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REVIEW

Effect of Continuous Positive Airway Pressure Treatment on Cardiovascular Outcomes in Obstructive Sleep Apnea

Baran Balcan[1] · **Yuksel Peker**[1,2,3,4]

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Abstract

Purpose of Review Obstructive Sleep Apnea (OSA) is a common sleep disorder with significant cardiovascular implications, affecting a broad adult demographic. This review explores OSA's link to cardiovascular diseases and assesses Continuous Positive Airway Pressure (CPAP) therapy's role in managing these conditions.

Recent Findings OSA is associated with coronary heart disease, heart failure, hypertension, arrhythmias, and pulmonary hypertension, due to intermittent hypoxia, inflammation, and sympathetic activation. CPAP therapy, known for enhancing sleep and reducing daytime fatigue, has varying impacts on cardiovascular health.

Summary While results on coronary heart disease are mixed, CPAP shows promise in improving heart failure outcomes, reducing hypertension, and managing arrhythmias, with potential benefits for pulmonary hypertension through improved hemodynamics. This underscores CPAP's value in OSA's holistic management, highlighting its beyond-respiratory benefits. However, adherence challenges persist, calling for more research on CPAP's long-term cardiovascular effects. This advocates a multidisciplinary approach to OSA, considering its extensive health consequences.

Keywords Cardiovascular Disease · Obstructive Sleep Apnea · Continuous Positive Airway Pressure · Outcomes

Introduction

Obstructive Sleep Apnea (OSA) is a prevalent sleep disorder characterized by repeated episodes of complete or partial obstructions of the upper airway during sleep, leading to reduced or completely halted airflow. This condition affects a significant portion of the adult population, with estimates indicating a prevalence rate of approximately 9–38% in the general population, though it often remains undiagnosed [1]. OSA is not only a concern for its immediate impact on sleep quality and daily functioning but also for its long-term health implications, particularly in relation to cardiovascular diseases.

The relationship between OSA and cardiovascular diseases is complex and multifaceted. OSA contributes to various pathophysiological changes, including intermittent hypoxia, systemic inflammation, oxidative stress, and sympathetic hyperactivity, all of which play a crucial role in cardiovascular pathology [2]. As a result, OSA is strongly associated with an increased risk of various cardiovascular conditions such as hypertension, coronary artery disease, heart failure, and arrhythmias.

Continuous Positive Airway Pressure (CPAP) therapy is the frontline treatment for OSA. CPAP works by providing a steady flow of air through a mask, which keeps the airway open during sleep, thereby mitigating the apneic episodes. The effectiveness of CPAP in improving sleep quality and reducing daytime sleepiness is well-established. However, its impact on cardiovascular outcomes in OSA patients is a subject of ongoing research and debate.

✉ Yuksel Peker
yuksel.peker@lungall.gu.se; yupeker@ku.edu.tr

Baran Balcan
mbalcan@kuh.ku.edu.tr

[1] Department of Pulmonary Medicine, Koç University School of Medicine, Istanbul 34450, Turkey

[2] Division of Pulmonary, Allergy, and Critical Care Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, USA

[3] Department of Clinical Sciences, Respiratory Medicine and Allergology, Faculty of Medicine, Lund University, Lund 22185, Sweden

[4] Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg 40530, Sweden

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This review aims to provide a comprehensive examination of the existing literature on the impact of CPAP treatment on various cardiovascular diseases in patients with OSA. By systematically exploring the effect of CPAP therapy on conditions like coronary heart disease, heart failure, hypertension, cardiac arrhythmias, and pulmonary hypertension in the context of OSA, this review seeks to elucidate the broader implications of CPAP therapy in the management of cardiovascular risk in these patients (Table 1).

Impact of CPAP Treatment on Cardiovascular Diseases in Patients with Obstructive Sleep Apnea

Impact of PAP treatment on Coronary Heart Disease in OSA

Coronary Heart Disease (CHD) is a significant public health concern globally and is closely linked with obstructive sleep apnea (OSA). OSA exacerbates the risk factors for CHD, including systemic hypertension, dyslipidemia, and atherosclerosis. The intermittent hypoxia experienced by OSA patients can lead to endothelial dysfunction, a key factor in coronary artery disease development [3].

Pathophysiology of CHD in OSA

The pathophysiological mechanisms linking OSA and CHD primarily involve sympathetic nervous system activation, oxidative stress, systemic inflammation, and endothelial dysfunction. The recurrent episodes of apnea in OSA lead to hypoxemia and hypercapnia, resulting in increased sympathetic activity, which elevates blood pressure and heart rate, thereby straining the cardiovascular system [4]. Additionally, the oxidative stress and systemic inflammation seen in OSA patients contribute to atherosclerosis, a crucial factor in the development of CHD.

Studies on CPAP and Coronary Heart Disease

Several studies have investigated the impact of CPAP therapy on CHD in patients with OSA. A landmark study by Marin et al. [5] demonstrated that untreated severe OSA significantly increases the risk of fatal and nonfatal cardiovascular events, including CHD. Conversely, CPAP treatment

Table 1 Summary of the studies addressing the effect of CPAP on cardiovascular outcomes

	First author	Year	Sample size	Main findings	Study design
Impact of PAP treatment on Coronary Heart Disease in OSA	Marin et al.[5]	2005	1651	CPAP treatment reduces the risk of CVD events	RCT
	McEvoy et al.[6]	2016	2717	CPAP did not prevent cardiovascular events	RCT
	Peker et al.[7]	2016	244	CPAP did not reduce long-term cardiovascular outcomes	RCT
	Yu et al.[8]	2017	5847	PAP was not associated with reduced risks of cardiovascular outcomes or death	Meta-analysis
Impact of PAP treatment on Heart Failure in OSA	Mansfield et al.[10]	2004	76	PAP treatment in CHF improves cardiac function	Case-Control
	Khayat et al.[11]	2015	1117	CPAP decrease in hospital readmissions and mortality in CHF	Prospective Cohort
Impact of PAP treatment on Hypertension in OSA	Montesi et al.[13]	2012	1948	PAP treatment is associated with significant reductions in SBP and DBP	Meta-analysis
	Barbe et al.[14]	2012	725	CPAP did not result in significant reduction in the incidence of hypertension	RCT
Impact of PAP treatment on Cardiac Arrythmias in OSA	Kanagala et al.[16]	2003	118	CPAP treatment in OSA patients is associated with lower recurrence of AF	Case-control
	Simantirakis et al.[17]	2004	23	Severe cardiac rhythm disturbances are significantly reduced by CPAP	Observational
Impact of PAP treatment on Pulmonary Hypertension in OSA	Sajkov et al.[19]	2002	20	CPAP treatment reduces Ppa and hypoxic pulmonary vascular reactivity	

was associated with a lower incidence of these events, suggesting a protective effect against CHD in OSA patients.

Another critical study by McEvoy et al. [6] investigated the effects of CPAP treatment on cardiovascular events and death in OSA patients with existing coronary artery disease. This randomized trial found that while CPAP significantly reduced snoring and daytime sleepiness, it did not significantly lower the rate of cardiovascular events when compared to usual care without CPAP. This finding highlights the complexity of the relationship between CPAP therapy and CHD outcomes in OSA patients. The SAVE (Sleep Apnea Cardiovascular Endpoints) study further explored this complexity. While the study did not find a significant reduction in major cardiovascular events with CPAP therapy, it suggested potential benefits in reducing stroke, mood disorders, and motor vehicle accidents among OSA patients [6].

The RICADSA trial further contributes to this discussion. It specifically looked at patients with coronary artery disease and non-sleepy OSA, assessing the impact of CPAP treatment on cardiovascular outcomes. This trial revealed that in this particular subset of patients, CPAP did not significantly reduce the rate of cardiovascular events compared to the control group, adding a nuanced perspective to the understanding of CPAP's role in managing CHD among OSA patients [7].

In addition to the aforementioned studies, the ISAAC trial represents another significant investigation into the effects of CPAP therapy on cardiovascular outcomes in patients with OSA. This trial, focusing on a broad population of OSA patients, aimed to evaluate whether CPAP therapy could reduce the incidence of cardiovascular events, including CHD, beyond the benefits of symptom relief. Preliminary findings from the ISAAC trial suggest that while CPAP therapy continues to show efficacy in improving sleep-related symptoms and quality of life for OSA patients, its direct impact on reducing cardiovascular events, specifically CHD, aligns with the complex and nuanced results observed in other studies [8].

A recent meta-analysis included data from 3 RCTs SAVE, ISAACC, and RICCADSA analyzed the impact of CPAP adherence on the risk of cardiovascular events in OSA patients, emphasizing that consistent CPAP use ($\geq$ 4 h per night) significantly lowers the risk of major adverse cardiac and cerebrovascular events. This highlights the importance of CPAP compliance for effective secondary cardiovascular prevention in individuals with OSA, underscoring the role of patient adherence in achieving the therapeutic benefits of CPAP therapy for cardiovascular health [9].

The relationship between CPAP therapy and its impact on coronary heart disease in OSA patients is a topic of ongoing research and discussion. While CPAP is undoubtedly effective in alleviating the symptoms of OSA, its role in reducing CHD risk and related cardiovascular events remains complex and multifaceted. Further large-scale, long-term randomized controlled trials are needed to conclusively determine the extent of CPAP's cardiovascular benefits in OSA patients with CHD.

Impact of PAP treatment on Heart Failure in OSA

Heart failure (HF) is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood. The coexistence of OSA and HF is of particular clinical importance due to the bidirectional relationship between these two conditions. OSA not only contributes to the development and worsening of HF but also HF can exacerbate OSA.

Pathophysiology of Heart Failure in OSA

In patients with OSA, repetitive episodes of apnea lead to intermittent hypoxia, increased sympathetic nervous activity, and fluctuations in intrathoracic pressure. These factors contribute to increased cardiac preload and afterload, leading to myocardial stress and, over time, potentially to myocardial injury and heart failure [10]. Additionally, the hypoxic episodes can induce pulmonary arterial vasoconstriction, which may contribute to the development of pulmonary hypertension, a condition that further complicates heart failure.

Studies on CPAP and Heart Failure

Numerous studies have evaluated the impact of CPAP therapy on heart failure in patients with OSA. One pivotal study demonstrated significant improvements in cardiac ejection fraction and reductions in sympathetic nerve activity among patients with OSA and HF who received CPAP treatment [11]. This suggests that CPAP therapy can not only improve sleep-related symptoms in these patients but also potentially mitigate some of the cardiopulmonary abnormalities associated with HF.

Another important study focused on the long-term effects of CPAP on patients with HF and coexisting OSA. The study found that CPAP therapy led to a decrease in hospital readmissions and mortality in this patient group, indicating a positive impact on overall prognosis and quality of life [12].

However, it's crucial to note that while CPAP therapy shows promise in managing heart failure in OSA patients, it is not a substitute for standard heart failure treatments. It should be considered a complementary therapy, particularly in those with severe OSA.

CPAP therapy plays a potentially beneficial role in the management of heart failure in patients with OSA. By improving cardiac function and reducing adverse cardiovascular outcomes, CPAP can be an important adjunct therapy

in this patient population. However, further research is needed to fully understand the extent of its benefits and to optimize treatment strategies for these patients.

Impact of PAP treatment on Hypertension in OSA

Hypertension is a common comorbidity in patients with obstructive sleep apnea (OSA), and the interplay between these two conditions can significantly impact cardiovascular health. The repetitive episodes of upper airway obstruction during sleep in OSA lead to intermittent hypoxia and hypercapnia, which contribute to increased sympathetic activity and, consequently, elevated blood pressure.

Pathophysiology of Hypertension in OSA

The pathophysiology of hypertension in OSA patients involves several mechanisms, including increased sympathetic nervous system activity, endothelial dysfunction, and hormonal changes. These pathophysiological changes result in sustained daytime hypertension and a non-dipping blood pressure pattern, which is a significant risk factor for cardiovascular morbidity and mortality [13].

Studies on CPAP and Hypertension

There is substantial evidence supporting the beneficial effects of CPAP therapy on blood pressure in OSA patients. A meta-analysis by Montesi et al. [14] demonstrated that CPAP therapy significantly reduces both systolic and diastolic blood pressure, particularly in patients with resistant hypertension. This reduction in blood pressure is not only clinically relevant but also suggests a potential mechanism through which CPAP may reduce cardiovascular risk in OSA patients.

Another noteworthy study by Barbé et al. [15] evaluated the effect of CPAP on the prevention of new-onset hypertension in patients with OSA. The results indicated that CPAP treatment significantly reduced the incidence of new hypertension cases, highlighting the preventive role of CPAP in this high-risk population.

CPAP therapy has a significant impact on managing hypertension in patients with OSA. By reducing blood pressure levels and potentially lowering the risk of associated cardiovascular complications, CPAP treatment emerges as an essential component in the comprehensive management of OSA patients with comorbid hypertension. However, adherence to therapy is crucial for achieving these beneficial effects, underscoring the need for patient education and support in CPAP use.

Impact of PAP treatment on Cardiac Arrythmias in OSA

Cardiac arrhythmias, including atrial fibrillation, nocturnal brady-arrhythmias, and non-sustained ventricular tachycardia, are frequently observed in patients with OSA. The association between OSA and cardiac arrhythmias is thought to be mediated through multiple mechanisms including autonomic instability, hypoxemia, and changes in intrathoracic pressure.

Pathophysiology of Cardiac Arrhythmias in OSA

The intermittent hypoxia characteristic of OSA leads to increased sympathetic activity and fluctuating parasympathetic tone, creating an environment conducive to arrhythmogenesis. Additionally, the recurrent upper airway obstructions cause significant swings in intrathoracic pressure, which can adversely affect cardiac loading conditions and lead to arrhythmias [16].

Studies on CPAP and Cardiac Arrhythmias

Several studies have highlighted the beneficial effects of CPAP therapy in reducing the incidence and severity of cardiac arrhythmias in OSA patients. A study by Kanagala et al. [17] demonstrated that OSA patients with atrial fibrillation had a higher recurrence rate of arrhythmias if left untreated with CPAP, compared to those who received CPAP therapy. This suggests that effective treatment of OSA with CPAP may reduce the burden of atrial fibrillation.

Furthermore, a study by Simantirakis et al. [18] showed that CPAP therapy significantly reduced the incidence of ventricular arrhythmias in patients with OSA, indicating a potential role of CPAP in managing life-threatening arrhythmias in this population.

CPAP therapy is effective in reducing the incidence and severity of various cardiac arrhythmias in patients with OSA. By stabilizing the autonomic and respiratory disturbances associated with OSA, CPAP treatment can play a crucial role in the cardiac management of these patients. However, the relationship between CPAP adherence and arrhythmia control warrants further investigation to optimize treatment strategies.

Impact of PAP treatment on Pulmonary Hypertension in OSA

Pulmonary hypertension (PH) is a concerning complication of OSA, characterized by increased pressure in the pulmonary arteries. The intermittent hypoxemia and hypercapnia

from recurrent apneas in OSA can lead to pulmonary artery constriction, resulting in elevated pulmonary artery pressures.

Pathophysiology of Pulmonary Hypertension in OSA

The pathophysiology of PH in OSA is primarily attributed to hypoxia-induced vascular changes. Chronic intermittent hypoxia leads to pulmonary arteriolar constriction, vascular remodeling, and subsequently increased pulmonary arterial pressure. These changes can lead to right ventricular overload and, eventually, right heart failure if left unmanaged [19].

Studies on CPAP and Pulmonary Hypertension

The role of CPAP in managing PH in OSA patients has been the subject of several studies. A study by Sajkov et al. [20] demonstrated that CPAP therapy significantly reduced pulmonary arterial pressures in patients with severe OSA, suggesting a direct beneficial effect of CPAP on pulmonary hemodynamics.

Another critical research by Arias et al. [21] showed that long-term CPAP use led to a reduction in pulmonary artery pressures and improved right ventricular function in patients with OSA and PH. This indicates that CPAP treatment not only ameliorates respiratory symptoms of OSA but also has a positive impact on the cardiovascular system, particularly in the context of PH.

CPAP therapy shows significant potential in managing pulmonary hypertension associated with obstructive sleep apnea. By mitigating hypoxia-related pulmonary vascular changes, CPAP can play an important role in reducing pulmonary artery pressures and improving cardiac function in these patients. Continued research is essential to further understand and optimize the role of CPAP in the treatment of PH in OSA.

Conclusions

This comprehensive review has explored the multifaceted impact of CPAP treatment on various cardiovascular diseases in patients with OSA. The interconnections between OSA and a range of cardiovascular conditions – including coronary heart disease, heart failure, hypertension, cardiac arrhythmias, and pulmonary hypertension – highlight the critical role of CPAP therapy not only in alleviating the respiratory symptoms of OSA but also in addressing its cardiovascular complications.

Coronary Heart Disease: CPAP treatment has shown potential in reducing cardiovascular events in patients with OSA, though the extent of its impact varies based on adherence to treatment and comorbidities.

Heart Failure: CPAP therapy appears beneficial in improving cardiac function and reducing hospital readmissions and mortality in OSA patients with coexisting heart failure.

Hypertension: The use of CPAP has been consistently associated with reductions in blood pressure, particularly in patients with resistant hypertension, thereby lowering cardiovascular risks.

Cardiac Arrhythmias: CPAP treatment can significantly reduce the incidence and severity of arrhythmias in OSA patients, potentially reducing the risk of atrial fibrillation recurrence.

Pulmonary Hypertension: CPAP therapy has shown efficacy in reducing pulmonary artery pressures and improving right ventricular function in patients with OSA and pulmonary hypertension.

The cumulative evidence underscores CPAP therapy's role in the holistic management of OSA, extending beyond respiratory symptom relief to encompass cardiovascular health benefits. However, it's important to note that adherence to CPAP therapy is critical in achieving these benefits, and challenges in adherence remain a significant barrier.

Further research is required to understand the full scope of CPAP's impact on cardiovascular diseases in OSA patients, particularly in the context of long-term outcomes and in specific patient subgroups. As our understanding evolves, so too will the strategies for integrating CPAP therapy into the broader framework of cardiovascular disease management in OSA patients.

In conclusion, CPAP therapy stands as a pivotal treatment modality in OSA, with substantial implications for cardiovascular disease management. It underscores the necessity for a multidisciplinary approach to treating OSA, considering both its respiratory and cardiovascular consequences.

Key References

Papers of particular interest, published recently, have been highlighted as:

• ***Of importance***.

*McEvoy, R.D., et al., *CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea.* N Engl J Med, 2016. **375**(10): p. 919 – 31. **This study is the largest randomized control trial of CPAP treatment in patients with coronary artery disease and/or stroke and OSA with neutral results.**

*Peker, Y., et al., *Effect of Positive Airway Pressure on Cardiovascular Outcomes in Coronary Artery Disease Patients with Nonsleepy Obstructive Sleep Apnea. The RICCADSA Randomized Controlled Trial.* Am J Respir Crit Care

Med, 2016. **194**(5): p. 613 – 20. **This study is the first randomized control trial of CPAP treatment in patients with coronary artery disease and OSA with neutral results in intention-to-treat analysis but with good effect in CPAP compliant participants.**

•• ***Of major importance***.

Sánchez-de-la-Torre, M., et al., *Adherence to CPAP Treatment and the Risk of Recurrent Cardiovascular Events: A Meta-Analysis.* Jama, 2023. **330(13): p. 1255–1265. **Findings from this meta-analysis suggests the importance of CPAP compliance for effective secondary cardiovascular prevention in individuals with OSA.**

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Compliance with Ethical Standards

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