



Original Article

Improvements of central respiratory events, Cheyne–Stokes respiration and oxygenation in patients hospitalized for acute decompensated heart failure



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ABSTRACT

Background: Sleep-disordered breathing (SDB), and Cheyne–Stokes respiration (CSR) in particular, are associated with reduced survival in patients with acute decompensated heart failure (ADHF). CSR cycle length (CL) has been shown to mirror heart failure severity and therefore may be a predictor of outcome. However, studies characterizing CSR in ADHF are rare and no study has investigated changes in CSR from admission to discharge in ADHF patients.

Methods: Consecutive patients admitted to our Academic Medical Center with ADHF were eligible. Study patients underwent two multichannel cardiorespiratory polygraphy (PG) recordings, one on admission and another during recompensation.

Results: 105 patients (age 71.5 ± 12.1 years, 66.7% male, NYHA class 3.2 ± 0.6 , left ventricular ejection fraction $38.5 \pm 13.3\%$, brain natriuretic peptide 1299 ± 1290 pg/ml); 77 had two fully analyzable PG recordings. CSA prevalence on the first PG was 77%. Based on the apnea-hypopnea index (AHI), CSA was mild, moderate or severe in 21%, 39% and 40% of patients, respectively. During ADHF treatment, AHI decreased non-significantly from $54 \pm 17/h$ to $48 \pm 9/h$ ($p = 0.06$), central hypopnea index from $20.9 \pm 14/h$ to $17.1 \pm 6.2/h$ ($p < 0.01$), and time spent in CSR from 65.5 ± 28.4 to 63.7 ± 17.8 min ($p < 0.01$); oxygenation improved from $91.4 \pm 2.6\%$ to $92.0 \pm 1.5\%$ ($p < 0.05$). There was no significant change in CL.

Conclusions: Patients with ADHF have a high prevalence of central respiratory events, which decreased during cardiac recompensation. Cardiac recompensation also non-significantly improved the AHI and time spent in CSR and oxygenation, but had no clear impact on CSR CL, which leaves clinical account open to further investigation.

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1. Introduction

Congestive heart failure (CHF) is a common disease worldwide, and its incidence is increasing. CHF is among the leading causes of death, and has a major economic health burden [1]. Hospital readmissions contribute to the health care burden of CHF and are also a marker of poor prognosis [1,2]. Although there have been a number of advances in therapy, including new pharmacological

agents and novel devices, there is an increasing focus on comorbidities as a target for improving prognosis and quality of life in patients with CHF [1]. One comorbidity that is gaining recognition is sleep-disordered breathing (SDB) [3].

SDB has been associated with poor prognosis in patients with CHF [4–7] and occurs at a high prevalence in this patient group [8–10]. Furthermore, there is strong epidemiological data linking SDB and ADHF [4,11,12], which indicates that there is growing interest in understanding this association [13]. It was recently reported that SDB is not a fixed or static concept but instead varies with changes in cardiac function [14]. SDB dynamics and characteristics have been linked with heart failure (HF) and severity [8], but the time course of changes in SDB characteristics during cardiac de- and re-compensation is still not well understood.

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There are two main types of SDB: obstructive sleep apnea (OSA) and central sleep apnea (CSA). In contrast to OSA, CSA is characterized by absent or decreased inspiratory effort and a lack of obstructive features, such as flattening, paradoxical thoracoabdominal movements or snoring [15]. A noteworthy but often neglected subtype of CSA is Cheyne–Stokes respiration (CSR), which is characterized by a crescendo/decrecendo breathing pattern followed by an apnea (absence of airflow) or hypopnea (decreased airflow) of at least 10 s [11,15].

The prevalence of CSR is high in patients with CHF, and increases in tandem with HF severity [8,10]. In this context, CSR cycle length (CL) is thought to mirror cardiac function and provide an indication of HF severity, with a reported correlation between CSR CL and the severity of left ventricular dysfunction in stable HF patients [16]. Patients with more severe CHF appeared to have longer CLs and spent more time in CSR overall compared to those with less severe disease, even when there is a similar apnea-hypopnea index (AHI; the traditional marker of SDB severity) [16].

Therefore, the AHI might not be the best metric of CSR severity in CHF patients. This study prospectively investigated respiratory event characteristics and CSR CL during recompensation in patients hospitalized for ADHF to identify markers of HF severity.

2. Methods

This prospective, observational trial included consecutive patients admitted to the Academic Medical Center in Bad Oeynhausen, Germany with ADHF between July 2012 and August 2013. Inclusion criteria were New York Heart Association (NYHA) functional class III or IV and clinical symptoms of ADHF as defined by current European Society of Cardiology (ESC) guidelines [1]. Exclusion criteria were dependent on oxygen insufflation, infections, intravenous catecholamine therapy, acute coronary syndrome, planned coronary interventions or surgery. The study protocol was approved by the institutional ethics committee and all patients gave written informed consent before being enrolled and undergoing SDB screening using multichannel cardiorespiratory polygraphy (PG).

2.1. PG screening

PG recordings were obtained using one of three different devices (Embletta, Embla, Rotterdam, The Netherlands; NoxT3, Nox Medical, Reykjavik, Iceland; SomnoScreen plus, Somnomedics, Randersacker, Germany). All recordings had to contain a minimum of six recording channels (nasal airflow, thorax and abdominal effort, body position, snoring and oxygen saturation). Recordings with a temporary loss of one channel, except for nasal airflow were acceptable. A minimum recording time of three hours was required. PG recordings were independently and blindly analyzed according to American Academy of Sleep Medicine (AASM) scoring recommendations [15]. CSR apneas were defined as a $\geq 90\%$ decrease in airflow and hypopneas as a $\geq 30\%$ decrease in airflow, followed by a desaturation of at least three percent. Arousals could not be measured due to the nature of PG. All patients were given a standardized questionnaire form after the PG recording night on which to record actual sleep time. The first PG recording was performed at the first night of admission. AHI/h is given as AHI per hour of recording time.

2.2. Definition of CSR and cycle length

CSR was scored when the recording showed at least three consecutive central events with typical crescendo-decrecendo breathing pattern, with at least five events per hour and a

minimum CL of ≥ 40 s or more [15]. CL in CSR apneas was defined as the time between the beginning of the apnea and the end of the following crescendo-decrecendo respiratory phase as previously described [16]. In CSR hypopneas, CL was defined as the time from one zenith in crescendo-decrecendo amplitude to the following [16]. Ventilation length (VL) was calculated by subtracting apnea/hypopnea length from the CL [16]. Circulatory delay (CD) was defined as the time between the end of apnea/hypopnea and the following nadir of oxygen saturation [16]. These parameters were determined for 30 typical cycles of CSR from the total recording, but only in patients with an AHI ≥ 10 /h (Figs. 1 and 2).

2.3. Cardiac recompensation

Recompensation was defined as resolution of symptoms that led to hospital admission, weight loss and return to pre-admission condition. Echocardiography was obtained within the first three days of hospital admission.

2.4. Statistical analysis

Statistical analysis was done with IBM SPSS 22, IBM Corporation, Armonk, NY, USA, for Mac, Apple Inc., Cupertino, CA, USA. Statistical significance was assumed when $p < 0.05$. Data are expressed as percentages for discrete variables and as mean \pm standard deviation for continuous variables. Continuous variables were compared by ANOVA. Categorical comparisons were compared using Chi-square analysis and non-parametric inferential statistical analyses were performed using Mann–Whitney U, Wilcoxon rank sum test and Spearman's rank correlation coefficient.

3. Results

3.1. Patients

A total of 105 patients were enrolled. Demographic and clinical characteristics at baseline for the total population and the subgroup with CSR are shown in Table 1. The prevalence of CSA was 77%, severity was rated as mild (AHI 5–14/h) in 21% of patients, moderate (AHI 15–29/h) in 39% and severe (AHI ≥ 30 /h) in 40%. For further analysis of CSA, 77 patients had PG recordings that fulfilling all predefined quality requirements, while for sufficient CSR CL analysis only 24 patients qualified.

Questionnaire data after PG recording suggested a sleep time of 226 ± 210 min on the first PG night and 242 ± 208 min on the second night of PG recording.

During recompensation BNP came down from 1299 ± 1290 pg/ml to 965 ± 1051 pg/ml, NYHA functional class improved from 3.2 ± 0.6 to 2.5 ± 0.8 and mean weight loss was 6 kg. Arterial blood gas analysis of our study population showed pH 7.45 \pm 0.03, pO_2 72.5 \pm 13.2 mmHg, pCO_2 35.9 \pm 5.1 mmHg, SO_2 95 \pm 2.9%. Glomerular filtration rate was 55.1 \pm 22.9 ml/min. Prevalence of atrial fibrillation was 45.7%.

3.2. SDB characteristics and analyses

During ADHF-related hospitalization, the recompensation phase was associated with a non-significant decrease in the AHI, significant decreases in the central hypopnea index and time spent in CSR, and a significant increase in oxygen saturation (Table 2). There were no relevant changes in CSR characteristics, including CL, CD and VL, throughout the period of hospitalization and treatment for ADHF (Table 2), and CL values were within the expected range.

To more specifically assess the relevance of CSR CL, the median value was calculated (55.5 s) and patients were divided into two

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