

Prevalence of Cheyne–Stokes respiration in modern treated congestive heart failure

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Abstract

Introduction The prevalence of sleep breathing disorders in patients with congestive heart failure is relevantly high. According to historical studies Cheyne–Stokes respiration is an oscillatory ventilation during sleep in up to 40% of patients with congestive heart failure. During the last decade the medical treatment of congestive heart failure has been improved. The aim of this investigation was to analyze the prevalence of Cheyne–Stokes respiration in patients with congestive heart failure and modern medical treatment.

Results and discussion In 50 patients with severe congestive heart failure receiving modern medical treatment a full night polysomnography was performed. All patients had β -blockers and angiotensin-converting-enzyme inhibitors or angiotensin-II-antagonists as standard treatment. The mean age was 63 ± 12 years and the mean left ventricular ejection fraction was $26 \pm 6\%$. Respiratory polygraphy revealed Cheyne–Stokes respiration with a respiratory disturbance index of $\geq 5/h$ sleep in 32 (64%)

of the seven female and 43 male patients. The prevalence of Cheyne–Stokes respiration defined by using the threshold of an apnea index of $\geq 10/h$ was 30%.

Conclusion Thus, no significant change of Cheyne–Stokes prevalence could be found in our modern treated severe congestive heart failure collective.

Keywords Sleep disordered breathing · Cheyne–Stokes-respiration · Congestive heart failure · Prevalence

Introduction

For a number of years a high prevalence of sleep breathing disorders has been known to exist in patients with congestive heart failure [1–3]. Congestive heart failure is one of the leading causes of morbidity and mortality in developed countries. Since the description of a waxing and waning breathing pattern by Cheyne and Stokes the occurrence of Cheyne–Stokes respiration is well-recognized in congestive heart failure [4–5]. Several investigators showed an increased mortality in congestive heart failure combined with Cheyne–Stokes respiration [6, 7]. This possibly results from increased neurohumoral stress on the heart [8]. The treatment of congestive heart failure patients has changed during the last decade when new therapeutic standards like beta-blockers and angiotensin-converting-enzyme inhibitors have been established [9]. Prognosis of congestive heart failure patients has been improved by these new treatment standards.

The aim of this study was to find out if modern medical treatment has diminished sleep disordered breathing like Cheyne–Stokes respiration in congestive heart failure patients.

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Materials and methods

All patients with severe heart failure enrolled in the study of the Department of Cardiology at University Hospital were eligible if they met the following criteria: a left ventricular ejection fraction of $\leq 35\%$ and at least one episode of cardiac decompensation in patient history. They all had to be in stable cardiac conditions at NYHA-classification class 2–3 and had to have a beta-blocker and an angiotensin-converting-enzyme inhibitor or an angiotensin-II-antagonist as standard medications. No primary lung dysfunction with a forced expiratory volume in 1 s $< 65\%$ was accepted for participants and no myocardial infarction should have been in the last 6 months. The patients had to be at a minimum age of 18 years. For recruitment the consecutive patients were primarily screened by echocardiographic ejection fraction and then the other criteria had to be fulfilled.

All patients provided informed consent to participate in the study, which was performed in accordance with the principles of the Declaration of Helsinki and approved by the ethics committee at the University of Goettingen. Each patient had to have a pulmonary function test as well as an electrocardiography and echocardiography.

Polysomnography was performed in one night at the sleep laboratory of the cardiology and pneumology department. No patient had a known history of sleep disordered breathing prior to our investigations. To determine the stages of sleep an electroencephalogram, a chin electromyogram and an electrooculogram were obtained. Thoracoabdominal excursions were measured with strain gauges placed on the rib cage and abdomen. Airflow was monitored with thermocouples. All polysomnographic data were collected by computer system (Alice 4, Heinen & Löwenstein, Germany). According to the manual criteria of the American Academy of Sleep Medicine there had to be at least three cycles of crescendo and decrescendo change in breathing amplitude and five or more central sleep apneas or hypopneas per hour of sleep to be scored as Cheyne–Stokes respiration [10]. Furthermore according to the international classification of sleep disorders (ICSD-2) the apnea index (AI) of $\geq 10/h$ was defined as relevant [11]. In all patients classified as having obstructive sleep apnea or Cheyne–Stokes respiration, that breathing disorder was the predominant pattern. Obstructive apnea or hypopnea was defined as an absence or a reduction of airflow for at least 10 s despite continued out-of-phase chest and abdominal movements. A mixed apnea was defined as an apnea with a combination of both central and obstructive components.

Statistical analysis was performed with SPSS (SPSS GmbH Software, Germany). The Mann–Whitney test was used to assess differences between patients with and without sleep disordered breathing, and chi-square anal-

ysis was used to analyze proportions. A two-sided *P* value of less than 0.05 was considered to indicate statistical significance. Values are reported as means.

Results

Fifty patients were included in the study (Table 1). Four of the six female and 22 of the 44 male patients had ischemic cardiomyopathy. Twenty patients had a dilated and four a hypertrophic nonobstructive cardiomyopathy. Sinus rhythm has been registered in 39 patients and arterial hypertension was prevalent in 31 patients. A documented diabetes mellitus has been observed in 14 patients, as often as nicotine abuse. More often the cardiac risk factor of hyperlipidemia were seen with 30 patients.

All of the patients were being treated with a beta-blocker-medication and 42 were treated with angiotensin-converting-enzyme inhibitor while eight had angiotensin-II-antagonists. All patients were being treated with diuretic medications and 12 with digitalis. Eighteen patients received an aldosteron antagonist.

According to the mentioned American Academy of Sleep Medicine (AASM)-manual-criteria there were eight patients with a respiratory disturbance index (RDI) of less than 5/h and 64% of all study patients had Cheyne–Stokes breathing patterns (Table 2). Twenty-two (44%) of all patients had a Cheyne–Stokes respiration with an AHI $> 15/h$. Ten patients (20%) had mainly obstructive sleep breathing disorders during sleep.

If ICSD-2-criteria for sleep investigations were used there would have been 34 patients (68%) with an AI of less than 10/h. Fifteen (30%) of all patients had a Cheyne–Stokes respiration with an AI $\geq 10/h$ (25 ± 13 vs 4 ± 10 , $p < 0.0001$).

Considering cardiac characteristics of all patients the mean ejection fraction was $26 \pm 6\%$ and the average left ventricular diastolic dimension was 64 ± 8 mm. Mean septal dimension was 11 ± 2 mm and left atrial dimension was 49 ± 8 mm. Divided into patient groups with and without

Table 1 Clinical data of the patients

Variable	Patients (<i>n</i> =50)	CSR (<i>n</i> =32)	NCSR (<i>n</i> =18)	<i>P</i> value
Age (years)	63±12	62±13	63±12	ns
Body mass index (kg/m ²)	26.6±4.3	26.3±3.7	27.1±5.3	ns
Height (cm)	175±10	177±9	172±10	0.1
Heart rate (bpm)	74±18	75±18	70±18	ns
FEV1/VC (% standard)	102±16	102±14	101±19	ns

CSR patients with Cheyne–Stokes respiration according to AASM-manual-criteria, NCSR non Cheyne–Stokes respiration patients, ns non-significant, FEV1/VC %Standard forced expiratory volume in 1 second/vitalcapacity in percent of standard value

Table 2 Characteristics of the patients during sleep

Variable	CSR (n=32)	NCSR (n=18)	P value
Total sleep time (min)	314±62	297±100	ns
NonREM (min)	280±55	254±79	ns
REM (min)	50±29	53±28	ns
RDI (/h TST)	26±16	10±14	0.001
AHI (/h)	23±15	8±14	0.001
Apnea-index (/h sleep)	13±14	5±14	0.04
Arousal-index (/h sleep)	25±15	29±17	ns
Mean oxygen saturation (%)	89±4	90±3	ns
Min. oxygen saturation (%)	81±7	84±8	ns

CSR patients with Cheyne–Stokes respiration according to AASM-manual-criteria, NCSR non Cheyne–Stokes respiration patients, TST total sleep time, REM rapid eye movement sleep, RDI respiratory disturbance index, AHI apnea-hypopnea index, ns non-significant

Cheyne–Stokes respiration according to AASM-manual-criteria the only significant difference was the septal dimension regardless of the kind of sleep disorders cutoff point (Table 3). For ICSD-2-criteria there was a tendency to a worse ejection fraction in patients suffering from Cheyne–Stokes respiration ($p < 0.1$).

Discussion

Cheyne–Stokes respiration has been common during sleep in congestive heart failure patients in previously published investigations [1–3, 12]. There are also hints for a poorer prognosis in those congestive heart failure patients with Cheyne–Stokes respiration [6, 7, 13]. Modern medical treatment has a prognostic impact in patients with congestive heart failure [14–19]. In a small study population of 8 patients Walsh and colleagues showed a reduction of apneic episodes as well as arousals and an increase of slow wave and REM sleep by treatment with captopril [20]. More recent studies by Koehnlein and colleagues as well as Tamura and colleagues stated a reduced prevalence in β -blocker-treated heart failure patients [21, 22]. Both investigations failed to request equal baseline therapy according to treatment guidelines.

In this investigation modern medication standards like beta-blockers and angiotensin-converting-enzyme inhibitors or angiotensin-II-antagonists showed no beneficial influence in the prevalence of Cheyne–Stokes respiration. As a limitation no own control data were used.

While there are widely accepted standards for analyses of sleep apnea the definition of Cheyne–Stokes respiration is less precise. If the actual AASM-manual-criteria of sleep breathing disorders with a cutoff respiratory disturbance index of $\geq 5/h$ would have been used, the incidence would be 64%. These results are almost similar to the retrospective study results of Sin et al. in 450 patients with an occurrence

of sleep breathing disorders of 72%, 61%, and 53% according to an apnea–hypopnea index cutoff point of 10, 15, and 20/h in congestive heart failure patients [3]. Still in that earlier study no standard medical treatment was given as recommended by modern heart failure treatment guidelines [9]. As the respiratory disturbance index is attributed to the total sleep time [23], it tends to be higher than the apnea–hypopnea index related to the total recording time in bed [7]. This termination has not been standardized so far, therefore an apnea–hypopnea index could have been related to time-in-bed or total sleep time in earlier investigations [2, 7, 24]. Furthermore the ICSD-2 definitions recommend an AI $\geq 10/h$ for Cheyne–Stokes respiration [11]. According to this definition there would be a lower number of patients with Cheyne–Stokes respiration in our study population, still this definition would not be comparable to previous studies.

In 203 German patients with congestive heart failure and left ventricular ejection fraction $< 40\%$ an apnea–hypopnea index cutoff about 10/h were seen by polysomnography in 71% with a majority in obstructive sleep apnea probably due to higher body mass index [25]. The prevalence of sleep breathing disorders according to common study criteria with an apnea–hypopnea index cutoff about 10/h and 15/h is approximately 56% and 48% in our study population. The prevalence in the historic collective of Javaheri et al. with an apnea–hypopnea index cutoff about 15/h has been about 50% for sleep breathing disorders [2].

Compared to the prevalence in the study population of Javaheri et al. the prevalence of Cheyne–Stokes respiration in the sleep breathing disorders was between 66% and 44% in our patients group depending on the cutoff versus 40% in Javaheri's patient group. The different inclusion criteria concerning the ejection fraction of $< 45\%$ in Javaheri's study and $\leq 35\%$ in our study may be the reason for the small difference.

A retrospective analyses in 450 consecutive patients with congestive heart failure with an apnea–hypopnea index cutoff about 10/h found a prevalence of sleep breathing disorders of 72% [3]. In that retrospective analyses the prevalence of Cheyne–Stokes respiration of 33% was comparable to the

Table 3 Cardiac characteristics of the patients

Variable	CSR (n=32)	Non-CSR (n=18)	P value
Ejection fraction (%)	26.3±6.3	25.8±6.7	ns
LVEDD (mm)	65.1±8.0	61.4±8.4	ns
Left atrial dimension (mm)	50.1±8.0	48.2±7.9	ns
Septal dimension (mm)	11.9±2.3	10.6±1.9	< 0.05
Remained sinus rhythm	24	15	ns
Bundle branch block	17	11	ns

CSR patients with Cheyne–Stokes respiration according to AASM-manual-criteria, Non-CSR non Cheyne–Stokes respiration patients, LVEDD left ventricular enddiastolic dimension, ns non-significant

German patients with 28% [25]. The differences to our as well as Javaheri findings are possibly related to a higher body mass index leading to an increased prevalence of obstructive sleep apneas as well as no predefined inclusion ejection fraction in Sins' patient collective.

Although the modern medical treatment improved prognostic outcome in congestive heart failure there appears to be no clear evidence of a reduction in Cheyne–Stokes respiration. The increasing prevalence of chronic heart failure is affecting patients' quality of life, and health resources, despite advances in management. Recognizing and treating comorbid illnesses is critical. Risk factors such as hypertension and diabetes are treated, but less importance is placed on the role of sleep apnea in heart failure. Apneic episodes during sleep can lead to profound disturbances to the sympathetic and parasympathetic nervous system.

Conclusions

In conclusion special therapeutic strategies in Cheyne–Stokes respiration may still be of importance for further prognostic benefit in congestive heart failure patients. There is no clear evidence for a reduction of Cheyne–Stokes respiration due to modern medical treatment in congestive heart failure.

Competing interests The authors declare that they have no competing interests.

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