REVIEW

Identifying Predictors of Central Sleep Apnea/Cheyne-Stokes Breathing in Chronic Heart Failure: a Pathophysiological Approach

Aneliya I. Draganova, Kiril V. Terziyski, Stefan S. Kostianev

Department of Pathophysiology, Faculty of Medicine, Medical University of Plovdiv, Plovdiv, Bulgaria

Correspondence:

Aneliya I. Draganova, Department of Pathophysiology, Faculty of Medicine, Medical University of Plovdiv, 15a Vassil Aprilov Blvd., 4002 Plovdiv, Bulgaria

E-mail:

adraganova@pathophysiology.info

Tel: +359 884 213 500

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Chronic heart failure (CHF) is a major health problem associated with increased mortality, despite modern treatment options. Central sleep apnea (CSA)/Cheyne-Stokes breathing (CSB) is a common and yet largely under-diagnosed co-morbidity, adding significantly to the poor prognosis in CHF because of a number of acute and chronic effects, including intermittent hypoxia, sympathetic overactivation, disturbed sleep architecture and impaired physical tolerance. It is characterized by repetitive periods of crescendo-decrescendo ventilatory pattern, alternating with central apneas and hypopneas. The pathogenesis of CSA/CSB is based on the concept of loop gain, comprising three major components: controller gain, plant gain and feedback gain. Laboratory polysomnography, being the golden standard for diagnosing sleep-disordered breathing (SDB) at present, is a costly and highly specialized procedure unable to meet the vast diagnostic demand. Unlike obstructive sleep apnea, CSA/CSB has a low clinical profile. Therefore, a reliable predictive system is needed for identifying CHF patients who are most likely to suffer from CSA/CSB, optimizing polysomnography use. The candidate predictors should be standardized, easily accessible and low-priced in order to be applied in daily medical routine.

The present review focuses on a pathophysiological approach to the selection of some predictors based on parameters reflecting the etiology, the pathogenesis and the consequences of CSA/CSB in CHF.

INTRODUCTION

Chronic heart failure (CHF) is a major health problem, associated with increased mortality in all age groups and especially among the elderly people (over 65 years) despite modern treatment.¹ It is increasingly prevalent, affecting 1-2% of the population in the developed countries.² Its clinical course and prognosis depend on the presence of various concomitant diseases and conditions, therefore, their proper identification and subsequent treatment are of primary importance.³

Among the most significant conditions accelerating the progression of CHF is the sleep-disordered breathing (SDB). It presents as repetitive episodes of a cessation (apnea) or a partial decrease (hypopnea) of the airflow, accompanied by desaturations and disturbed sleep architecture. Central sleep apnea (CSA) usually develops as a result of an instabil-

ity in the breathing control system, manifesting with an absence of respiratory effort during the apneic phase. Cheyne-Stokes breathing (CSB) is a form of periodic breathing in which periods of crescendo-decrescendo ventilatory pattern alternate with central apneas and hypopneas, often referred to as CSA/CSB.

A review of the studies on SDB in CHF shows a high prevalence of sleep apnea among this population. Moreover, CSA/CSB was detected in 30-50% of the patients, while obstructive sleep apnea (OSA) – in 20-40%.⁴ The great variability in the prevalence, the type and the severity of the SDB among the CHF population could be attributed to several factors. The focus of attention should be directed to the significant methodological differences, the lack of universal diagnostic criteria, the heterogeneity in the patients' characteristics, including different types of

heart failure – with preserved or reduced ejection fraction, and the diversity in the therapy (**Table 1**).

The matter is further complicated by the possibility that a single patient may present with predominantly one type, both types of sleep apnea (OSA and CSA), or even a shift between them within a single night.^{6,16} Furthermore, elements of the Cheyne-Stokes breathing pattern with waxing and waning ventilation can be observed even during obstructive events. Accordingly, Tkacova et al. hypothesize that both central and obstructive events are a part of a vicious cycle, including cardio-vascular, pulmonary and autonomic nervous mechanisms, adding to the progressive heart function decline.¹⁶

PATHOGENESIS OF THE CHEYNE-STOKES RESPIRATION ACCORDING TO THE LOOP GAIN THEORY

According to the chemoreflex instability hypothesis CSA is explained as a self-sustaining oscillation resulting from an alteration in the closed breathing control system.^{17,18} It is based on the concept of “loop gain” - an engineering term, used to describe the stability of a system regulated by a negative feedback mechanism. The loop gain can be defined as the ratio between the magnitude of the response to a change in a certain controlled variable and the subsequent effect exerted on the amplitude of the latter. Thus, the loop gain reflects the propensity of

the system for destabilization, and, in terms of the respiratory control – for development of periodic breathing. The relationship between the alterations occurring in CHF and the pathogenesis of CSB according to the loop gain theory is shown in **Fig. 1**.

The loop gain consists of three components: controller gain, plant gain and feedback gain. In fact, the controller gain represents the classical understanding of the control of breathing through central and peripheral chemoreceptors and reflects the ventilatory response to CO₂ changes. The plant gain accounts for the efficiency of ventilation in eliminating CO₂. A prerequisite for the destabilization of a negative feedback system is the time delay in the response of the control mechanisms, represented by the feedback gain. Enhancement in any of these three components would result in ventilatory instability expressed as CSA/CSB (**Fig. 1**).

ENHANCED CONTROLLER GAIN

The main pathological factor leading to and maintaining the CSB is the instability in CO₂ concentration, fluctuating around the apneic threshold.^{19,20} In CHF patients, however, there are several other factors, contributing to the development of periodic breathing, such as decreased partial pressure of carbon dioxide (pCO₂) levels, both during sleep and wakefulness, as well as the absence of adequate decrease in the apneic threshold.^{18,21} Lorenzi-Filho

Table 1. Some of the most important studies reporting the prevalence of sleep-disordered breathing in chronic heart failure

Study	n	Age (years)	Method	AHI (count.h ⁻¹)	SDB%	CSA%	OSA%
Arzt, 2016 ³	6876	69 ± 11	PG	≥15	46	NA	NA
Macdonald, 2008 ⁵	108	57 ± 11	PG	>15	61	31	30
Javaheri, 1998* ⁶	81	66 ± 9	PSG	≥15	51	40	11
Ferrier, 2005 ⁷	53	60 ± 10	PSG	≥10	68	15	53
Christ, 2007 ⁸	102	60 ± 14	PG	≥10	55	37	17
Oldenburg, 2007 ⁹	700	65 ± 10	PG	≥5	76	40	36
Schulz, 2007 ¹⁰	203	65 ± 1	PG	≥10	71	28	43
Yumino, 2009 ¹¹	218	56 ± 13	PSG	≥15	47	21	26
Vazir, 2007 ¹²	55	61 ± 12	PSG	>15	53	38	15
Bitter, 2012 ¹³	1500	68**	PSG/PG	>5	71.1	48.9	22.2
Gellen 2016 ¹⁴	376	59 ± 13	PG	≥15	55	NA	NA

Legend: PG – polygraphy; PSG – polysomnography; AHI – apnea-hypopnea index, SDB – sleep-disordered breathing, CSA – central sleep apnea, OSA – obstructive sleep apnea (data give the percentages of patients with SDB/CSA/OSA out of the total number of patients in the respective study), *data for the SDB group; **data for the CSA group.

Legend: PCWP – pulmonary capillary wedge pressure, SAA – sympathetic-adrenal activation, FRC – functional residual capacity.

Figure 1. The relationship between the alterations occurring in CHF and the pathogenesis of CSB according to the loop gain theory (based on Naughton⁵).

et al. managed to eliminate successfully the CSB (AHI 38.7 ± 17.0 vs 2.3 ± 2.9) and the associated desaturations in 10 CHF patients by exposing them to small concentrations of CO_2 through inhalation, which was accompanied by a slight increase in the transcutaneous pCO_2 . This experiment further implies the significance of even minimal fluctuations of pCO_2 for the development and maintenance of periodic breathing in CHF patients.²²

ENHANCED PLANT GAIN

Based on the hypothesis that increased left ventricular volume in CHF is associated with pulmonary congestion and a predisposition to CSB, Tkacova et al.²³ investigated patients with non-ischemic cardiomyopathy and demonstrated that the end systolic and the end diastolic volumes of the left ventricle are twice as big in the CSB group compared to those without CSB. Solin et al.²⁴ reported similar results, demonstrating approximately the two-fold increase in the pulmonary capillary wedge pressure (PCWP) in patients with CHF and CSA, accompanied by hypocapnia, as compared to those with OSA or without SDB. Furthermore, PCWP was found to correlate negatively with the level of pCO_2 and positively with the severity and frequency of the central apneas.²⁴ Therefore, increased PCWP could be an alarming signal for the presence of CSA, especially taking into account the increased mortality among CHF

patients with increased vascular pressures.

ENHANCED FEEDBACK GAIN

The prolonged circulation time causes a delay in the transmission of the changes in the arterial blood gases to the chemoreceptors. Theoretically, this can lead to a destabilization of the respiratory control. The increased arterial circulatory time, caused by heart failure, changes the loop gain activity in a way that it enhances the possibility for the development of respiratory oscillations, thus stimulating controller gain to execute a “right answer at the wrong time”. However, the data concerning the significance of time delay in the pathogenesis of CSA are contradictory. Several studies suggest its importance in the development of CSA.^{17,18,25,26} In a study of 10 patients with idiopathic CSA and normal cardiac function and 10 CSA/CSB patients with CHF, Hall et al. demonstrated that SDB is due to the dips of CO_2 levels below the AT, but are not associated with the degree of circulatory delay. The authors concluded that rather than initiating periodic breathing, the circulatory delay determines hyperpnea length and cycle duration once it has already been established.¹⁷

THE NEED FOR PREDICTIVE FACTORS

Irrespective of the exact intricate pathogenetic mechanisms of CSB, its presence in CHF patients

worsens the overall prognosis^{27,28} and needs targeted treatment^{29,30}. Therefore, a reliable screening system for its timely detection is required. At present, the golden standard for diagnosing CSA/CSB is laboratory polysomnography, which can differentiate the various types of SDB⁷ and determine the need of treatment. However, polysomnography is an expensive, laborious and highly specialized procedure. Besides, the available laboratories are not able to meet the diagnostic demand of all the patients with CHF.^{12,26} Type 4 screening devices (one or two channels) are a meaningful solution to detect patients with SDB. However, they are not available to most of the general practitioners and even cardiologists who take care of patients with CHF. A practical approach to overcome these problems is the establishment of a predictive system, aiming at selecting the appropriate patients for optimal use of polysomnography, rather than avoiding it. The “obvious” “candidate predictors” are those derived from the clinical history, the physical examination, as well as some distinctive characteristics of the disease or laboratory parameters. The chosen ones should be clearly defined, informative, standardized, easily accessible and low-priced, in order to be applied in the medical routine.

A pathophysiological approach for the selection of the predictors is their classification into 3 main groups: 1) The presence/absence of risk factors for the development of CSA in CHF patients (etiological); 2) Parameters, reflecting the pathogenesis of CSA in CHF patients (pathogenetic) and 3) Parameters,

reflecting the consequences of the existing CSA in CHF patients (symptomatic).

Such an approach, applied to the available literature data and the potential predictors, in our view, is presented in **Fig. 2**.

ETIOLOGICAL PARAMETERS

ANTHROPOMETRIC MEASUREMENTS – AGE, GENDER, BODY MASS INDEX (BMI), NECK CIRCUMFERENCE

Older age and male gender have been clearly identified as significant independent risk factors for the presence of CSA in CHF patients^{13,27}, irrespective of BMI, left ventricular ejection fraction (LVEF) and New York Heart Association (NYHA) class.¹¹

The factors behind the gender differences are not entirely elucidated. Central phenomena usually appear in light sleep or in the transition wakefulness-sleep, especially after an arousal or sleep-phase change. Consequently, the fact that men have more fragmented sleep, with less stable sleep structure, less slow wave sleep and an increased number of sleep-wake transitions^{31,32}, could be a possible explanation. On the other hand, central events are usually triggered by a phenomenon that causes hyperventilational hypocapnia, such as an obstructive apnea.^{4,11,16} Therefore, the higher prevalence of OSA in males can partially explain the higher prevalence and severity of CSA in male patients with CHF.³²

Obesity is a classical risk factor for OSA.¹³ It could be speculated that it is among the risk factors for CSA as well, taking into account the influence of adipokines on respiratory control³³ and the fact

PREDICTORS

Etiologic	Pathogenetic			Symptomatic
<ul style="list-style-type: none"> ✓ Anthropometry ✓ Medical history ✓ EchoCG ✓ NYHA class ✓ Laboratory parameters 	Controller gain	Plant gain	Mixing gain	Symptoms
	<ul style="list-style-type: none"> ✓ Respiratory control 	<ul style="list-style-type: none"> ✓ PFT ✓ EchoCG 	<ul style="list-style-type: none"> ✓ EchoCG 	<ul style="list-style-type: none"> ✓ ESS ✓ MLHFQ
	Loop gain in general <ul style="list-style-type: none"> ✓ Cardiopulmonary exercise testing (CPET) ✓ Hypoxic provocation ✓ BGA 			Complications
				<ul style="list-style-type: none"> ✓ ECG/ HRV ✓ CPET

Legend: EchoCG – Echocardiography, NYHA – New York Heart Association, BGA – blood gas analysis, PFT – pulmonary function test, ESS – Epworth Sleepiness Scale, MLHFQ – Minnesota Living With Heart Failure Questionnaire, ECG – electrocardiography, HRV – heart rate variability, CPET – cardiopulmonary exercise testing

Figure 2. A pathophysiological approach to identify predictors for the presence of central sleep apnea in patients with chronic heart failure.

that obstructive events can also trigger CSA in case of a predisposition.^{4,11,16}

The neck circumference is a simple anthropometric parameter that has been used in the prediction of OSA. As it was summarized by Bradley et al.³⁴, it is influenced by the rostral fluid shift during the night, present in patients with CHF. The rostral fluid shift, however, affects also the lungs (increasing pulmonary congestion), which is a part of the CSA pathophysiology. Thus, increased neck circumference, although not causatively related to the occurrence of CSA, may still correlate with it.

LABORATORY PARAMETERS – BRAIN NATRIURETIC PEPTIDE (BNP), C-REACTIVE PROTEIN (CRP)

BNP levels proportionately increase with CHF progression and are routinely used to assess the severity of the syndrome.³⁵ The mechanisms by which CSA/CSB influences the levels of BNP are not well-understood. The sympathetic overactivation, observed in CSA, could cause repetitive surges of blood pressure and heart rate, thus increasing the left ventricular afterload. Furthermore, the hypoxemia can also stimulate BNP secretion.³⁶ Carmona-Bernal et al. report a three-fold increase in BNP levels in CHF patients with CSA, as compared to those without CSA and similar NYHA class and LVEF.²⁸ Bitter et al. also report higher levels of NT-BNP in the CSA group compared not only to patients without SDB, but also to OSA patients.¹³

Several studies report increased levels of CRP in CHF patients.^{37,38} According to the cytokine hypothesis, the activation of the immune system plays a certain role in the pathogenesis of CHF, underlining the importance of some pro-inflammatory cytokines in the development of the ventricular dysfunction.³⁸ Anand et al. demonstrated that elevated CRP levels correlate with greater CHF severity, regardless of its cause (ischemic or non-ischemic), and also with the subsequent adverse events and mortality.³⁹ The mechanisms linking increased levels of CRP and CHF remain not entirely understood. A possible explanation is that IL-6, secreted by the cardiac myocytes when exposed to hypoxic stress, is a direct stimulus for CRP production by the hepatocytes.^{38,40}

PARAMETERS REFLECTING THE SEVERITY OF CHF – ECHOCARDIOGRAPHY (ECHO CG), NYHA CLASS

The standard measurements used for assessment of the severity of CHF (NYHA class and ejection fraction) do not considerably differ between CHF patients with and without accompanying SDB.^{8,41,42} Despite the correlation between the severity of CHF

and the prevalence of CSA, the latter is present in patients with milder forms of CHF, which makes NYHA class an unreliable criterion for determining the CSA risk.⁴²

CSA/CSB has also been found in CHF patients with preserved EF (HFPEF). In a study of 244 consecutive patients with HFPEF, Bitter et al. found that sleep apnea (apnea-hypopnea index (AHI) ≥ 15 /hour) was present in 48% of the patients (25% OSA and 23% CSA).⁴³ Therefore, EF is inapplicable as a predictive tool for the presence of CSA/CSB.

PATHOGENETIC PREDICTORS (ASSOCIATED WITH ELEMENTS OF THE CSA PATHOGENESIS IN CHF)

INDICATORS OF ENHANCED CONTROLLER GAIN

The measurement of arterial blood gases provides indirect information about the controller gain (in association with the plant gain). According to Szollosi et al., arterial hypoxia is an important prognostic factor for the presence of CSA in CHF.⁴⁴ The authors report that patients with CSA had significantly lower values of pCO_2 and diffusing capacity, compared to the OSA and the stable-breathing groups.⁴⁴ Since decreased diffusing capacity is a mechanism for the occurrence of hypoxia and hypocapnia, the role of the partial pressure of oxygen (pO_2) as an independent risk factor could be questioned. However, lower pO_2 values in CSA patients have not been found to be an independent risk factor, in the study of Bitter et al.¹³ On the contrary, the hypocapnia ($pCO_2 < 35$) is a major criterion in the suggested screening algorithm in CHF patients and in the subsequent recommendation for polysomnography. It should be stated that the arterial blood gases (pO_2 and pCO_2) are indicative not only for the controller gain and the plant gain, but being the main controlled parameters, represent the loop gain system as a whole.

INDICATORS OF ENHANCED PLANT GAIN

Increased plant gain reflects the excessive efficiency of the ventilation in regard to the exhaled CO_2 . The plant gain is dependent on pulmonary gas reserves, tissue oxygen and CO_2 reserves and metabolism intensity.⁴⁴

Breathing at a decreased functional residual capacity (FRC) makes CO_2 elimination more effective. Reduced pulmonary volumes promote breathing instability, which can explain the increased propensity to CSA/CSB in supine position.⁴ The decreased FRC in CHF patients leads to a premature closure of the airways during tidal breathing⁴⁵, which results

in an irregular distribution of the ventilation and a disturbed gas transfer in the lungs. The impaired gas exchange is partially compensated by an increase in the pulmonary ventilation at the expense of hyperpnea and tachypnea.⁴⁵ In other words, the decreased FRC is a prerequisite for a relative hyperventilation and the development of CSA/CSB.

According to the study by Szollosi et al., the decreased diffusion capacity is an important and independent predictor for the presence of CSA in CHF patients showing a moderate correlation with the AHI.⁴⁴ In this study, however, the patients within the CSA group had considerably lower levels of pCO₂, a fact that questions the independent predictive value of the decreased diffusion capacity.

INDICATORS OF ENHANCED FEEDBACK GAIN

An indirect assessment of the circulatory delay could be acquired from parameters reflecting the impaired hemodynamics in CHF, such as LVEF and BNP, which have been discussed earlier.

The direct evaluation of the circulatory delay is expressed as LECT (lung-to-ear circulation time), which is defined as the time from the end of the apneic pause to the nadir of saturation measured at the ear lobe.⁴⁶ However, the methodology of LECT measurement is too complex to be applicable as a screening tool.

PARAMETERS OF ENHANCED LOOP GAIN (AS A WHOLE)

Presence of periodic breathing while awake (during rest or cardio-pulmonary exercise testing (CPET))

CSB in CHF has also been observed during wakefulness^{26,47} and has been associated with increased mortality and shorter transplant-free survival. It is determined by low cardiac index and prolonged circulation time²⁶ and has been related to sympathetic overactivation and increased BNP levels.⁴⁷ The association of daytime CSB with more severe clinical course, lower LVEF, decreased functional capacity and hypoxemia at rest, suggests common pathogenetic mechanisms for the development of daytime and nighttime CSB in CHF patients.

Periodic breathing has been registered also during CPET. In the study by Roche et al., the presence of periodic breathing at rest and during the first 4 minutes of veloergometry showed strikingly high sensitivity (92.9%), specificity (94.1%) and predictive strength (93.3%) for the presence of CSA in CHF.⁴⁸

SYMPTOMATIC PARAMETERS (ASSOCIATED WITH THE CONSEQUENCES OF CSA+CHF)

ATRIAL FIBRILLATION (AF)

A relation between atrial fibrillation and the presence of SDB has been demonstrated.¹⁵ This association is probably bi-directional, since AF could be described as a complication of CSA and, at the same time, as a part of its pathogenesis. It is possible that AF is a consequence of CHF, because of the sympathetic overactivation, which influences the cardiac conduction system. On the other hand, CHF and AF may share common etiology, e.g. coronary artery disease, which may also affect the cardiac conduction system.

HEART RATE VARIABILITY (HRV)

The dysregulation of the autonomic nervous system, assessed by HRV analysis, is one of the most pronounced alterations, occurring in CHF.⁴⁹ Vazir et al. reported that the HRV is considerably increased in CHF patients with SDB, as compared to those without SDB.⁴¹ Tateishi et al. also found increased prevalence of very low frequency (VLF) oscillations in CHF patients with CSB and demonstrated that changes in the HRV (expressed as a ratio CSB/VLF oscillations-80%), are a marker of poor prognosis.⁵⁰ A serious disadvantage of the method is its inapplicability in the presence of AF or other conductive disorders. Another factor influencing HRV parameters is the drug therapy and especially beta-blockers, commonly prescribed to CHF patients.

EXCESSIVE DAYTIME SLEEPINESS (EDS) AND QUALITY OF LIFE (QoL)

Unlike OSA, the clinical profile of CSA is poor. Usually, patients do not report the typical loud snoring and/or EDS.^{7,41,42} In most cases, the precise evaluation of EDS is problematic, since the available methods rely mainly on subjective assessment, therefore, ESS alone could not identify patients with SDB. In addition, the symptoms of CHF can also cause sleep fragmentation and bad sleep quality and provoke some daytime complaints, even in the absence of CSA.⁷ The prevalence of ESS varies with age, showing an increased predominance and morbidity among the elderly, who actually constitute the main CHF contingent.⁵¹

CHF patients have considerably impaired quality of life as compared to patients with other chronic conditions.⁵² Hoekstra et al. demonstrated that QoL is a predictor of 3-year mortality in CHF patients.⁵³ However, according to Ferrier et al., the QoL in

CHF patients, measured by Minnesota Questionnaire (MLHFQ), does not show any differences between the groups with and without CSA.⁷

PHYSICAL CAPACITY (CARDIO-PULMONARY EXERCISE TEST)

OSA has been associated with decreased physical capacity, because of sleep alterations, including: 1) Hypoxia (leading to endothelial dysfunction, sympathetic activation and neuronal loss), 2) Arousals (associated with peripheral and muscle vasoconstriction), 3) Sleep fragmentation (ESS), 4) Increased breathing effort (left ventricle damage). The first three factors are present in CSA as well and, therefore, decreased physical activity is expected in CSA. However, there are only a few small studies on the topic reporting contradictory results.^{41,42}

CONCLUSION

There is a striking contrast between the substantial medical, social and economic impact of the CSA/CSB in CHF and the lack of well-established guidelines and algorithms for its diagnosis and treatment. Most of the recent efforts have been directed towards improvement of the treatment modalities, while strict criteria to go by in treatment are absent. Another important problem is the incapability of the available sleep laboratories to meet the overwhelming demand for polysomnography of CHF patients. Taking into account the reported prevalence of CSA in CHF, a reliable screening system, based on certain predictive factors, would greatly unload the healthcare system. Thus, the lack of an easily available and cheap screening method is a significant problem that has been only modestly addressed in the last years. We propose an approach, reflecting the pathophysiology of the respiratory control instability in CHF, based on the loop gain concept, in the process of looking for new predictors (**Table 2**). The proposed structure for a screening system may be used as a theoretical background for prospective studies on the topic.

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Идентификация предикторов центрального сонного апноэ (дыхание Чейна-Стокса) при хронической сердечной недостаточности: патофизиологический подход

Анелия И. Драганова, Кирилл В. Терзийски, Стефан С. Костянев

Кафедра патофизиологии, Факультет медицины, Медицинский университет, Пловдив, Болгария

Адрес для корреспонденции:

Анелия И. Драганова, Кафедра патофизиологии, Факультет медицины, Медицинский университет - Пловдив, бул. Васила Априлова № 15А, Пловдив, 4002, Болгария
E-mail: adraganova@pathophysiology.info
Тел.: +359884213500

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Хроническая сердечная недостаточность (ХСН) представляет серьезную проблему для здоровья, связанную с повышенной смертностью, несмотря на современные возможности лечения. Центральное сонное апноэ (ЦСА) / дыхание Чейна-Стокса (ДЧС) является часто встречающимся и, несмотря на это, в значительной степени редко диагностируемым сопровождающим заболеванием, которое играет существенную роль в неблагоприятном прогнозе в случаях ХСН ввиду наличия ряда острых и хронических эффектов, включая периодическую гипоксию, симпатическую сверхактивность, нарушения архитектуры сна и нарушения физического толеранса. Характеризуется повторяющимся проявлением ромбовидного систолического шума выброса (кресчендо-декресчендо), вслед за которым наступает центральное апноэ и гипонейя. Патогенез ЦСА/ДЧС основан на концепции цикла усиления, состоящего из трех основных компонентов: респираторный контроллер, эффективность выделения CO₂ и задержка, проистекающая в результате соединения гемоглобина и кровообращения. Лабораторная полисомнография является золотым стандартом при диагностике нарушений дыхания во время сна (НДС), но на данный момент является дорогостоящей и высокоспециализированной процедурой, не способной удовлетворить большой спрос в области диагностики. По сравнению с обструктивным сонным апноэ ЦСА/ДЧС отличается низким клиническим профилем. Поэтому необходима надежная предиктивная система для идентификации пациентов с ХСН, по всякой вероятности страдающих ЦСА/ДЧС, за счет оптимизации использования полисомнографии. Возможные предикторы должны быть стандартизованными, легко доступными и недорогими, в целях их применения в повседневной медицинской практике.

Данный обзор фокусируется на патофизиологическом подходе к выбору предикторов, в основе которого стоят параметры, отражающие этиологию, патогенез и последствия ЦСА/ДЧС при наличии ХСН.