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Review

Relationship between central sleep apnea and Cheyne—Stokes Respiration

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ABSTRACT

Central sleep apnea (CSA) in patients with heart failure (HF) occurs frequently and shows a serious influence on prognosis in this population. The key elements in the pathophysiology of CSA are respiratory instability with chronic hyperventilation, changes of arterial carbon dioxide pressure (pCO_2) and elongated circulation time. The main manifestation of CSA in patients with HF is Cheyne–Stokes Respiration (CSR). The initial treatment is the optimization of HF therapy. However, many other options of the therapeutic management have been studied, particularly those based on positive airway pressure methods. In patients with heart failure we often can observe the overlap of CSA and CSR; we will discuss the differences between these forms of breathing disorders during sleep. We will also discuss when CSA and CSR occur independently of each other and the importance of CSR occurring during the daytime in context of CSA during the nighttime.

Contents

1. Introduction and definitions

Central sleep apnea is a relatively wide term, which includes sleep pathologies regardless of main etiology (Table 1). These various disorders differ in a key pathophysiological point and that is the baseline arterial carbon dioxide level [1,2]. The core issue in our discussion for this article is patients with HF and CSA, particularly with Cheyne–Stokes Respiration (CSR). This article will focus on the following problems: main differences and similarities between CSR and CSA; when they mean the same and when they are independent phenomena; and the relevance of central sleeping disorders during day and night.

According to the definition, apnea is defined when the following conditions are met: registration of 90% or more drop in airflow signal, lasting at least 10 s. A central apnea is characterized when respiratory effort is absent [3,4]. Hypopnea is defined (preferably) as the reduction in airflow amplitude by 30% or more with time duration ≥10s and the accompanying saturation drop by ≥3% or with an arousal. Alternatively a 50% drop in amplitude may be used as the cutoff point [3,4].

Cheyne–Stokes Respiration is the special pattern of breathing disorders with cyclic returning periods of hyperventilation in "crescendo–decrescendo" manner of tidal volume changes alternately with central apnea/hypopnea events (Fig. 1). For recognition, a minimum of 3 consecutive cycles with the aforementioned breathing pattern and with accompanying AHI at least 5/hour (h) with a monitoring period of at least 2 h [3,4]. The recommended definition of cycle length in CSR is the time from the beginning of central apnea event to the end of the following "crescendo–decrescendo" respiratory period. In the case of a central hypopnea associated with hyperventilation events, the cycle length may be estimated as the distance between peaks of adjoining hyperventilation phases. Cycle lengths for CSR are usually at least 40s [3,4].

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Table 1
Type of CSA (according to 1, 2, 4).

Hypercapnic CSA		Nonhypercapnic CSA
Disorders on central breathing control level	Disorders on axis between motor neurons and respiratory muscles	Cheyne–Stokes Respiration (CSR)
Central apnea inducted by narcotic drugs	Neuromuscular diseases: amyotrophic lateral sclerosis, myopathies, myasthenia gravis	Idiopathic central apnea
Ondine's curse (CCHS—congenital central hypoventilation syndrome		Complex apnea
Obesity hypoventilation syndrome (OHS)		High altitude sleep apnea

CSA and CSR are closely related but they are not equal. CSA is a broader term, which can be correlated either with hypercapnic or hypocapnic respiratory disorders, whereas CSR is a specific type of CSA with a typical oscillatory pattern of ventilation. Moreover, CSR can occur not only during sleep but also in course of a daily activity (at rest as well as during exercise). When it occurs during wakefulness, only the term CSR should be used and not CSA [3–5]. Additionally, CSR is often equated with periodic breathing (PB). Some opinions recommend the use of CSR when apnea or hypopnea is accompanied with hyperventilation and PB when only hypopneas exist between two "crescendo–decrescendo" respiratory periods [6].

In patients with heart failure, sleep-disordered breathing (including CSA) is a very common comorbidity. CSA can occur without breathing fluctuations characteristic for Cheyne–Stokes Respiration model (Fig. 2). However patients with HF present mostly CSA with CSR (Fig. 1), which has respiratory instability as a crucial pathomechanism, so these two terms are often used interchangeably in the HF population. There is even a special term CSA–CSR which has been used to name syndrome of breathing disorders specific for patients with HF [5]. In short, CSR in which every hyperventilation is associated with an apnea and presents "crescendo–decrescendo" pattern, may be referred to as CSA–CSR. Otherwise CSR (CSR with hypopnea, not apnea) and CSA should be treated as separate terms.

2. Pathophysiology

The essential axis for the pathogenesis of CSA–CSR is apnea threshold and pCO_2 fluctuations around it with respiratory control system instability in the background. Control of breathing is maintained by a negative feedback loop. Crucial elements here are: controller gain, which is understood as chemosensitivity at the central and peripheral chemoreceptor level; effector mechanism (respiratory muscles, lung, chest wall) which is responsible for correct ventilation response to signals from controller and determines efficiency of gas tension changes in blood; and finally, pinning the pathology together is an appropriate transmission of information about pO_2 and pCO_2 changes to chemoreceptors [6–9].

A naturally weak point in the breathing control system which predisposes to respiratory instability is the moment of transition from wakefulness, when respiration is mainly under behavioral control, to sleep (particularly NREM 1 and 2 stages) when abovementioned neural drive is substantially reduced and breathing is strictly dependent on metabolic stimulants [6–9].

Pinna et al. validated the correlation between the transition state (wakefulness–NREM–wakefulness) and alternating phases of central apnea and hyperventilation in CSR model. Ninety two percent of central apneas occurred at the same time as recorded wakefulness to NREM transition. Also, the ventilatory response was observed in relation with simultaneous transition to a wakefulness state, which was associated with increased values of tidal volume and minute ventilation (respectively 3× and 2×) [10].

In normal conditions after falling asleep, the apnea threshold (minimal pCO_2 level which is necessary to activate respiration) rises in

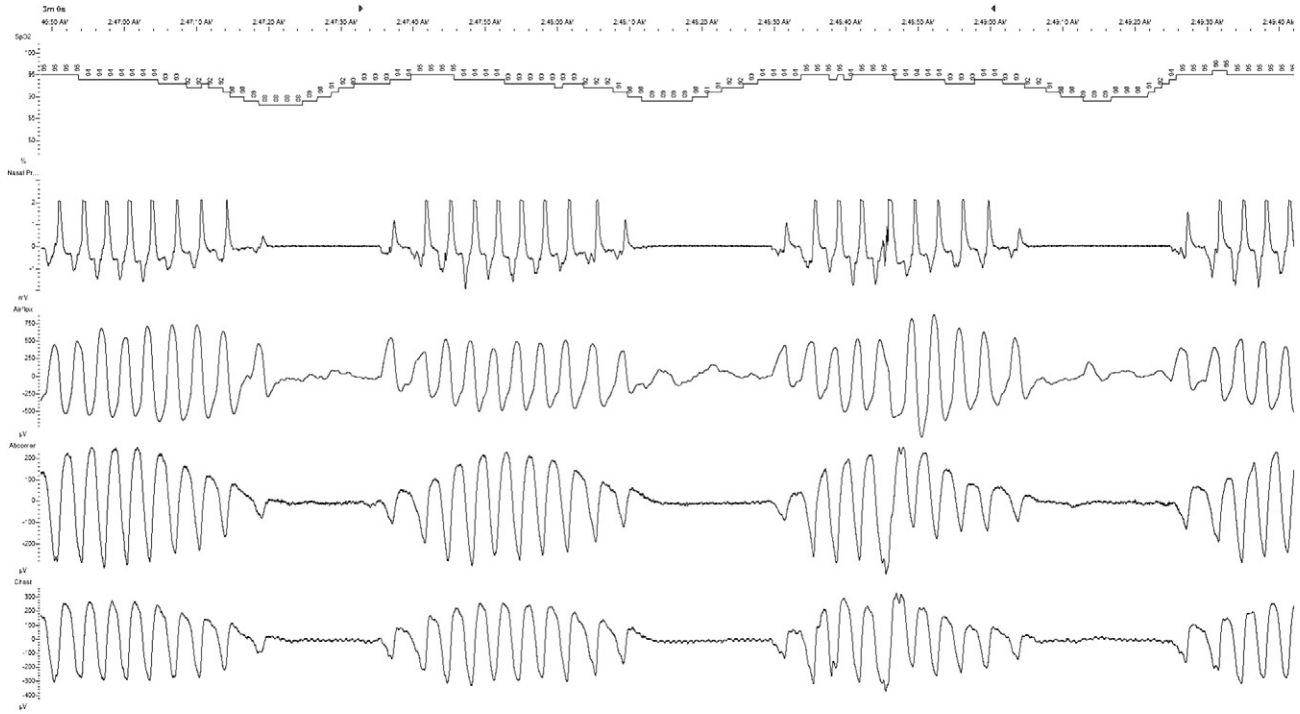

Fig. 1. CSR–CSA.