Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/ihj

Sleep-disordered breathing and cardiovascular disease

Stefan D. Anker [a,*], Stephan von Haehling [a], Robin Germany [b]

[a] Innovative Clinical Trials, University Medical Centre Göttingen, Göttingen, Germany
[b] University of Oklahoma, Oklahoma City, OK, USA

ARTICLE INFO

Article history:
Received 8 October 2015
Accepted 5 November 2015
Available online 10 December 2015

Keywords:
Sleep-disordered breathing
Obstructive sleep apnea
Central sleep apnea
Review

ABSTRACT

Sleep-disordered breathing (SDB) is a common comorbidity in a number of cardiovascular diseases, and mounting clinical evidence demonstrates that it has important implications in the long-term outcomes of patients with cardiovascular disease (CVD). While recognition among clinicians of the role of SDB in CVD is increasing, it too often remains neglected in the routine care of patients with CVD, and therefore remains widely undiagnosed and untreated. In this article, we provide an overview of SDB and its relationship to CVD, with the goal of helping cardiovascular clinicians better recognize and treat this important comorbidity in their patients. We will describe the two major types of SDB and discuss the pathophysiologic, diagnostic, and therapeutic considerations of SDB in patients with CVD.

1. Introduction

Worldwide, the incidence of cardiovascular disease (CVD) continues to increase, and despite ongoing therapeutic advances, it continues to be associated with high rates of morbidity, hospitalization, and mortality.[1,2] In India alone, CVD is responsible for an estimated 20% of the nation's total annual deaths—a number that is likely to climb as the nation's rapid economic development and changing lifestyles fuel known risk factors for CVD, such as obesity, diabetes, dyslipidemia, and hypertension.[3,4]

The onward march of CVD throughout the world clearly illustrates the need for new and innovative management strategies to further improve patient outcomes. One area under active investigation is the treatment of sleep-disordered breathing (SDB), which is now recognized as a common comorbidity in a number of CVDs. Mounting clinical evidence suggests that the presence of SDB may have important implications on the long-term outcomes of patients with CVD.

In this article, we provide an overview of SDB and its relationship to CVD, with the goal of helping cardiovascular clinicians better recognize and treat this important comorbidity in their patients. Below, we describe the two major types of SDB and discuss the pathophysiologic, diagnostic, and therapeutic considerations of SDB in patients with CVD.

2. Definitions

SDB is characterized by cycles of significant pauses in breathing followed by hypoxia and partial neurological arousals that disrupt sleep. An expanding body of research shows that repeated episodes of apnea, hypoxia, and arousal from sleep are associated with a number of pathophysiological effects that have important clinical consequences, including

* Corresponding author.
E-mail address: s.anker@cachexia.de (S.D. Anker).
http://dx.doi.org/10.1016/j.ihj.2015.11.018

abnormal lipid and glucose metabolism, hypertension, stroke, and CVD.[5]

Terms commonly used to describe the abnormal breathing patterns associated with SDB include: apnea, the complete absence of breathing (≥10 s); hypopnea, an abnormally slow or especially shallow breathing; and hyperpnea, an abnormally rapid or deep breathing. The apnea-hypopnea index (AHI) is a commonly used clinical index that describes the severity of SDB. The AHI is defined as the average number of apnea and/or hypopnea episodes that occur during sleep expressed in events per hour. SDB severity is commonly defined as mild with an AHI ≥5 and <15, moderate with an AHI ≥15 and ≤30, or severe with an AHI >30.

3. Types, prevalence, and pathophysiology

SDB is classified into two types: obstructive sleep apnea (OSA) and central sleep apnea (CSA). Although it is not uncommon to see a mixture of both types in a patient with CVD (especially in patients with heart failure), one type usually predominates throughout the sleep period. OSA is caused by partial or complete upper airway collapse and obstruction during sleep. Each episode of airway obstruction is associated with decreased or absent air entry into the lungs and subsequent hypoxia despite ongoing respiratory effort. Airway obstruction is eventually terminated by an arousal from sleep. OSA is a relatively common sleep disorder worldwide, occurring in an estimated 3–8% of men and 1–5% of women.[6] Although research into the prevalence of OSA in the Indian population is limited, one study found that 7.5% of middle-aged urban Indian men may have OSA.[7] In otherwise healthy individuals, the presence of OSA is recognized as an important risk factor for the development of a number of CVDs, including hypertension,[8,9] coronary artery disease,[10,11] and stroke.[12,13] OSA is also a common comorbidity in patients with established CVD, occurring in an estimated 30% of hypertensive patients,[14,15] 35% of heart failure patients,[16,17] and 30% of coronary artery disease patients.[10,18] In these individuals, OSA has been found to be an independent risk factor for the progression of CVD and adverse outcomes.[5] In patients with heart failure, co-morbidities play an important role in the progression of cardiac dysfunction and overall patient status,[19–21] and OSA, together with CSA, appear to be one of most prevalent co-morbidities in these patients.

CSA is characterized by the temporary withdrawal of central neurological respiratory drive, resulting in the cessation of respiratory effort and airflow. Whereas OSA is common in the general population and is a comorbidity in a number of CVDs, CSA is more uniquely seen in patients with heart failure or following stroke.[5] In these patients, CSA is typically accompanied by Cheyne-Stokes respiration. CSA with Cheyne-Stokes respiration is recognized by the simultaneous absence of air flow and respiratory effort (central apnea or hypopnea) followed by characteristic hyperventilation in a crescendo-decrescendo pattern. CSA in patients with heart failure has been particularly well-studied. Because of its unique relationship to heart failure and recent developments in this area, our discussion of CSA will be limited to its presence in heart failure. CSA is highly prevalent in heart failure, occurring in about 35% of cases.[16,22] Studies suggest that CSA is an independent risk factor for cardiac transplantation and death in patients with heart failure.[23,24]

Underlying the development of CSA in heart failure is respiratory control system instability due to oscillation of the arterial blood carbon dioxide level ($PaCO_2$) above and below the central threshold of ventilation termed the apneic threshold.[25] A number of factors contribute to respiratory control system instability and predispose heart failure patients to fluctuations in $PaCO_2$, including lung congestion-related J-receptor activation, hypersensitive central and peripheral carbon dioxide chemoreceptor gain, hypoxia-related arousals, as well as reduced cardiac output leading to prolonged circulation time.[26] When the $PaCO_2$ is periodically driven below the apneic threshold by an episode of hyperpnea—such as that which occurs with hyperventilation during arousal or changes in sleep stage—central neural outflow to the respiratory muscles is temporarily suppressed and central apnea ensues.[25,26]

Despite differing mechanisms underlying the development of OSA and CSA, both disorders are characterized by repeated, prolonged apneas that result in hypoxia and partial neurological arousals that significantly disrupt sleep. These repeated episodes of apnea, hypoxia, and arousal trigger a number of neurohormonal, hemodynamic, metabolic, thrombotic, and inflammatory mechanisms that place patients with SDB at significantly greater risk for hypertension, myocardial ischemia, arrhythmias, and ventricular dysfunction (Fig. 1). Together, these effects ultimately contribute to the increased morbidity and mortality seen in patients with SDB.[5,26,27]

4. Risk factors and clinical presentation

Risk factors associated with the development of OSA include obesity, male gender, advancing age, genetic predisposition to OSA, smoking and alcohol consumption, and craniofacial/pharyngeal anatomical anomalies.[6] Obesity is a major risk factor in part because obese individuals often have pharyngeal fatty deposits that contribute to pharyngeal obstruction. Pharyngeal anatomical anomalies are another major risk factor because they reduce the size of the posterior airway, which increases the chance of obstruction during sleep. The classic signs and symptoms of OSA are loud snoring, disrupted sleep, and daytime drowsiness. Other symptoms may include nocturnal gasping, restless legs, morning headaches, mood changes, and trouble concentrating.[5,27] On clinical examination, patients with OSA are typically middle-aged, overweight, and/or may have craniofacial or pharyngeal features (e.g., presence of redundant pharyngeal tissue, elongated soft palate, enlarged uvula, and/or small or receding jaw) that contribute to upper airway obstruction.[5,27] Additionally, they often have elevated daytime systolic blood pressure.[5] In this regard, it should be noted that many patients with drug-resistant hypertension have undiagnosed OSA; thus, clinicians should maintain a high level of suspicion of OSA when encountering these patients.[5]

Risk factors for CSA are closely associated with those of heart failure, and include male gender, higher New York Heart Association class, lower left ventricular ejection fraction, waking hypocapnia, presence of atrial fibrillation, higher brain natriuretic peptide (BNP) levels, and frequent nocturnal