Review

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The pulse of sleep: novel interventions in understanding the sleep-cardiovascular connection: a literature review

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Introduction: Sleep disorders represent common complaints in different medical illnesses. They encompass a risk for diverse inflammatory, metabolic, and cardiovascular diseases. Sleep disorders include disorders of hypersomnolence, insomnia, parasomnias, sleep-related movement disorders, circadian rhythm sleep-wake-disorders, and sleep-related breathing disorders, each one of which was associated with increased cardiovascular disease risk in a different mechanism. In this review, the authors address the most recent research on the correlation between sleep and CVD.

Methods: The literature on sleep disorders and their potential links to various cardiovascular diseases was reviewed in narrative form. For the published papers up to June 2023, the authors searched the databases of PubMed and Google Scholar. Literature demonstrating the relationship between these illnesses, pathophysiological mechanisms, diagnosis, and various therapeutic approaches was included.

Results: Sleep disorders were significantly linked to heart rate variability, hypertension, and obesity, which can eventually result in cardiovascular consequences and affect mortality and morbidity. The disruption in sleep cycles, which can be noticed in different sleep disorders, can obviously result in blood pressure, heart rate, and other cardiac functions. The clinical assessment acts as the cornerstone in the diagnosis of different spectrums of sleep disorders. The management of sleep disorders ranges from cognitive-behavioral therapy to continuous positive airway pressure (CPAP).

Conclusion: Additional research on the topic is needed to pinpoint any potential links and pathological processes. To improve clinical treatment and preventive measures, further observational studies should emphasize the reliability of early diagnostic signs.

Keywords: cardiovascular diseases, obstructive sleep apnea, pulmonary hypertension, sleep disorders

Introduction

Sleep is an essential component of health. It is characterized by reduced muscle activity and relative sensory inhibition[1]. Sleep consists of two phases rapid eye movement (REM) phase and the non-REM phase[1]. Approximately every 90 min 1 cycle of REM and non-REM phases occur[1]. Disturbances in the amount of sleep, misalignment of the circadian clock, or other sleep abnormalities constitute the basis of sleep disorders. The exact

HIGHLIGHTS

- Sleep disorders represent common complaints in different medical illnesses. They encompass a risk for diverse inflammatory, metabolic, and cardiovascular diseases.
- Sleep disorders are categorized into six main disorders. The clinical evaluation beside the sleep diary and the questionnaires are the cornerstone in the diagnosis of insomnia and the different spectrum of sleep disorders.
- The serum biomarkers and laboratory test still have limited value and specificity in the diagnosis and follow-up of different sleep illnesses. Even so, OSA led to an elevation in some serum markers, including kallikrein-1, uromodulin, urocortin-3, and orosomucoid-1, which can be used in combination as diagnostic tests.
- Some sleeping disorders, especially sleep-related breathing disorders, have direct and indirect linkage with cardiovascular diseases risks. Some studies showed the presence of significant increase in pressure and heart parameters and risk of heart disease in patients with sleep illnesses or sleep deprivation.

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prevalence of these disorders is based on the specific disorder. There is not enough data on the total prevalence of all sleep disorders combined. However, they are recognized as one of the most common medical complaints. Insomnia alone constitutes about a third of all medical complaints in adults, however insomnia, as a diagnosis, is estimated to be about 10%[2]. Current literature highlights sleep disorders' role in diverse disease processes especially inflammatory, metabolic, and cardiovascular diseases (CVDs)[1,3,4]. CVD are very important to consider as they are the most common cause of death globally[5].

Sleep is an important regulator of cardiovascular function[4]. Recent literature has been assessing the association of sleep with cardiovascular disease and accumulating evidence suggests that sleep is a closely related modifiable risk factor for CVD and may help in preventing CVDs[4]. On the other hand, multiple studies provide contradicting evidence between sleep health and the risk of developing CVD[6]. In this review, we discuss the recent literature on the connection between sleep and CVD. We also review mechanisms, diagnostics, and treatments of such diseases.

Sleep disorders and cardiovascular risk factors

The international classification of sleep disorders divides sleeping disorders into six categories: 1-central disorders of hypersomnolence, 2-insomnia, 3-parasomnias, 4-sleep-related movement disorders, 5-circadian rhythm sleep-wake disorders, and 6-sleep-related breathing disorders[2]. 1- Central disorders of hypersomnolence are disorders of excessive sleepiness during the daytime[2,7]. These disorders are due to abnormal central nervous system control of sleep-wake cycles[2]. On the other hand, 2-insomnia is difficulty initiating or sustaining sleep[2]. The exact etiology of insomnia remains unknown, but insomnia is usually triggered by stress[2,8]. Insomnias that are triggered by stress are usually acute and resolve with no intervention, however, some patients may develop chronic insomnia disorder[8]. 3-Parasomnias are abnormal behaviors during sleep[8]. They are divided into Non-REM and REM parasomnias and are summarized in Figure 1[8]. Non-REM parasomnias are arousal disorders and are attributed to an inability to arise from the non-REM phase[8]. Thus, patients with non-REM parasomnias can walk and talk while sleeping, these actions are referred to as somnambulism and somniloquy, respectively[8]. The other REM parasomnias include nightmares, recurrent isolated sleep paralysis, and REM sleep behavior disorder (RBD)[7]. These disorders occur because of emotions or REM phase and wake dissociation[7]. For example, RBD is characterized by loss of motor inhibition, thus patients with RBD may report aggressive movements such as kicking and punching while asleep[2,8]. RBD can also be a manifestation of other disease processes such as synucleinopathies which are more prevalent in old age[8]. 4-Sleep-related movement disorders include restless leg syndrome (RLS) and periodic limb movement disorder[2,8]. Patients with RLS have an excessive urge to move their legs[2,8]. The urge is triggered by rest and relieved by moving the legs, making it difficult to fall asleep[2,8]. 5- Circadian rhythm sleep-wake disorders describe conditions in which internal circadian rhythm is mismatched with the external environment[2]. These disorders are caused by jetlag, irregular sleep-wake rhythm, shift work delayed sleep phase disorder, or advanced sleep phase disorder[8]. It is important to note that delayed sleep phase and advanced sleep phase are considered disorders only if it affects the patient negatively[8]. 6-Sleep-related breathing disorders include obstructive sleep apnea, central sleep apnea syndromes, sleep-related hypoventilation disorders, and sleep-related hypoxemia disorder[2,7,8]. In central sleep apnea CNS neurons are incapable of activating phrenic and intercostal muscles[2,8]. In obstructive sleep apnea, a collapse of the upper airway decreases oxygen saturation and may cause arousal, and cardiovascular complications[2,8]. Sleep-related hypoventilation disorders can be due to multiple causes including medication, obesity, and other medical disorders[7]. Lastly, sleep-related hypoxemia disorder is a separate diagnosis from hypoventilation, diagnosed if oxygen saturation is less than or equal to 88% for more than 5 min without elevation of arterial carbon dioxide[7] (Fig. 1).

An important function of sleep that is usually overlooked is cardiovascular health regulation[4]. Heart rate and blood

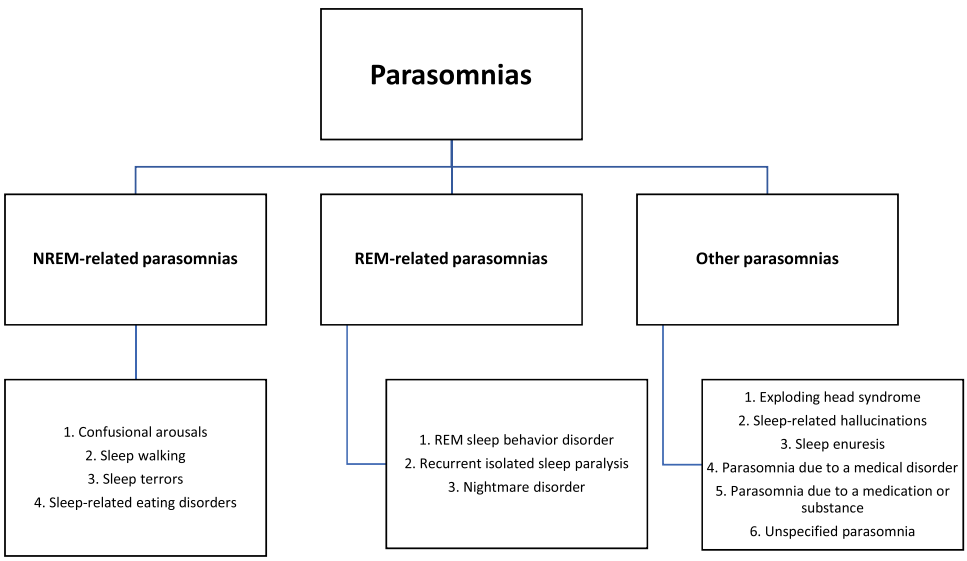

Figure 1. Summarizes the classification of parasomnia.

pressure vary during different phases of sleep and thus, there has been an interest in discovering the association between disordered sleep and CVD risk factors[4]. Evidence shows that sleep abnormalities are associated with multiple cardiovascular risk factors including hypertension, metabolic disorders, and obesity[1,3,9]. Hypertension has a strong association with sleep-related breathing disorders and insomnias, however, evidence of association with sleep deprivation and fragmentation requires further investigation[4,9]. Sleep disorders create metabolic and hormonal stressors that promote higher metabolic intake and eventually obesity[1]. There is evidence of diabetes association with circadian misalignment, sleep, deprivation, sleep fragmentation, and sleep-related breathing disorders.

Heart rate variability has a lot of conflicting studies on whether sleep disorders cause abnormal heart rate variability[10]. One explanation proposed by Nano *et al.*[11] is that autonomic regulation seems to be consistent when patients with insomnia are divided into subgroups based on their phenotype, thus heart rate variability impairment alone is not reliable.

Sleep-related breathing disorders and insomnia have been linked to hypertension. Such disorders reduce non-REM sleep which is correlated to blood pressure dipping and further studies associated reduced non-REM with the incidence of hypertension[9]. In terms of obesity, the amount of sleep and circadian alignment are important in regulating energy expenditure and appetite[1]. Insufficient sleep increases energy expenditure, however, energy intake is higher especially later in the day[1]. Late meals are associated with low thermic effects and with obesity[1]. Circadian misalignment contributes to obesity by reducing energy expenditure and releasing appetite-promoting hormones[1]. In addition, some behaviors associated with both insufficient sleep and circadian misalignment such as poor food choices can contribute[1]. These mechanisms allow weight gain without changes in energy intake[1].

Sleep and immune function are recognized to be closely related[3]. Sleep regulates immune markers and in return, immune markers were shown to promote sleep[3]. This relation is important and is thought to be implicated in immune dysregulation[3]. Continuous disturbance of normal sleep allows a sustained inflammatory state thus possibly increasing the risk of CVD[3].

Mechanisms of sleep disorders' impact on cardiovascular health

To assess the impact of testing for sleep issues and enhancing sleep hygiene on heart disease outcomes, research studies are also required. Here, we demonstrate that short sleepers are more prone to experience sleep disorders and to participate in other harmful sleep-related behaviors, indicating a potential clustering of sleep-related issues. Consequently, more research is needed to determine the effectiveness of using self-reported sleep duration screening as a practical and quick way to evaluate sleep in enhancing CVD risk prediction[12].

Important changes in heart rate (HR) and blood pressure (BP) are linked to sleep and arousal. Arousal, rapid eye movement (REM) sleep and nonrapid eye movement (NREM), and transitions between the different stages of sleep are all regulated by multiple neuronal groups in the basal forebrain, hypothalamus, and brainstem. The brainstem is responsible for controlling behavioral arousal, cardiovascular activity, respiratory system, and the timing of wakefulness and sleep cycle[13]. Active wakefulness causes the orexin/hypocretin neurons to fire, and through targeting the brainstem, they play a significant part in coordinating arousal and circulatory and respiratory activation. The orexin/hypocretin neurons of the posterior lateral hypothalamus provide inputs to activate all wake-promoting neurons (Fig. 1)[14]. Orexins are required for the physiological alterations in BP and HR that take place as a result of shifting between awake and asleep, NREM sleep, and REM sleep. BP and HR drop during the transition from awake to NREM sleep and consequently rise again during REM sleep to waking levels[15] (Fig. 2).

GABAergic neurons in the ventrolateral and median preoptic areas, which send inhibitory projections to wake-promoting regions of the hypothalamus and brainstem, are principally responsible for the shift from awake to sleep[16]. In the hypothalamus, melanin-concentrating hormone (MCH) neurons possess extensive brain connections, including those to arousal neurons. Optogenetic activation of MCH neurons promotes sleep despite the presence of a powerful urge to stay awake, by inhibiting wake-active neurons[17,18].

As opposed to daytime wakefulness, it has been established that nocturnal sleep provides protection against acute cardiovascular syndromes[19]. Sudden spikes in BP and HR to wakefulness levels and higher, occur during (REM) sleep, in addition to an increase in peripheral tone. On the other hand, non-REM (NREM) sleep, commonly referred to as slow wave sleep (SWS), is linked to lower levels of BP, HR, cardiac output, and systemic vascular resistance, as well as vasodilation, which also lowers blood pressure as a result. Additionally, sleep apnea and other sleep disorders that lead to the lack of SWS are associated with an increased risk of cardiovascular dysfunction, particularly a higher incidence of hypertension. The preoptic region of the hypothalamus, which promotes sleep, and the posterior hypothalamus, which promotes wakefulness, both play major roles[4,19].

The autonomic nervous system (ANS) plays a pivotal role in modulating cardiovascular functions throughout various sleep stages[20]. Serotonergic neurons of the midline raphe in the pons, the orbital frontal cortex, the hippocampus, the hypothalamus, and the amygdala are among the brain regions most crucial for controlling both sleep and heart rate. Additionally, the hypothalamic suprachiasmatic nucleus (SCN) serves as the primary pacemaker for all cardiometabolic processes, including circadian rhythms (Fig. 3)[4].

Sleep apnea, whether obstructive or central in origin, is the most common sleep-related problem in cardiovascular diseases (CVD)[21]. Studies on chronic insomnia and sleep-deprived

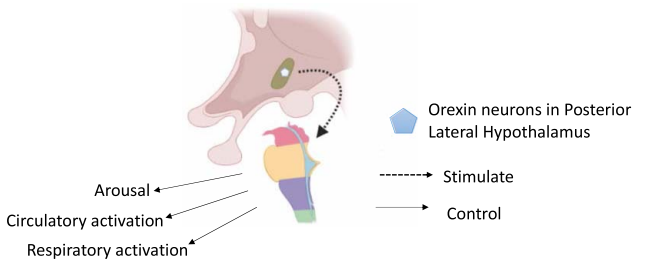

Figure 2. The involvement of orexin neurons in sleep regulation and cardiovascular control.

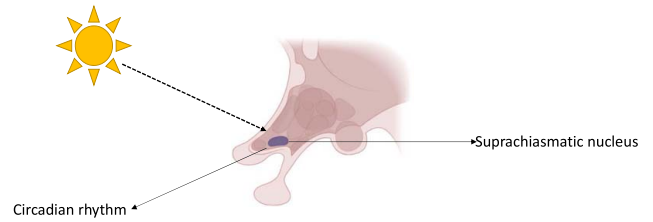

Figure 3. The location of suprachiasmatic nucleus involved in circadian rhythm in the hypothalamus.

healthy people have found elevated cortisol levels, lowered immunity, and elevated sympathetic activity indicators (Fig. 4)[22]. Cardiac remodeling was also attributed to exposures to hypoxemia, notably in obstructive sleep apnea[23].

Overview of key studies investigating the impact of sleep disorders on cardiovascular health

Gottlieb *et al*. followed 1927 men and 2495 women over the age of 40 who did not have coronary heart disease or heart failure at the beginning of the study. A baseline polysomnography (a sleep study) was performed on each participant, and they underwent follow-up exams for around 8.7 years. The study aimed to investigate the potential association between obstructive sleep apnea (OSA) and the onset of heart failure and coronary heart disease (CHD). The researchers discovered that OSA emerged as an important indicator of incident CHD in men aged 70 years or younger after controlling for several risk variables. Per 10-unit rise in the apnea-hypopnea index (AHI) in these individuals, the probability of having CHD rose by 10%. However, neither older men nor older women showed any evidence of a connection between OSA and incident CHD[24].

Kadier *et al*.[25] suggests those under the age of 60 who have sleep disorders have a risk for CVD. A possible protective factor against CVD in females is a shorter sleep-onset latency.

Quan and Gersh[26] conducted a workshop, of which the primary objective was to make new research recommendations for improving our comprehension of the pathophysiological mechanisms that link sleep disorders and CVD, as well as the magnitude of this association from an epidemiological standpoint.

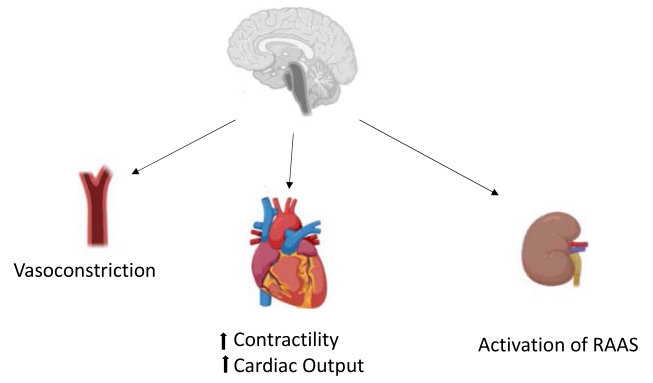

Figure 4. Mechanisms of sympathetic system to increase blood pressure.

As per Patrick *et al*.'s review, insufficient sleep has been observed to induce a proinflammatory state characterized by elevated release of interleukin (IL)-6 and tumor necrosis factor (TNF). In addition, it has been shown to affect leukocyte inflammatory gene expression and the likelihood of developing inflammatory diseases through nuclear factor (NF)-B activation, a molecular pathway. Stress activation, involving sympathetic and/or cortisol activation, could be responsible for these proinflammatory effects. Additionally, most sleep disorders are associated with intermittent hypoxia, leading to oxidative stress. The monocytes and lymphocytes are further activated by this inflammatory cascade, which further enhances the production of adhesion molecules. The degree of an impairment of endothelial-dependent vasodilation was linked with endothelial cell apoptosis. Disrupted endothelial function and atherosclerosis develop as a result[27].

Tobaldini *et al*.[28] associated the risk of CVD in sleep-disorder patients to several physiologic mechanisms, including oxidative stress, cardiovascular autonomic regulation, inflammatory reactions, and endothelial function.

Greater attention should be paid to complementary basic scientific research. For example, approaches such as tissue culture or mouse models with microarray, genomic, and proteomic approaches offer valuable insights into the molecular mechanisms involved in intermittent hypoxia and its impact on cardiovascular function. Furthermore, children with sleep disorders are excellent candidates for studying the correlation between sleep disorders and CVD because they generally lack other predisposing risk factors. Additionally, there is a crucial need for developing innovative screening methods capable of identifying sleep disorders in large populations[26].

Diagnostic tools for sleep disorders and cardiovascular assessment

Sleep disorders are categorized into six main disorders[29]. The clinical evaluation beside the sleep diary and the questionnaires are the cornerstone in the diagnosis of insomnia and the different spectrum of sleep disorders[30].

The evaluation of severity and planning for management can be met with objective assessment using different set of tools and tests, including polysomnography (PSG), portable monitor (PM), sleep latency test (MSLT), and actigraphy as an adjunct to portable monitors in moderate cases[31].

Polysomnography is the gold standard sleep study assessment tool. It gives a record of multiple parameters of 8 h of sleep: heart status, EEG waves, movement of the eye, mouth, legs, abdomen, thorax, airflow, and oxygenation to assess different stages of sleep[32]. Home sleep apnea test (HSAT) helps to evaluate sleep with 4 or 7 of the previously mentioned parameters. HSAT is ideal for patients with a higher possibility of obstructive sleep disorder and in the absence of comorbidities including cardiovascular diseases[32]. Likewise, actigraphy provides an objective assessment of sleep patterns and evaluation of efficacy of treatment using a wrist device monitor. However, it has limited validity compared to other tests and tools[33]. On the other hand, (MSLT) charts the speed and latency of falling asleep and conducts a sleep study in five scheduled naps, usually accompanied by actigraphy to assess any abnormal sleep pattern[34].

The serum biomarkers and laboratory test still have limited value and specificity in the diagnosis and follow-up of different sleep illnesses. Even so, OSA led to an elevation in some serum markers, including kallikrein-1, uromodulin, urocortin-3, and orosomucoid-1, which can be used in combination as diagnostic tests[35].

Sleep deprivation and sleep disorders, such as OSA, significantly increase cardiovascular disease risks, morbidity, and mortality[35]. The duration of sleep was directly associated with increased heart rate, blood pressure, level of cortisol, LDL, and total cholesterol. Furthermore, oxygen desaturation, which can be noticed in some sleep disorders, was associated with exaggerated sympathetic nervous system activity, which results in the increase of systemic inflammatory response, such as C-reactive protein (CRP), Factor VIII, intercellular and vascular adhesion molecules (ICAM) and (VCAM-1) of the endothelium, IL-6, and IL-10[35,36]. Moreover, short sleep increases the level of serum amyloid A (SAA) and glucagon-like peptide 1(GLP-1), which can predispose to decreased insulin production and eventually lead to insulin resistance[37]. Accordingly, sleep disorders can represent an independent risk factor for serious cardiovascular events through different biochemical and mechanical mechanisms involving various sets of biomarkers that could be used as diagnostic or prognostic indicators (Fig. 5).

Nonpharmacological interventions for sleep disorders and their cardiovascular implications

Nonpharmacological interventions for sleep disorders are interventions that do not require the use of medications to improve sleep and sleep quality[38]. They can also be referred to as remedies for sleep disorders that do not require medicines or therapeutics. Nonpharmacological interventions for sleep disorders include cognitive-behavioral therapy for insomnia and continuous positive airway pressure (CPAP) therapy for sleep apnea. They have been shown to improve sleep and sleep quality[39].

Cognitive-behavioral therapy for insomnia (CBT-I): CBT-I is a nonpharmacological intervention for improving sleep and sleep quality in individuals suffering from insomnia[40]. It focuses on improving sleep through the modification of sleep habits and behaviors, which includes the identification of sleep problems (insomnia) and changing the thoughts and behaviors that affect the ability to sleep and sleep well. This intervention is made up of components that are described as key components. They include sleep restriction (deprivation), stimulus control, sleep hygiene, and cognitive therapy. Using these components to improve sleep also has consequences for cardiovascular health[41].

Sleep restriction (deprivation) is the reduction of sleep hours to greater than or equal to 24 h. This is usually done in the daytime, as sunlight decreases the ability to fall asleep. This component requires trained personnel's assistance, which could be done through telemedicine or physically. Sleep restriction, or deprivation, has been associated with coronary heart disease. Studies have shown that an association exists between sleep restriction and coronary heart disease, cardiovascular death, and myocardial infarction. This is through causing the death of myocardial cells through complex mechanisms such as inflammatory response, lipid metabolism, oxidation, etc.[41] (Fig. 6).

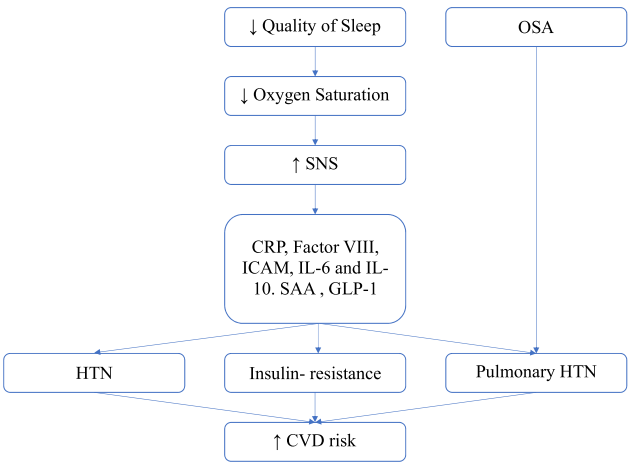

Figure 5. Sleep disorders and CVD risk.

Continuous positive airway pressure (CPAP) therapy for sleep apnea

By maintaining pressure on the airways throughout the respiratory cycle (both inspiration and expiration) while sleeping in persons who are breathing naturally, CPAP lowers the chance of developing fatal and severe cardiovascular problems[42,43]. CPAP is further referred to as an airway pressure where individuals with apnea use a device to maintain positive end-expiratory pressure (PEEP), which is the pressure in the alveoli above atmospheric pressure at the end of expiration. Centimeters of water pressure (cm H2O) are used to measure CPAP. Machines created expressly to deliver a flow of constant pressure are used in CPAP therapy. It can be delivered using a facemask, nasal, or nasopharyngeal interface depending on the mask being worn. A full-face mask that forms a tight seal over the lips and nose is used for the face mask. It can be applied to mouth breathers or to preoxygenate individuals who are spontaneously breathing before intubation. Patients who need a nasal procedure wear nasal prongs that go into their nostrils or a little mask that covers their nose. Patients who need a nasopharyngeal procedure have a tube inserted through their nose with the tip ending in the nasopharynx. Bypassing the nasal cavity offers the benefit of delivering CPAP farther away. In addition to straps to hold the mask in place, a CPAP machine also has a motor that blows air into the tube, an air filter to clean the air entering the nose, and a hose or tube that links the mask to the machine's motor[44].

Neonates and infants use bubble CPAP. Here, the pressure in the circuit is maintained by immersing the distal end of the expiratory tubing in water. The depth of the tubing in water determines the pressure (CPAP) generated. Blended and humidified oxygen is delivered via nasal prongs or nasal masks, and as the gas flows through the system, its 'bubbles' out of the expiratory tubing into the water, giving a characteristic sound. The pressures used are typically between 5 and 10 cm H_2O. It requires skilled nurses and respiratory therapists to maintain effective and safe use of the bubble CPAP system[44]. Continuous positive airway pressure (CPAP) is a standard therapy approach for OSA that has the potential to significantly reduce both fatal and nonfatal cardiovascular consequences. Oral appliances and surgical procedures are alternative treatments for those with more severe OSA who have CPAP sensitivity or mild symptoms, albeit there is less data on their effectiveness[45].

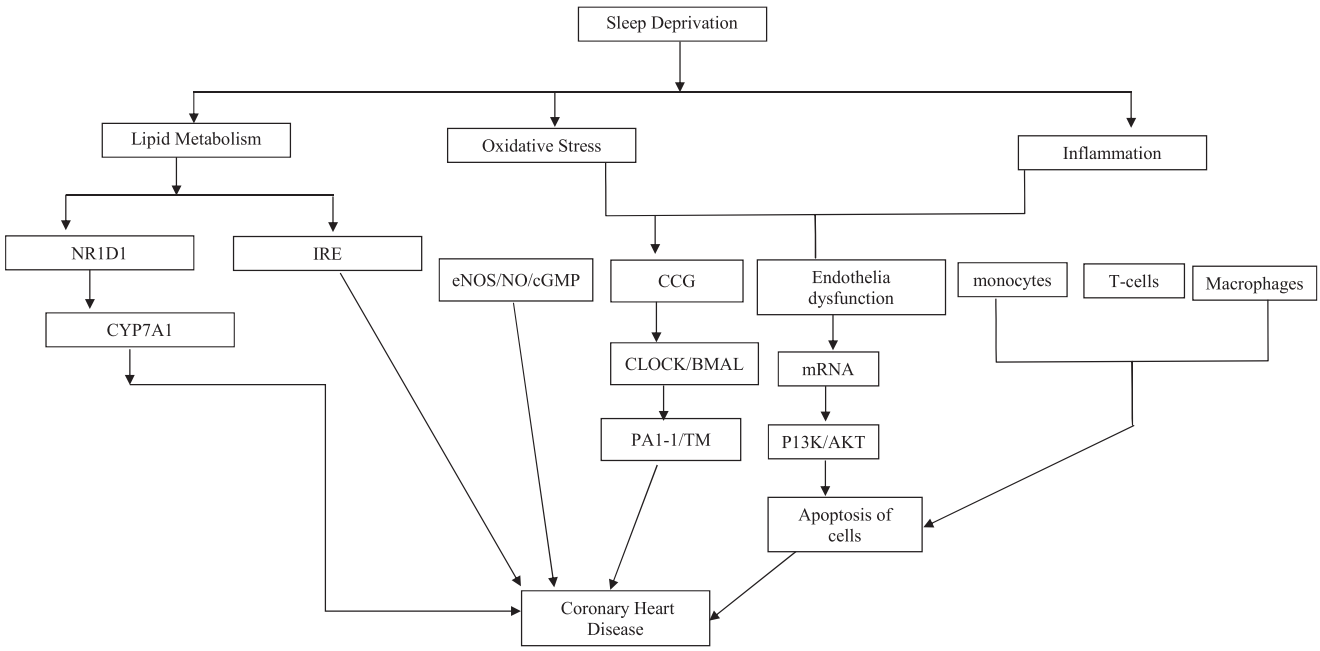

Figure 6. Sleep deprivation and pathogenesis of coronary heart disease.

Future research examining these pertinent outcomes is required, even though there is no proof that CPAP therapy enhances CV outcomes. Issues with CPAP adherence, bias, and the sample comprised in each randomised controlled trial may have diminished the reliability of the findings that indicate the benefit in all patients[45].

Pharmacological treatments targeting sleep disorders and cardiovascular health

Drugs that can be used to treat sleep disorders include benzodiazepines and benzodiazepine receptor agonists (BZDs), dual orexin receptor antagonists (DORAs), melatonin receptor agonists, and histamine antagonists. These medications are additionally effective to treat insomnia. Doxepin (which is marketed under the name Silenor), Daridorexant, Temazepam (marketed under the name Restoril), Eszopiclone (marketed under the name Lunesta), Ramelteon, Suvorexant, Triazolam, Trazodone, Estazolam, etc. are a few of the medications. Oral or intravenous administration of these medicines is available[46]. Several oral and intravenous methods are used to deliver benzodiazepines. As required by protocol and patient presentation, they can also be given intramuscularly, intranasal, and rectally. When administering benzodiazepines, it is possible to administer modest dosages of the drug until the desired effect—such as drowsiness, a halt to seizure activity, or anxiolysis—is realized. A CNS drug concentration sufficient to produce the desired effect with intravenous delivery, however, may take 3–5 min to reach. In order to prevent over sedation of the patient, sufficient time should be allowed between doses. Additionally, during the administration of benzodiazepines, clinicians must have easy access to resuscitation and airway management tools. As permitted by the emergency management service providers' training, airway management tools may include nasopharyngeal or oropharyngeal airways, bag valve masks, blind insertion airway devices, laryngeal mask airways, or endotracheal intubation[9]. Daridorexant is given orally, usually 2–3 times per day for 3–4 weeks to individuals with persistent insomnia. These drugs may cause withdrawal symptoms and anxiety as side effects. To avoid over sedating the patient, enough time should pass between dosages. Additionally, when administering benzodiazepines, clinicians must have quick access to tools for resuscitation and airway management. Depending on the emergency management service providers' training, airway management tools may include laryngeal mask airways, bag valve masks, blind insertion airway devices, nasopharyngeal or oropharyngeal airways, or endotracheal intubation[47]. Orally administered daridorexant is given to patients with chronic insomnia 2–3 times per day for roughly 3–4 weeks. These drugs might cause withdrawal symptoms and anxiety, which may have a major impact on blood pressure and have cardiovascular system consequences as well.

Therapies aimed at managing underlying cardiovascular risk factors

The management of underlying cardiovascular risk factors is accomplished by medication and lifestyle interventions. Exercise, dietary changes, and lifestyle modification are all parts of lifestyle therapy. Exercise has been found to promote cardiovascular health in patients and lower the risk of chronic cardiovascular disease consequences. It has also been demonstrated that changing lifestyle habits, such as giving up smoking and eating foods high in fiber and low in calories, can lower cardiovascular risks[4].

Future directions and implications

The focus of most sleep disorders studies was on the scope of apprehension of the causal and pathophysiological relationship

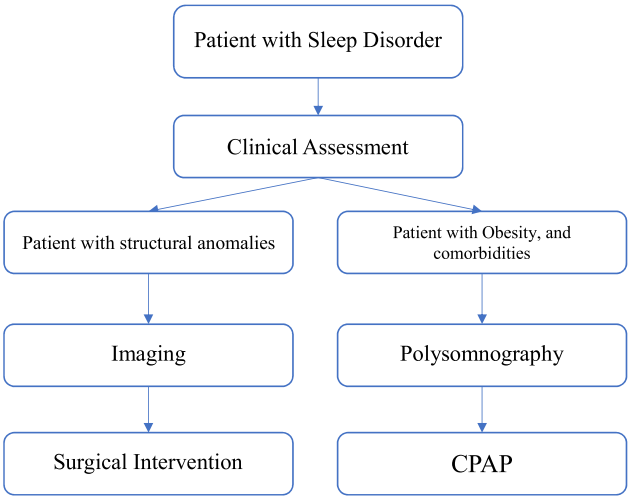

Figure 7. Application of personalized medicine in sleep disorders evaluation and management.

between morbidity and mortality. The literature highlighted possible mechanisms of increased cardiovascular risks with sleep disorders and deprivation. Sleep was considered as a cardiometabolic and cardio-mechanical modulator of the heart physiology which played an essential role. Thus, that explains the pathophysiology of OSA and different cardiovascular diseases, such as increased pulmonary arterial pressure, right ventricular failure, and different kinds of arrhythmias[48,49]. Additionally, cardiovascular disease and different sleep illnesses had two-way effects in predisposition to each other[50]. The efficacy of treatment and prevention of the emergence of critical cardiovascular disorders were points of interest to a different scope of studies, in which they tried to note different approaches to the management and prevention of sleep disorders and ultimately cardiac problems that could result from[51].

The plans and interventions for the management of sleep disorders are usually standard approaches that are supposed to fit all patients with sleep illness. However, different ethnicities, genetic predispositions, age groups, patients with comorbidities, and different severities should be considered during the diagnosis and treatment so every patient should be evaluated and the factors to be managed for each patient as a different entity[52] (Fig. 7).

Although sleep habits showed a crucial role in cardiac health and cardiac diseases, cardiologists usually have limited exposure to sleep disorders and sleep medicine. Therefore, it was necessary to develop a training program that allows the practice of sleep medicine and dealing with classes of sleep disorders in the cardiology field. The American Academy of Sleep Medicine developed such a program for eligible cardiologists. Which can be reflected on more fruitful cooperation and early management and prevention[52].

Limitations

There are a number of restrictions on the research that links sleep to cardiovascular disease. Above all, most research has been done using a single measurement time point. To analyze the effects of exposure and trajectories, longitudinal sleep testing is required, particularly considering the lengthy time course of cardiovascular pathology. For instance, well-controlled opportunities exist to model the acute effects of sleep deprivation on subclinical illnesses through laboratory-based studies involving sleep restriction lasting 3–14 days[4]. However, these studies are unable to model the long-term impact of chronically short periods of sleep on clinical cardiovascular events. Increasing exposure to sleep disturbances, such as persistent insomnia either by itself or in conjunction with short sleep duration, has been linked to clinical illness, according to observational studies[4]. Sleep extension paradigms offer a means of investigating the enduring consequences of brief sleep exposure; yet, prior treatments have also been short-lived (e.g. 2 weeks) and have involved restricted physiological evaluations[4].

Conclusion

The spectrum of sleep disorders encompasses different classes of illnesses that are classified according to the clinical presentation and severity, which ranges from simple habits to chronic and disabling disorders. Some sleeping disorders, especially sleep-related breathing disorders, have direct and indirect linkage with cardiovascular diseases risks. Some studies showed the presence of significant increase in pressure and heart parameters and risk of heart disease in patients with sleep illnesses or sleep deprivation. For secondary prevention as well as primary cardiovascular protection in the general population, good sleep hygiene, and the right amount of sleep should be encouraged. It has been demonstrated that chronotherapeutic methods work. The better efficiency of certain medications is specifically related to the timing of the medication in relation to the circadian fluctuations of physiologic variables and the pharmacokinetic and pharmacodynamic properties of the drug. However, the majority of the data available now concentrate on the short-term effects on BP, while there is little information available on the long-term prognostic influence of such techniques. Supplementing with dietary melatonin has been linked to beneficial cardiometabolic alterations, such as an enhanced lipid profile and the metabolism of glucose.

However, more studies on the subject should be conducted to identify possible pathological processes and associations. More observational studies should highlight the validity of early diagnostic markers to enrich clinical practice and improve the preventive measure.

Ethical approval

Ethics approval was not required for this article.

Consent

Informed consent was not required for this article.

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Author contribution

All authors approved the final manuscript, conceptualization of ideas, critical reviews with comments, and final draft.

Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

Research registration unique identifying number (UIN)

1. Name of the registry: not applicable.
2. Unique identifying number or registration ID: not applicable.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): not applicable.

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Data availability statement

Not applicable.

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