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# SLEEP DISORDERS AS A RISK FACTOR FOR CARDIOVASCULAR DISEASE: A COMPREHENSIVE REVIEW

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## ABSTRACT

**Background.** Sleep disorders represent a heterogeneous group of conditions that impair sleep quality, duration, and architecture, leading to significant daytime dysfunction and increased global morbidity. Epidemiological data indicate that approximately 30–40% of adults experience sleep disturbances, including insomnia and obstructive sleep apnea (OSA), which are increasingly recognized as modifiable risk factors for cardiovascular disease (CVD).

**Aim.** The aim of this narrative review was to synthesize current evidence on the association between sleep disorders and major cardiovascular outcomes and to identify the biological mechanisms underlying these relationships.

**Material and methods.** A narrative review of the literature was conducted using PubMed, ScienceDirect, JAMA Network, OUP, and open-access repositories. Epidemiological studies, cohort studies, and meta-analyses evaluating the impact of insomnia, sleep-disordered breathing, and circadian rhythm disturbances on hypertension, coronary artery disease, heart failure, arrhythmias, and stroke were analyzed.

**Results.** The reviewed evidence demonstrates that insomnia and obstructive sleep apnea are consistently associated with an increased risk of cardiovascular diseases, particularly hypertension, atrial fibrillation, coronary artery disease, heart failure, and stroke. The underlying mechanisms include sympathetic nervous system overactivation, oxidative stress, systemic inflammation, endothelial dysfunction, and dysregulation of glucose and lipid metabolism.

**Conclusions.** Sleep disorders have great effects on the cardiovascular system and should be considered independent, modifiable risk factors for CVD. Early diagnosis and treatment of sleep disorders may play a crucial role in cardiovascular disease prevention and risk reduction.

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## KEYWORDS

Sleep Disorders, Insomnia, Obstructive Sleep Apnea, Cardiovascular Disease, Hypertension

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## CITATION

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## Introduction

Sleep disorders are composed of a group of conditions that disrupt normal sleep quality, duration, and architecture. It leads to impaired functioning during the day and contributes to global morbidity. Due to WHO data, approximately 30-40% of adults suffer from one of these disorders - including insomnia, obstructive sleep apnea (OSA), parasomnia, and circadian rhythm disturbances. Lately, these conditions are increasingly recognized as important, modifiable risk factors for cardiovascular disease (CVD). This narrative review synthesizes current evidence on the relationship between sleep disorders and major cardiovascular outcomes. Literature from PubMed, ScienceDirect, JAMA Network, OUP, and open-access repositories was analyzed, with emphasis on epidemiological studies, cohort analyses, and meta-analyses assessing the association between sleep pathology and hypertension, coronary artery disease, heart failure, arrhythmias, and stroke. Consequently, insomnia and OSA are believed to be one of the strongest and most consistent links with CVD, with studies demonstrating increased risks of hypertension, atrial fibrillation, coronary artery disease, and cerebrovascular events. The biological processes underlying these associations include sympathetic overactivation, oxidative stress, systemic inflammation, endothelial dysfunction, and dysregulation of glucose and lipid metabolism. Therefore, this review demonstrates that sleep disorders impose profound adverse cardiovascular effects and should be pointed out as independent, modifiable contributors to CVD risk.

## **The impact of sleep disorders on cardiovascular risk**

### **What are sleep disorders?**

Sleep disorders are a group of conditions characterized by disruption of normal sleep patterns—its duration, quality, continuity, or structure—leading to impaired daytime functioning. These include difficulty falling asleep and maintaining sleep (insomnia), episodes of pathological daytime sleepiness, breathing disorders occurring during sleep (such as obstructive or central sleep apnea), abnormal sleep behaviors (parasomnias), and disturbances in the regulation of circadian rhythms. They constitute a widespread health problem—it is estimated that various forms of sleep disorders affect up to 30–40% of adults—and are associated with significant clinical consequences. Insufficient or fragmented sleep negatively impacts cognitive, immune, and metabolic functioning, and numerous studies also indicate a link between sleep disorders and an increased risk of cardiovascular, metabolic, and psychiatric diseases. Growing knowledge about the role of sleep in maintaining body homeostasis makes sleep disorders an increasingly important area of research in clinical medicine and public health.

Sleep consists of 4-5 cycles. Each cycle consists of two phases: NREM and REM. NREM sleep consists of three stages. The proper quality and duration of each of these cycles is crucial for a healthy life. To achieve this, adults should sleep 7 to 9 hours per day.

The most common somatic disorders associated with insomnia and cardiovascular disorders include coronary heart disease and arrhythmias.

### **The Importance of the Cardiovascular System**

The proper functioning of the cardiovascular system is crucial to health. Blood circulates throughout the body, delivering nutrients and cleansing tissues of waste products. However, it cannot circulate properly and fulfill its function if the blood transport system—the intricate connections between veins, arteries, and the heart—is not functioning properly. Cardiovascular diseases inevitably cause life-threatening conditions such as heart attacks, strokes, heart failure, and more. These are among the most common causes of death among patients.

Each year, cardiovascular diseases cause approximately 3.9 million deaths in Europe and approximately 18 million deaths worldwide. It accounts for 45% of all deaths in Europe and 32% of deaths globally [1][2]. According to WHO statistics, approximately 10,000 deaths are caused by heart and vascular diseases every day [3].

More than 60 million Europeans struggle with the consequences of cardiovascular disorders [4]. All the numbers mentioned above demonstrate the scale of the problem. It's no wonder the medical world is constantly analyzing all risk factors for the problem, such as sleep problems.

### **Sleep Problems and CVD**

Modern medicine strives to prioritize prevention. For this reason, scientists and physicians are searching for modifiable risk factors, the minimization of which can reduce morbidity. Many recent studies indicate that sleep disorders are significantly associated with the risk of CVD [5]. They point out that not only sleep duration (too much or too little), but also its quality and regularity are important in the prevention of cardiovascular disease [6]. Therefore, it should be no surprise that sleep has attracted significant attention in the medical world, particularly in cardiology.

### **Methodology**

This narrative review was developed based on the available scientific literature on the association between sleep disorders and cardiovascular disease (CVD). Publications were analyzed from databases such as PubMed, ScienceDirect, JAMA Network, OUP, and open access repositories (e.g., PMC). Review papers, cross-sectional studies, cohort studies, and meta-analyses on insomnia, sleep-disordered breathing, circadian rhythm disorders, and their impact on hypertension, coronary artery disease, heart failure, arrhythmias, and stroke were included. Risk ratios and odds ratios (OR, HR, RR) were intentionally used to compare the strength of associations between specific sleep disorders and clinical cardiovascular outcomes. The primary goal was to synthesize the available evidence, describe the biological mechanisms underlying these associations, and assess the consistency of results across studies.

### **The main sleep disorders that contribute to cardiovascular disease**

The sleep disorders that have well-documented impact on cardiovascular diseases are insomnia and obstructive sleep apnea [18]. We will describe these connections in more detail below.

#### **Insomnia**

Insomnia is a sleep disorder characterized by persistent difficulty falling asleep, staying asleep, waking up too early, or experiencing poor sleep quality despite adequate sleep conditions. These symptoms lead to clinically significant impairment in daytime functioning and persist at least three times per week for at least three months.

People with insomnia have been shown to have a greater than 40% increased risk of developing CVD [7], indicating that insomnia is a strong risk factor for cardiovascular disorders, not just a comorbid symptom. The strongest effect of this sleep disorder has been shown to induce hypertension (OR=1.16). A link was then demonstrated with coronary artery disease (OR=1.14). Lower associations were demonstrated for heart failure (OR=1.04) and ischemic stroke (OR=1.09). There are also some studies that clearly link insomnia with atrial fibrillation (OR=1.02) and intracranial hemorrhage (OR=1.16). No evidence provides connections between insomnia and small vessels stroke [8].

#### **Obstructive Sleep Apnea**

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by repeated episodes of complete (apnea) or partial (hypopnea) closure of the upper airways, despite sustained respiratory effort. This results in decreased oxygen saturation, arousals, and sleep fragmentation. Diagnosis is based on an apnea-hypopnea index (AHI) of  $\geq 5$  episodes/hour on polysomnography in conjunction with clinical symptoms, or an AHI of  $\geq 15$  episodes/hour regardless of symptoms.

Patients with obstructive sleep apnea have approximately 1.8 times higher risk of cardiovascular disease than the control group [9]. According to research, the chances of stroke are 1.86 times higher in people who suffer from this condition, and the chances of developing coronary artery disease are 1.46 [10]. Another article indicates an indirect relationship between obstructive sleep apnea and the increased chances of developing heart failure via increased ApoB, which is estimated at 1.26. Researchers also show an association with hypertension (OR=1.24) and atrial fibrillation (OR=1.21) [11].

### **Biological Mechanisms Linking Sleep with the Cardiovascular System**

#### *Sympathetic and Parasympathetic Nervous System*

The body functions best when it achieves homeostasis, or a balance between the various processes occurring in the human body. The same principle applies to the balance between the sympathetic and parasympathetic nervous systems. Heart rate, blood pressure, and vascular function are then normal. However, in sleep disorders, the sympathetic nervous system predominates, increasing catecholamine levels, heart rate, and blood pressure. There is no specific balance that allows the body to "rest" and regenerate during sleep [12]. This is most noticeable in Obstructive Sleep Apnea, where there is constant oxygen deprivation and increased CO<sub>2</sub>. These trigger the activation of chemoreceptors, which send signals that stimulate the sympathetic nervous system [13]. This leads to nocturnal elevations in blood pressure and heart rate, which, over time, result in persistent sympathetic overactivation. Hypertension is also noticeable during the day. This translates into a risk of arrhythmia, vascular remodeling, and other cardiovascular diseases [14]. Additional harmful mechanisms are involved, such as oxidative stress, endothelial dysfunction, and inflammation. All these conditions further fuel the development of conditions such as atherosclerosis, which is a proven risk factor for heart and vascular disease [15]. On the other hand, the lack of complementary action of the parasympathetic system results in the inability to reduce heart rate and vascular resistance. First, there is no physiological "nighttime drop in blood pressure" that has a protective effect on the vessels and the heart [16]. The lack of homeostasis between the sympathetic and parasympathetic systems in people suffering from chronic sleep disorders significantly affects changes in the vascular system.

#### *Oxidative Stress*

Sleep problems disrupt the balance between factors promoting oxidative stress and the protective mechanisms that regulate redox balance, favoring the former [17], [19]. Obstructive Sleep Apnea (OSA) involves alternating periods of normal and abnormal blood oxygenation, which activate enzymes that promote free radical production. Excessive amounts of free radicals can lead to endothelial cell damage, hypertension, atherosclerosis, and other CVDs [20]. Studies show that people with sleep disorders have fewer antioxidants in their bodies.

### *Inflammation*

Long-term sleep disruption also triggers an activation of the inflammatory response [21]. This is another pathophysiological mechanism that supports the idea that sleep problems are a risk factor for cardiovascular disease. Studies have shown that the inflammatory marker CRP dramatically increased after sleep deprivation [22]. This marker is already a proven risk factor for conditions such as heart attack and hypertension. Furthermore, in obstructive sleep apnea, it has been observed that the severity of the disease—the intensity of apneas at rest—is directly proportional to the increase in CRP. It has also been demonstrated that chronic sleep deprivation triggers the secretion of interleukin-6, which also activates the immune system. Both the CRP marker and the cytokine IL-6 lead to chronic low-grade inflammatory response. Inflammation is a known factor in endothelial dysfunction and increased inflammatory cell adhesion, which subsequently leads to the development of atherosclerosis. Combined with the other mechanisms mentioned above, this increases the risk of adverse cardiovascular events.

### *Endothelial Dysfunction*

In the previous sections, the impact of sympathetic-parasympathetic imbalance, oxidative stress, and inflammation has been discussed [23]. It has been emphasized that all of these are a result of sleep disorders and contribute to endothelial dysfunction [24]. A systematic review of scientific papers demonstrated that sleep deprivation affects most endothelial functions. A study of normal brachial artery contraction and dilation, which assesses vascular endothelial function, demonstrated that after 24 hours of sleep deprivation, arterial wall dilation and the secretion of proinflammatory cytokines IL-6 and IL-1 were impaired. This indicates impaired endothelial function and the creation of conditions that could, in the long term, lead to chronic low-grade inflammatory response [25]. The lack of homeostasis in the autonomic nervous system (sympathetic and parasympathetic) disrupts the circadian decrease and increase in blood pressure, which disrupts endothelial function. Chronic inflammation leads to the overactivation of adhesion molecules such as VCAM-1 and ICAM-1. This facilitates leukocyte adhesion to the endothelium, and their subsequent mitosis and activation. This disrupts endothelial cell contraction, pro- and antithrombotic activity, and repair. Further consequences can include atherosclerosis, decreased vascular susceptibility to vasoconstriction, and hypertension [24].

### *Blood Pressure Regulation*

Poor sleep quality and limited sleep duration contribute to dysregulation of the sympathetic-parasympathetic nervous system, favoring the sympathetic nervous system. This increases blood pressure, which, without the protection of the parasympathetic nervous system, can lead to hypertension [26]. One study showed that 24-hour sleep deprivation resulted in increased diastolic blood pressure. Sleep disorders also affect circadian blood pressure fluctuations, causing it to be regularly above normal for a given time of day. This results in a physiological drop in blood pressure at night, and a sudden rise in BP upon awakening [27]. Of particular importance in this case is insufficient sleep duration or poor sleep quality, which leads to fatigue. The NREM sleep phase is crucial here, as it is dominated by parasympathetic activation and whose duration may be impaired in insomnia and other sleep-related conditions. The predominance of activity tends to be towards the sympathetic nervous system [28]. Chronic sleep deprivation leads to higher average blood pressure throughout the day. This can lead to hypertension and, consequently, cardiovascular disease. Improving the quality and length of sleep reduces BP, indicating that sleep is an important risk factor for cardiovascular disease [29].

### *Glucose and Lipid Metabolism*

Sleep play a key role in regulating not only the nervous and immune systems, but also in regulating the homeostasis of glucose and lipid metabolism [30], [31]. Studies show that sleep deprivation is associated with the risk of developing insulin resistance, type 2 diabetes, obesity, and metabolic syndrome. Lack of adequate sleep quantity and quality can negatively impact metabolic and hormonal balance, consequently worsening lipid profiles and increasing blood glucose levels [32], [33]. Sleep deprivation and poor quality reduce tissue sensitivity to insulin and worsen glucose tolerance. This leads to hyperglycemia. Interestingly, sleep-deprived patients chose higher-calorie foods. Researchers attribute this to changes in leptin and ghrelin levels, hormones that regulate appetite. Increased ghrelin and decreased leptin contribute to a decreased feeling of satiety, which leads to increased calorie intake and, ultimately, obesity [30]. Increased adrenaline secretion, by stimulating the sympathetic nervous system, predisposes glucose production and impairs insulin secretion, directly leading to insulin resistance. Some studies show that inappropriate daily sleep fluctuations, such as shift work or circadian rhythm disruptions, lead to an 8% increase in fasting glucose levels and a 14% increase after a meal. Researchers attribute this to a decline in beta cell function [34].

## Clinical Evidence

### *Sleep Disorders and Hypertension*

Sleep disorders, particularly obstructive sleep apnea and insomnia, are significant risk factors for elevated blood pressure. A cross-sectional study involving nearly 230,000 individuals demonstrated that short sleep duration significantly increased the risk of hypertension (OR, 1.21; 95% confidence interval [CI], 1.09 - 1.34;  $P < 0.001$ ). Interestingly, prolonged sleep duration also increased the risk of hypertension (OR, 1.11; 95% CI, 1.04-1.18;  $P = 0.003$ ). It is worth emphasizing that a study that monitors patients for a longer period found an association between short sleep duration and hypertension (RR, 1.23; 95% CI, 1.06-1.42;  $P = 0.005$ ). Nevertheless, it did not prove a significant association between excessive sleep duration and hypertension (RR, 1.02; 95% CI, 0.91-1.14;  $P = 0.732$ ) [35]. Another study found that people who chronically do not sleep for over 7 hours have a 2,8-fold higher risk of developing hypertension than the population sleeping more than 7 hours [36]. The link between OSA and hypertension is also noteworthy. The odds ratios in studies range from OR=1.79 to OR=1.98 [37]. In any case, they show that people with obstructive sleep apnea have a significantly greater chance of developing hypertension. Other studies also show a relation between poor sleep quality (OR=1.38) and snoring (OR=1.94). Although in comparison to sleep quality, the results were inconsistent across case-control studies [38].

### *Sleep Disorders and Coronary Artery Disease*

It is interesting that over 70% of patients with acute coronary artery disease have undiagnosed OSA. The same study found that 67% of OSA patients had coronary artery calcifications detected in diagnostic tests (compared to only 31% of those without OSA). Such changes in heart arteries are risk factors for coronary artery disease [39]. Another study indicates that the severity of OSA symptoms increases the odds of developing coronary artery disease at its highest stage by up to 1.42 [40]. A study examining insomnia and coronary heart disease revealed that short sleep duration statistically increased the risk of developing the disease (HR=1.13). It's worth noting that difficulty falling asleep or taking medications to aid this process also increased the risk of the disease (HR=1.4). Long sleep duration did not affect the disease's incidence [41]. However, another study on a similar topic found that both short sleep and long sleep increased cardiovascular events, 1,45 and 1,38 times respectively. In conclusion, the research on too much sleep is ambiguous, but too little sleep is a definite risk factor [42].

### *Sleep Disorders and Heart Failure*

A study on the relationship between heart failure and sleep disorders showed that overall sleep disorders increase the odds of developing heart failure (OR=1.22). This included insomnia (OR=1.26) and sleep apnea (OR=1.21) [43]. Other studies show that people with obstructive sleep apnea (OSA) are more likely to develop heart failure. This is particularly true for men with severe disease, who have a 58% increased risk of developing HF [39]. Another analysis found that insomnia, particularly difficulty falling asleep, significantly increased the risk of developing HF (HR=1.26;  $p = 0.001$ ) [44].

### *Sleep Disorders and Arrhythmias*

OSA is suspected to be a risk factor for atrial fibrillation in patients without other cardiovascular diseases. This is indicated by the four-times increased incidence of this arrhythmia in patients with severe OSA [39], [45]. It has been shown that people with a broad range of sleep disorders were associated with a higher risk of developing atrial fibrillation (1,21 times more). That includes insomnia with a 1.26-times increased risk [46]. Another study found that patients with sleep-disordered breathing are particularly susceptible to arrhythmia. Their risk of arrhythmia is estimated at OR=2.24 (95% CI 1.48-3.39), with atrial fibrillation having the quadruple risk. Other arrhythmias, such as non-sustained ventricular tachycardia, sinus pauses, and atrioventricular block, occur less frequently, but are common enough to warrant consideration [47].

### *Sleep Disorders and Strokes*

The incidence of stroke is estimated to be higher in people with OSA. This severity increases with more sleep apneas [39]. A review study found that obstructive sleep apnea increases the risk twice of a vascular event leading to stroke, when compared with a healthy population [48]. The same literature review reported a link between sleep duration of less than 5-6 hours and a 15% increased risk of stroke.

### Final Conclusions

The accumulated data clearly indicate that sleep disorders, including insomnia, obstructive sleep apnea, and circadian rhythm irregularity, represent a significant, modifiable risk factor for cardiovascular disease. Poor sleep affects many key biological mechanisms: it activates the sympathetic nervous system, disrupts blood pressure regulation, increases oxidative stress, promotes chronic inflammation, and impairs endothelial function. These mechanisms increase the risk of hypertension, atherosclerosis, and cardiovascular events, as confirmed by numerous epidemiological studies demonstrating elevated OR and HR values for the most common CVDs. Particularly strong associations are observed for OSA, which significantly increases the likelihood of hypertension, atrial fibrillation, stroke, and heart failure. These results emphasize the need to treat sleep disorders as independent cardiovascular risk factors. Integrating sleep disorder diagnosis and treatment into routine cardiology practice and preventive strategies can significantly reduce the global burden of CVD and improve patient outcomes.

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