigations are systematically trying to determine type and extent of relationships. Much of the data linking sleep and the cardiovascular system have focused on obstructive sleep apnea (OSAS), which receives relatively greater attention here. However, we will also explore putative associations between other sleep disorders and the cardiovascular system and, in fact, the possible impact of reduced sleep duration itself on the cardiovascular system. Space limitations prevent an exhaustive review of sleep disorders and the cardiovascular system.

Obstructive Sleep Apnea Syndrome

Obstructive sleep apnea syndrome (OSAS) manifests with repeated upper airway near occlusions or temporary complete occlusions. It is estimated that some 18 million Americans have OSAS, which can lead to neurocognitive, pulmonary, and cardiovascular consequences. OSAS can be treated conservatively with weight loss, by minimizing alcohol and sedative use, as well as by unambiguously warning patients not to drive while sleepy. Beyond conservative recommendations, the most common treatment options include nasal continuous positive airway pressure (CPAP) which employs a blower machine, tubing and mask assembly that acts as an upper airway air splint; oral appliances; and surgery. Surgical options can include soft tissue upper airway surgery, jaw surgery, and bariatric (weight loss) surgery.

The Heart and Sleep

Hypertension and Sleep

Roughly two thirds of Americans over the age of 60 have hypertension (Yoon et al., 2012). Sleep is normally associated with lowered blood pressure but this may not be so in patients with obstructive sleep apnea (so called non-dipping). The majority of data suggest that OSAS can cause elevations in blood pressure and that treatment of OSAS lowers blood pressure. Research from Australia in 1998 demonstrated that approximately 40% of patients with high blood pressure have sleep apnea, and a Wisconsin study (Peppard et al., 2000) found a “dose response” relationship.
between the severity of sleep apnea at baseline and the development of high blood pressure over the next four years. In addition, treatment resistant hypertension has been associated with OSAS in between 70 and 80% of cases. Therefore, if one has high blood pressure and, particularly, treatment resistant hypertension, OSAS must be considered.

The preponderance of data suggests that treatment of OSAS does appear to lower blood pressure. Although the absolute amount of blood pressure reduction appears to be modest, these reductions are believed to be meaningful. Most of the data showing improvements in blood pressure with treatment of OSAS derive from CPAP studies. However, there is also evidence demonstrating that oral appliances and surgery for OSAS may lead to reductions in blood pressure. Recent data suggest that sleep clinicians should look beyond just the diagnosis of obstructive sleep apnea when they consider the intersection of sleep and hypertension.

RLS, PLMS, and Sleep

Restless legs syndrome (RLS) patients describe an urge to move (predominantly the lower extremities), at rest, most prominent at night and relieved quickly by movement. Some 5-10% of Americans may have RLS and it occurs roughly twice as often in women as in men. Most RLS subjects and clinicians focus on the impact of RLS on causing insomnia. However, there are now some (but not all) studies that suggest an association of RLS with hypertension. A 2011 study of over 65,000 middle-aged nurses demonstrated that RLS increased the odds of hypertension by 20% and that there was a dose response relationship between the frequency of RLS each month and the prevalence of hypertension. We must note that this study could not prove a cause and effect relationship nor did it apply to males, although earlier research in Sweden did associate RLS and hypertension in men.

Periodic limb movements of sleep (PLMS) are stereotypical lower extremity movements that occur in approximately 85% of patients with RLS, but such movements can be seen in numerous other situations, such as taking certain anti-depressants and being over 65 years of age. It may be that these leg jerks increase sympathetic nervous system activity, thereby leading to hypertension during the day. It is known that PLMS themselves have been associated with hypertension. For example, one study revealed that subjects with more severe hypertension had more PLMS than did those with lower levels of hypertension; other data reveal the complementary, namely, linking greater frequencies of PLMS with hypertension. These and other studies can be found as references in a comprehensive review of RLS and PLMS and cardiovascular consequences by Walters & Rye (2009).

We may also put ourselves at risk simply by achieving too little sleep. Studies have revealed that insufficient sleep may be associated with hypertension; i.e., sleep of less than or equal to five hours a night doubled the risk of hypertension among subjects between the ages of 32 and 59. Of interest, insufficient sleep has also been associated with diabetes and obesity, both of which, in turn, have been linked to heart disease and cardiovascular disease.

Coronary Heart Disease and Sleep

Hypertension, diabetes mellitus, and obesity have all been associated with obstructive sleep apnea and all are risk factors for coronary heart disease (CHD). Numerous changes that occur as a consequence of sleep disordered breathing are deleterious to the vascular system. Accordingly, researchers have investigated potential associations between sleep apnea and CHD. Overall, the data linking OSAS and CHD do not appear as striking as with OSAS and other cardiovascular diseases (e.g., hypertension, congestive heart failure, and atrial fibrillation). Nevertheless, there are some provocative data linking OSAS and CHD and the possibility that treating OSAS may benefit these cardiac patients. Data from the Sleep Heart Health Study demonstrated that severe obstructive sleep apnea increased the risk of developing CHD in males between the ages of 40 and 70 years; this finding was not replicated in either females or males older than 70 years (Gottlieb et al., 2010).

Women are not exempt from this association between OSAS and CHD, as an older study from Sweden of more than 100 women with CHD found that over 50% had sleep apnea versus only 20% in controls. A recent study found no differences in frequency of OSAS between females and males with CHD (Zhao et al., 2014); but, in this study, the females were older and more frequently were afflicted.
by kidney disease and diabetes mellitus.

In one Japanese study, the major index of sleep apnea severity was twice as high at the time of an acute myocardial infarction (heart attack) as compared to just 14 days later. OSAS may confer a worsened prognosis in patients with coronary heart disease and, thus, it is of interest to determine the impact of treating OSAS. Data suggest but do not unequivocally prove that CPAP treatment, for example, improves the outlook for those with both OSAS and CHD (Marin et al., 2005).

There is relatively little research investigating restless legs syndrome (RLS) and CHD. The Sleep Heart Health Study did find that RLS increased the likelihood for CHD. Interestingly, there was a dose response relationship for severity and frequency of RLS and risk for CHD (Winkelman et al., 2008).

Congestive Heart Failure and Sleep

The American Heart Association estimated in 2010 that just under six million Americans have congestive heart failure (CHF), with most of these being ages 65 and older. CHF can occur both with and without reductions in ventricular ejection fraction (heart muscle pump function). CHF has been associated with both obstructive and central sleep apnea (repetitive temporary pauses in breathing during sleep without upper airway narrowing/occlusion). One study revealed that roughly half of 81 patients with CHF (systolic dysfunction type) had sleep apnea, with central sleep apnea being more frequent in this study than obstructive sleep apnea. In addition, it appears that the presence of OSAS may confer a worsened prognosis in some with systolic dysfunction (reduced ejection fraction).

In a recent study, those who had CHF secondary to coronary heart disease had an increased mortality risk associated with sleep apnea. OSAS may lead to numerous alterations in physiology that are detrimental to the heart and, more certainly, to the diseased heart. Increased activity of the sympathetic nervous system, increased work requirements of the heart, repetitive drops/returns to baseline in oxygen level, increased oxidative stress, and increased production of inflammatory mediators all occur secondary to OSAS. CPAP administration has been shown to reverse these changes and there are some data that indicate that treating OSAS may, over time, lead to improvements in cardiac function, such as better ejection fraction.

Given the improvements in physiology with CPAP in heart failure patients, it would appear that CPAP therapy should reduce the burden of mortality. Some data from Japan support this contention but a recent review of OSAS and CHF cautions that results to date should be treated with caution (Kasai & Bradley, 2011). It is interesting to note that the relationship between OSAS and CHF may be bidirectional. Return of extra fluid from the lower extremities during sleep can increase neck circumference and thereby further destabilize the upper airway during sleep and worsen OSAS.

Central sleep apnea and Cheyne-Stokes breathing (a waxing and waning breathing pattern often associated with congestive heart failure) have also been associated with CHF and, further, portend worse prognosis. Although CPAP with or without supplementary oxygen can be utilized, a more sophisticated (and expensive) positive airway pressure device called adaptive servo-ventilation looks to be more effective in treating these central sleep breathing disorders. Importantly, a multi-center and randomized study is underway to evaluate the possible effectiveness of this machinery in improving such important end points as mortality and hospitalization.

A burgeoning research literature suggests (but does not prove) that restless legs syndrome (RLS) and periodic limb movements of sleep (PLMS) may be associated with hypertension, a risk factor for CHF. Data from the Sleep Heart Health Study suggest a relationship between RLS and cardiovascular disease, including coronary heart disease, congestive heart failure, and stroke (Winkelman et al., 2008). However, this study’s methodology could not establish a cause and effect relationship. Another study of RLS subjects found that those with more PLMS had greater risk for left ventricular hypertrophy (thickened left ventricular wall). This is important, for left ventricular hypertrophy appears to increase the risk for both heart failure and mortality. Indeed, this same study found increased rates of both heart failure and mortality in those with frequent PLMS; this study was retrospective and more data are needed to determine if RLS and
PLMS put patients at increased risk for negative cardiovascular outcomes and warrant more aggressive scrutiny and treatment by clinicians.

Atrial fibrillation and Sleep

A number of different disorders of cardiac rhythm have been associated with sleep disordered breathing. That abnormal electrical activity of the heart might occur is hardly surprising given some of the physiologic consequences of apnea that we have previously mentioned. Atrial fibrillation (an irregular heart rhythm associated with the atrium or top chamber of the heart) is increasingly common and has been noted to be even more so in older adults. Atrial fibrillation is important, in part, because it increases the risk of stroke and mortality. Studies have demonstrated that OSAS and atrial fibrillation are associated, with one study finding almost half of their atrial fibrillation patients had OSAS, and another finding that OSAS predicted an increased likelihood of atrial fibrillation after cardiac bypass for coronary heart disease (Qaddoura et al., 2014).

Treating OSAS may have salutary effects on atrial fibrillation. Patients with OSAS who are cardioverted (electrically shocked) out of atrial fibrillation are less likely to return to that abnormal rhythm if they use their CPAP than if they do not, with one study finding that those who used CPAP to treat OSAS were about half as likely to return to atrial fibrillation after catheter ablation than those who did not have OSAS.

The above clearly suggests that physicians and patients alike should be aware of the association of this frequent arrhythmia with OSAS, and the potential benefits of addressing sleep apnea along with atrial fibrillation. We have previously also mentioned central sleep apnea and its association with congestive heart failure. A new study reports that congestive heart failure patients with severe central sleep apnea were more likely to have atrial fibrillation.

Ventricular Arrhythmias and Sleep

Limited data suggest that irregular heart rhythms that emanate from the lower chamber of the heart (ventricle) can also be associated with OSAS and/or central sleep apnea. The Sleep Heart Health Study data revealed that patients with heart failure and central sleep apnea manifested more ventricular arrhythmias at night. Cardiologists can use implantable cardioverter defibrillators (ICD) to shock patients out of potentially lethal ventricular arrhythmias. Data demonstrate that central and obstructive sleep apnea patients are more likely to require ICDs and more likely to require “appropriate” activation of the ICD for irregular heart rhythms. A 2010 study from Japan demonstrated that after ablation therapy for ventricular dysrhythmias, patients with sleep apnea were more likely than those without sleep apnea to have recurrent disease. A recent review from the Journal of Clinical Sleep Medicine suggests that much more work is needed in this important area (Raghu et al., 2014).

Sudden Cardiac Death and Sleep

We are, generally, most at risk for abrupt death from heart disease in the morning hours. OSAS confers negative consequences such as recurrent drops in oxygen level, increased clotting, and surges in blood pressure. It might follow, then, because sleep is typically an overnight experience, that patients with sleep apnea would be at greater risk for death in the middle of the night (normally a protected time) than patients without apnea. This is exactly what Gami and colleagues have shown in their 2005 research paper in the New England Journal of Medicine; examining the potential impact of sleep apnea on time of sudden death, they found that patients with OSAS were twice as likely to have sudden death between midnight and 0600 as those who did not carry such a diagnosis. Further, the more severe the sleep apnea (as defined by the AHI, the number of partial or com-
complete pauses in breathing per hour of sleep), the more likely one was to pass away suddenly in the middle of the night.

Case Study #1

Mr. W., a 77-year old retired accountant, comes to the sleep medicine office at the request of his primary care physician. His wife accompanies him. Mr. W. notes that at a recent primary care visit his blood pressure was elevated. He states that both his primary care physician and his wife suspect that he may have a sleep disorder. Mr. W.’s wife describes her husband as having a long history of snoring and, more recently, she has witnessed him to have gasping respirations during sleep. Mr. W. states that he has been more apt to nap during the day, but ascribes his day napping to boredom. He is currently taking medications for hypertension and hyperlipidemia. He drinks alcohol only modestly and never smoked.

On physical exam, he is obese, with a body mass index of 31kg/m². His vital signs are normal except for a blood pressure of 156/98. His cardiovascular exam is normal. The sleep medicine specialist describes the association of hypertension with sleep apnea. A nocturnal polysomnogram (sleep study) reveals severe sleep apnea that responds in large part to the application of continuous positive airway pressure (CPAP). Mr. W. initiates nasal CPAP after discussion with both his sleep medicine specialist and primary care physician, with positive results.

Case Study #2

Ms. D., a 74-year old widowed, part-time nurse, presents for consultation at the request of her cardiologist. Her cardiologist is evaluating and treating Ms. D.’s congestive heart failure and atrial fibrillation. The cardiologist and patient both wonder if the patient’s atrial fibrillation could relate to an intrinsic sleep disorder. Ms. D. notes that she obtains about 7-8 hours of sleep each night, but that her sleep is not restorative and she takes a prescribed sleeping pill approximately once a week. She obtains about 45 minutes more sleep with sleeping pill administration but feels no more refreshed for using it. Ms. D. does not share the bed and cannot report if she currently snores or has witnessed pauses in respiration during sleep.

Physical exam reveals normal body mass index, evidence of an irregular heart rhythm (atrial fibrillation) and clear lungs. Records from the cardiologist’s office confirm the diagnosis of atrial fibrillation and document significantly diminished cardiac pump function with an ejection fraction of 30%. The sleep medicine physician orders a sleep study, which demonstrates evidence of both obstructive and central sleep apnea (AHI moderately elevated at 27) with only modest drops in oxygen level. There are also mild (20/hour) periodic limb movements of sleep. Ms D. elects to utilize a continuous positive airway pressure (CPAP) machine for her sleep apnea and to follow conservatively her mild periodic limb movements of sleep. After a month of treatment, she reports improved sleep and awaits follow-up by her cardiologist for input on her cardiac status.

Conclusion

Those in sleep medicine and throughout medicine are increasingly aware of the impact of sleep and sleep disorders on our health. It is important for older adults to do the same. Insufficient sleep itself has negative metabolic and cardiovascular effects. A gradually maturing literature demonstrates the association of sleep disordered breathing (both obstructive and central apnea) and numerous cardiovascular consequences. It is also apparent that treating sleep disordered breathing may be cardio-protective. More research is needed in this important area. What is less clear is if restless legs syndrome (RLS) and periodic limb movements of sleep (PLMS) are also problematic for our cardiovascular system. Given the high prevalence of RLS/PLMS, further research in this area would also be instructive.

Study Questions:

1. What are the options for treating OSAS?
2. Does treating obstructive sleep apnea reduce blood pressure?
3. What is the most dangerous time of day from the standpoint of our cardiovascular system? Does it differ for those with obstructive sleep apnea?

References

(Space limitations required an abridgement of references supporting this paper. For a full list of the 48 references originally cited, please contact the author at [email] or 5)}


**About the Author**

Robert Vorona, M.D., is an Associate Professor in the Division of Sleep Medicine at Eastern Virginia Medical School (EVMS) in Norfolk, Virginia. In addition, he is the Program Director for the EVMS Sleep Medicine fellowship. He has cared in practice for adults with the gamut of sleep disorders for over 25 years. His primary research interest of late has been the impact of high school start times on teens’ sleep and safety.