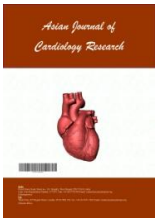

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Sleep and its Relationship with Cardiovascular Diseases

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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ABSTRACT

Cardiovascular diseases are the leading cause of global morbidity and mortality. Besides imparting enormous human suffering, they inflict huge direct and indirect financial costs on the worldwide society. With the ready availability of affordable therapeutics globally, and the relative slowdown in the introduction of newer modalities, lifestyle interventions are gaining importance to further control this epidemic. Sleep is one such modifiable lifestyle factor. Improper sleep is consistently and strongly related with a higher risk of cardiovascular disease incidence and mortality. Therefore, maintenance of a good sleep regimen and treatment of sleep related disorders has become an important goal in the quest for further improving global cardiovascular health. This paper briefly reviews the effects of sleep on cardiovascular diseases.

Keywords: Cardiovascular diseases; global morbidity; mortality; sleep.

1. INTRODUCTION

Restorative sleep is necessary for good health and well-being [1]. Healthy sleep is based on several dimensions – a sleep duration between 7-9 hours per day, falling asleep easily and staying asleep without interruption, waking up feeling refreshed and staying awake during the day [2]. Sleep disorders are common all over the world [3,4]. Insomnia and reduced sleep duration

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are pervasive. Disruptive sleep and sleep disorders are also widespread [5].

Sleep disorders include insomnia, hypersomnolence, parasomnias, sleep related movement disorders and circadian rhythm sleep-wake disorders [6]. Sleep-related breathing disorders or sleep-disordered breathing are characterized by abnormal respiration during sleep [7].

Several studies have reported an association between the duration of sleep (<7 or >9 hours) and several chronic conditions [8-10]. Sleep disorders decrease the quality of life in these patients [11]. Sleep disorders also increase mortality [12-14]. Two meta-analytic studies have estimated a 10% to 12% increased risk of mortality for short sleep duration and a 30% to 38% increased risk of mortality for long sleep duration [13,14].

Sleep-health relationship is often bidirectional. Chronic illnesses and hospitalization are common causes of disease induced sleep disorders [15]. Most chronic illnesses, such as asthma, cancer, depression, epilepsy, kidney disease and sickle cell disease, impact restorative sleep in a negative way [16]. Hospitalization, especially the intensive care units are notorious for inducing disturbed sleep [17]. Sleep defects may persist in critically ill patients up to 12 months after hospital discharge [18].

Chronic sleep deprivation is a major financial burden on the society with costs expected to reach between $318 to $456 billion in 2030, in the US alone [19].

2. DISCUSSION

Cardiovascular diseases (CVD) include coronary artery disease (CAD)/coronary heart disease (CHD) high blood pressure (HTN), stroke, heart failure (HF), cardiac arrhythmias (including atrial fibrillation (AF) and sudden cardiac death (SCD)), peripheral artery disease (PAD), deep vein thrombosis (DVT) and vasculogenic erectile dysfunction (ED) [20,21]. CVDs impart the greatest non-communicable diseases burden in the world [22]. They account for almost 18 million deaths annually [23]. These deaths represent 31% of the total global mortality (23) making CVDs the leading cause of worldwide mortality [24]. CVDs are also a leading cause of loss of disability-adjusted life years (DALYS) globally [25]. CVD imparts considerable loss of productivity and health care spending, which results in a huge financial burden on all societies [26].

Sleep, which is a basic human behavior, if non-restorative, is reported to be associated with the risk of cardiovascular disease and poor CVD outcomes [27-29]. The data on the relationship between both short and long sleep durations and poor cardiovascular health is persuasive [30]. A growing number of studies have demonstrated that short sleep duration increases the risk of cardiovascular disease, even after adjustment for potential confounders [31]. A few studies have also shown that poor sleep quality is also harmful for the cardiovascular system [32]. Disturbed sleep is reported by up to 70% of patients with heart disease [33]. Several disorders of breathing associated with sleep also impart a higher cardiovascular risk [34]. Obstructive sleep apnea (OSA) can lead to several CVDs and cause premature cardiovascular mortality [35-37]. Data also indicates that impaired sleep may also affect prognosis in CVD patients [38]. CVDs can themselves disrupt sleep [39]. The sleep-CVD relationship is therefore often bi-directional.

Although the pathogenesis of poor sleep and CVD is not fully understood, there are multiple mechanisms underlying this relationship, including dysregulation of the hypothalamic-pituitary axis, abnormal modulation of the autonomic nervous system with increased sympathetic nervous system activity, systemic inflammation, and enhanced atherogenesis [40-43].

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2.1 Sleep and HTN

HTN is an independent predisposing factor for several other CVDs including CAD, stroke, HF, AF, PAD, and chronic kidney disease (CKD) [44]. Hypertension is a major modifiable cause of death worldwide [45].

HTN is more common in patient with insomnia, when compared to those without insomnia [46]. Vgontzas and colleagues found five-fold higher odds for hypertension in insomniacs sleeping <5 hours than in normal sleepers [47]. It is estimated that for each hour of decrease in sleep, there is a 37% increase in the risk of developing HTN [48]. Even long sleep duration detrimentally affects the blood pressure (BP) (49). Overall, the sleep hypertension relationship appears to be U-

shaped [48,49]. Abnormal sleep duration attenuates the normal nocturnal dipping in BP [50]. Sleep deficiency also increases mortality and shorter the sleep duration, higher the risk of mortality [51].

Several studies indicate that besides insomnia and short or long sleep duration, poor sleep quality, is also associated with a higher risk of HTN [52]. Obstructive sleep apnea (OSA), restless legs syndrome, and shift work have all been linked with an increased risk of HTN [53-55].

2.2 Sleep and Coronary Heart Disease

CHD is the leading cause of disability and death in the world [56]. The underlying pathology is usually arterial atherosclerosis [57].

Epidemiological studies indicate that abnormal sleep duration is a risk factor for CHD [58-60]. This risk is U-shaped [59,61-63]. In the Behavioral Risk Factor Surveillance System survey, both ≤6 hours/night or ≥10 hours/night of sleep was associated with a higher prevalence of CHD, when compared to a reference group sleeping 7 to 9 hours [59]. In the Finnish population, sleep lengths of < 6 hours/night and >9 hours/night were associated with a higher history of myocardial infarction [61]. Compared to 7–8 hours of sleep per night, self-reported sleep of <5 hours or >10 hours, was associated with a 25% and a 43% respectively, raised risk for CHD in the Women's Health Initiative Study [62]. In another study, risk of CHD, at the end of a 10-year follow-up was 1.39-fold higher in women reporting <5 hours/night and 1.37-fold higher in those sleeping >9 hours compared to those sleeping 8 hours/night [63].

Sleep is also associated with mortality [64]. In a study by Cappuccio and group, fatal CHD risk was greater with a habitual sleep duration above or below 7 to 8 hours [65]. Similar U-shaped associations were seen in women in Singapore [63]. Life expectancy is better for individuals reporting sleeping between 7-8 hours per night on a regular basis [65].

2.3 Sleep and Stroke

Stroke is a major cardiovascular disease that strikes a new patient every 2 seconds in the world [66]. It is one of the leading causes of long-term disability and is responsible for 16.4% of all cardiovascular deaths [67,68].

Both short and long sleep duration increase the risk for stroke, indicating a U-shaped relationship between the two [69]. Sleep apnea increases the risk of AF, a major risk factor for stroke [70].

2.4 Sleep and Heart Failure

Heart failure is a leading cause of global morbidity and mortality [71]. Its prevalence continues to increase [72]. HF is a serious disease requiring frequent hospitalizations - 25% of patients are re-hospitalized within 30 days, and 50% are re-hospitalized within six months [73]. Survival remains poor [74].

Sleep disorders are associated with HF [75]. Insomnia increases the risk of incident heart failure [76]. Self-reported short sleep (<6 hours) in men with CVD increases the risk of developing HF [77]. Day time sleepiness or daytime napping of longer than 1 hour is also associated with greater risk of HF [78]. Levels of the established marker for HF, N-terminal pro-brain natriuretic peptide are increased in patients with sleep disturbances [79].

However, HF also increases sleep disturbances [80]. Individuals with HF often experience excessive sleepiness during the daytime [80]. Almost 63% of HF patients also report poor sleep quality [81]. HF is associated with elevated anxiety, depression and these contribute to the insomnia [82]. They may also have Cheyne-Stokes breathing and some HF medications may also interfere with sleep [83]. Poor sleep efficiency in HF patients predicts higher mortality [84].

2.5 Sleep and Arrhythmias

Cardiac arrhythmia is defined as any change from the normal sequence of electrical impulses [85]. Arrhythmias often lead to complications, such as heart failure, stroke, or cardiac arrest [86].

Sleep disorders and AF are bidirectionally linked [87-92]. In two major studies, short self-reported sleep was associated with a 6% to 7% higher risk of incident AF [87,88]. It is estimated that each 1-h reduction in sleep duration results in a 17% greater risk of prevalent AF and 9% greater risk of incident AF [89]. Sleep disruption cause alterations in sympathetic tone, and this may be responsible for the increased risk factor for AF in these patients [90]. OSA is also associated with

an increase risk of incident AF [91]. AF affects sleep quality in almost 50% of the patients [92]. Most of these patients experience a shorter sleep duration [93]. Sleep disturbed breathing has been noted in young patients with both paroxysmal and persistent AF with normal LV function [94].

OSA is associated with increased rates of ventricular tachyarrhythmia [95]. Ventricular arrhythmias are responsible for almost 80% of SCD [96]. SCD is higher in patients with OSA [97].

2.6 Congenital Heart Disease

The prevalence of congenital heart disease (CoHD) in the United States is estimated to be 8 in 1,000 live births [98]. Improved techniques in the treatment of CoHD have markedly increased the survival rate [99]. It is estimated that in the United States, 1 in 150 adults are born with some kind of CoHD [100]. In 2012, US had an estimated 1.5 million adult survivors of CoHD, and this number is expected to continue to increase [101].

Several studies support that poor sleep may have negative effects on the fetus and may result in growth restriction and decreased gestational length [102]. Poor maternal sleep if present on >4 days per week, compared to <1 day per week is also associated with an increase in neural tube defects [103]. Maternal sleep disorders also increase the risk of CoHD [104]. Short sleep duration and/or poor sleep quality during the peri-conceptional period is an independent risk factor for CoHD [104]. Adult patients with CoHD also have a high prevalence of sleep apnea [105].

2.7 Sleep and Heart Transplant

Heart transplantation is now an established therapy for end-stage heart failure [106]. Heart transplantation improves the prognosis of patients with HF and improves their quality of life [107].

Heart transplant patients do not sleep well [108,109]. Pediatric transplant patients often have sleep-disordered breathing and require a longer peri-transplant respiratory support and have a longer length of hospital stay [109]. Adolescent transplant recipients also report poor sleep quality compared with healthy peers [108]. Overall, sleep disturbances post-transplantation further decreases the already low QOL in these patients [110].

2.8 Sleep and Peripheral Artery Disease

PAD is an atherosclerotic vascular disease and is associated with a significant morbidity and mortality [111-113]. Its prevalence increases with advancing age [114]. PAD patients may experience ischemic rest pain, exertional claudication, leg ulcerations, frequent hospitalizations, revascularization procedures and amputation surgery [115]. These patients also have a greater likelihood of sustaining getting major CVD events (myocardial infarction or stroke) compared to patients without PAD [116]. It imparts a significant decrease in the quality of life [117].

Both short and long duration of sleep is associated with PAD. In the MESA (Please mention full out) study, there was a 2-fold higher prevalence of PAD in individuals when compared with those who slept 7 h/night [118]. Sleep disordered breathing is also associated with an increased risk of developing clinical PAD [119,120]. OSA promotes the development of arterial atherosclerosis in the entire vascular system, including the pelvic and leg arteries [120].

2.9 Sleep and Erectile Dysfunction

ED is characterized by a persistent inability to attain and/or maintain an erection sufficient for sexual performance [121]. Several causes have been implicated, including increasing age, side effects of medical treatment, and emotional disorders [122]. Atherosclerosis of the pelvic and penile vasculature is often an underlying cause [123]. Sleep-related involuntary erection occurs normally during REM (rapid eye movement, please mention full out) sleep [124].

Most cases of sleep disturbances and associated ED have been attributed to low testosterone levels induced by the former [125]. Patients with insomnia and fragmented sleep may experience sexual dysfunction [126,127]. This is also seen in non-standard shift workers [128]. OSA is strongly linked with ED and besides a decrease in testosterone levels, peripheral neuropathy due to hypoxemia, or vascular endothelial dysfunction have also been implicated in these patients [129,130]. CPAP (continuous positive airway pressure, please mention full out)therapy has beneficial effects in these patients [131]. Other

sleep disorders connected with ED include restless leg syndrome, periodic limb movements during sleep, narcolepsy, and nocturia [132135].

2.10 Sleep and Venous Disease

Venous thromboembolism (VTE) is a common cardiovascular disease [136]. Venous thrombosis in the legs may result in pulmonary embolism [137]. Pulmonary embolism is a serious and often fatal disease [138].

In a population-based study by Lippie et al., patients with OSA exhibit a higher risk of DVT and PE [139]. OSA may increase coagulability via elevated platelet activity, fibrinogen levels, and platelet aggregation and this causes an increase in VTE rate and recurrence [140]. Other sleep disorders are also known to be associated with chronic venous insufficiency of the legs [141].

2.11 Sleep and CVD Risk Factors

Sleep disorders are also associated with many other CVD risk factors, such as DM, obesity, depression, metabolic abnormalities, and CKD [142-146]. Poor lifestyle and behavior are believed to be the leading causes of cardiovascular disease, and individuals experiencing poor sleep often have poorer adherence to recommended lifestyle behaviors [147-149].

3. CONCLUSION

Poor sleep health is highly prevalent in the world. Abnormal sleep duration and quality is associated with significant morbidity and mortality. Adverse outcomes include weight gain and obesity, diabetes, accidents and injuries, increased pain, neurocognitive dysfunction, psychiatric problems, and premature mortality. Sleep problems also increase the risk for several cardiovascular diseases. Sleep hygiene is a modifiable, and sleep disorders respond to treatment with several ancillary clinical benefits. Good restorative sleep between 7 – 8 hours is important for protecting the cardiovascular system.

CONSENT

It's not applicable.

ETHICAL APPROVAL

It's not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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