Journal of Cardiology 66 (2015) 218–223

Contents lists available at ScienceDirect

Journal of Cardiology

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

Original article

Assessment of respiratory disturbance index determined with a non-restrictive monitor and of autonomic nervous system parameters in heart failure patients: A pilot study

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ARTICLE INFO

Article history:
Received 1 October 2014
Received in revised form 23 December 2014
Accepted 27 December 2014
Available online 3 February 2015

Keywords:
Sleep-disordered breathing
Heart rate variability
Autonomic nervous activation
Screening
Acute decompensated heart failure

ABSTRACT

Background: There is a link between sympathetic overactivity and sleep-disordered breathing (SDB), and both of which are important indicators of the development of heart failure. To manage the increasing numbers of heart failure patients, any method used to check for them needs to be as non-invasive, simple, and cost-effective as possible. The purpose of this study is to assess screening of SDB with a non-restrictive monitor and the autonomic nervous system in heart failure patients.
Methods: The subjects were 49 patients (mean age: 67 years; male: 78%) hospitalized for worsening heart failure. After stabilization with appropriate medical therapy, each patient simultaneously underwent sleep apnea syndrome (SAS) screening with the SD-101 (Kenzmedico Co. Ltd., Saitama, Japan), which is a novel, non-restrictive, sheet-like monitor for SAS screening, and assessment of heart rate variability (HRV) with a Holter monitor. In addition, we assessed daytime sleepiness by using the Epworth Sleepiness Scale.
Results: The mean respiratory disturbance index (RDI) was 21.9 events/h. Males had significantly greater RDI values than females (24.5 ± 11.2 events/h vs. 13.0 ± 6.2 events/h, $p < 0.001$). RDI on SD-101 testing was closely correlated with cyclic variation of heart rate index obtained with a Holter electrocardiogram scanner ($r = 0.843$). Although plasma brain natriuretic peptide level was not correlated with HRV, plasma norepinephrine level was moderately well correlated with the total low- to high-frequency ratio of HRV ($r = 0.529$).
Conclusions: SAS screening is important for heart failure patients, because absence of subjective sleepiness is not reliable in ruling out SDB. The SAS screening with SD-101 might apply for managing heart failure.

Introduction

Despite recent advances in the management of heart failure, mortality rates in heart failure patients remain high [1]. Heart failure is a global epidemic in health care and a leading cause of mortality and morbidity worldwide [2]. In Japan an estimated 1.0 million individuals have heart failure [3,4] and the number of Japanese outpatients with left ventricular (LV) dysfunction is predicted to increase gradually from 979,000 in 2005 to 1.3 million by 2030 [3].

In acute heart failure, adrenergic activation initially occurs in response to hemodynamic overload or/and an intrinsic reduction in pump failure [5]. In addition, obstructive sleep apnea (OSA) and central sleep apnea (CSA) interfere with neuro-humoral systems and thus may worsen heart failure by increasing sympathetic and renin–angiotensin–aldosterone activity [6]. Furthermore, there is a link between sympathetic overactivity and sleep-disordered breathing (SDB) [7], and both of which are important indicators of the development of heart failure [8]. Therefore, assessment of both SDB and cardiac autonomic nervous system is important for managing new-onset heart failure or preventing recurrent heart failure at as early a stage as possible. To manage the increasing

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http://dx.doi.org/10.1016/j.jjcc.2014.12.018
0914-5087/

numbers of heart failure patients, any method used to check for SDB and activation of the adrenergic nervous system needs to be as non-invasive, simple, and cost-effective as possible.

Although complete laboratory technologist-attended polysomnography (PSG) remains the accepted standard for evaluation of SDB [9], such assessments are complicated. The SD-101 sleep recorder (Kenzmedico Co. Ltd., Saitama, Japan) is a newly developed type-4 respiratory monitoring device that can be used to quantify the subject's respiratory movements and monitor for SDB under the Japanese medical insurance system. The device uses an array of pressure sensors embedded in its sheet-shaped core [10,11]. This device does not restrain the patient with tubes or cords, and it can be used easily by simply being placed on the bed.

Analysis of heart rate variability (HRV) has been used widely as a reliable tool for evaluating cardiovascular autonomic control in health and disease [12]. The Cardy 303 pico (Suzuken Co. Ltd., Nagoya, Japan) is one of the world's smallest and lightest (W 28 × D 42 × H 9 mm, 13 g) Holter monitors used for this purpose.

Here, we used these two novel devices—the SD-101 and the Cardy 303 pico—as screening tools to check for SDB and assess the autonomic nervous system in patients with acute decompensated heat failure (ADHF) who were in a stable condition after appropriate medical treatment. To our knowledge, this is the first study to use these novel devices simultaneously to screen for SDB and assess the autonomic nervous system in patients with heart failure. The purpose of this study is to assess screening of SDB and the autonomic nervous system by these non-invasive and minimally restrictive methods in ADHF patients.

Methods

Study design and ethical considerations

Forty-nine patients hospitalized for worsening heart failure were enrolled in the study. We excluded patients with atrial fibrillation, implanted pacemakers, or dementia. When all patients had been stabilized after appropriate medical treatment, they underwent laboratory measurements [including plasma brain natriuretic peptide (BNP) and norepinephrine], echocardiography, 24-h Holter electrocardiography (ECG) with the Cardy 303 pico, and a sleep study for sleep apnea syndrome (SAS) screening with the SD-101. We assessed daytime sleepiness by using the Epworth Sleepiness Scale (ESS) [13]. The Ethical Review Board of Nagoya University School of Medicine approved the study protocols. All patients provided written informed consent with regard to the study procedures and potential risks.

Sleep testing

The SD-101 is a newly developed type-4 portable respiratory monitor with a sheet-like shape approved under the Japanese government medical insurance system, as previously described [14]. Respiratory events were defined as a ≥50% decrease in respiratory effort waveforms lasting >10 s from the preceding baseline value. We defined the respiratory disturbance index (RDI) obtained from the SD-101 data as the number of respiratory events divided by the amount of time spent in bed, because total sleep time could not be estimated from the SD-101 data alone. The definition of moderate to severe SDB using the RDI parameter was set to ≥15 events/h.

HRV

On the same day as they underwent the SD-101 sleep test, all patients underwent Holter electrocardiography. HRV was analyzed by using the Cardy Analyzer 05 electrocardiogram data viewer (Suzuken Co. Ltd., Nagoya, Japan), as previously described [15]. HRV was assessed by examining the R–R interval in the time-domain analysis and the power spectral analysis. Hayano et al. [16,17] have reported that the cyclic variation of heart rate (CVHR) index obtained by using the autocorrelated wave detection with adaptive threshold (ACAT) algorithm is closely correlated with the apnea–hypopnea index (AHI) and shows good performance in identifying patients with moderate-to-severe OSA. The ACAT algorithm is a time-domain method that uses only interbeat interval data. The processes of the ACAT algorithm were as follows: Interbeat interval time series were smoothed by second-order polynomial fitting, and all dips in the smoothed trend with widths between 10 and 120 s and depth-to-width ratios of >0.7 ms/s were detected. Also, the upper and lower envelopes of the interbeat interval variations were calculated as the 95th and 5th percentile points, respectively, within a sifting window with a width of 130 s. Then, the dips that met the following criteria were considered CVHR: (1) a depth >40% of the envelope range at that point (adaptive threshold), (2) interdip intervals (cycle length) between 25 and 130 s, (3) a wave form similar to those of the two preceding and two subsequent dips with a mean morphological correlation coefficients >0.4 (autocorrelated wave), and (4) three cycle lengths between four consecutive dips that meet the following equivalence criteria: $(3 - 2l_1/s)(3 - 2l_2/s)(3 - 2l_3/s) > 0.8$, where l_1, l_2, and l_3 are three consecutive cycle lengths and $s = (l_1 + l_2 + l_3)/3$ [16]. The algorithm of CVHR has been incorporated into the data obtained with a Holter ECG scanner before [17].

In the power spectral analysis, the low-frequency (LF) and high-frequency (HF) components of HRV in the daytime (9 AM to 9 PM) and at night (midnight to 6 AM) and for the total period were calculated for each subject. Spectral measures were computed by using the fast-Fourier transform method. A component band in the frequency range from 0.04 to 0.15 Hz was considered an LF component. A component band in the frequency range from 0.15 to 0.40 Hz was considered an HF component.

Statistical analysis

Data are presented as means ± standard deviation (SD). Continuous variables were compared between two groups with the use of Student's t-test for unpaired data. Categorical variables are presented as numbers (percentages), and were performed by a Fisher exact test. BNP, LF, and HF were naturally logarithmically transformed to approximately normalize the distribution and then used in the analysis. A Pearson product moment correlation analysis method was used to assess correlations between continuous variables. Prespecified subgroups were defined by gender; cut-off values for median age (70 years), body mass index (25 kg/m^2), plasma BNP (200 pg/ml), and left ventricular ejection fraction (50%); initial or repeat hospitalization for worsening heart failure; presence or absence of ischemic heart disease; and presence or absence of diabetes. All analyses were performed with the SPSS 21.0 software package (SPSS/IBM, Chicago, IL, USA). A p-value of <0.05 was considered statistically significant.

Results

Baseline characteristics of patients are shown in Table 1. The group included 24 (49.0%) patients with age ≥70 years, 16 (32.7%) with BMI ≥25 kg/m^2, 31 (63.3%) with plasma BNP level ≥200 pg/ml, and 40 (81.6%) with an LV ejection fraction <50%. The frequency distribution of the RDI in 5-unit intervals for the 49 (male 38, female 11) heart failure patients is depicted in Fig. 1. SDB was present in 47 of our ADHF patients (95.9%); only 4.1% of patients did not present