



Original Article

Changes of heart rate variability predicting patients with acute exacerbation of chronic obstructive pulmonary disease requiring hospitalization after ED treatment

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Abstract

Background: Indexes of heart rate variability (HRV) appear to reflect severity and may have prognostic value in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). We hypothesized that AECOPD without adequate treatment response would demonstrate impaired cardiac autonomic regulation and changes in HRV after emergency department (ED) treatment.

Methods: A prospective study of measuring HRV in admitted and discharged patients with AECOPD shortly after ED arrival and again 24 h after treatment.

Results: Total consecutive 33 patients (18 admitted and 15 discharged, age 77.1 ± 1.6 years) were enrolled. Among admitted patients, high frequency in normalized unit (HF%) was significantly lower ($P < 0.001$) while Ratio of LF to HF (LF/HF ratio) was significantly higher ($P < 0.001$) than discharged. 24 h after treatment, admitted patients had a significantly larger increase in HF% ($P < 0.002$) and larger decrease in LF/HF ratio ($P < 0.05$) than discharged. ROC curve analysis show the relative potential of the Δ HF% and Δ LF/HF% in the discrimination of groups. The area under the ROC curve between the 2 groups was 0.807 ($P < 0.01$) and 0.722 ($P < 0.05$), respectively. The best cut-off value for the admission between groups was Δ HF% > 7.1 and Δ LF/HF% ≤ -0.39 .

Conclusion: Patients with AECOPD requiring admission after ED treatment had a greater increase in HF% and greater decrease in LF/HF ratio compared to those discharged. Our study demonstrates patient with Δ HF% was > 7.1 or a Δ LF/HF% ≤ -0.39 require admission despite 24 h of ED treatment.

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Keywords: Acute exacerbation; Chronic obstructive pulmonary disease; Emergency department; Heart rate variability

1. Introduction

Chronic obstructive pulmonary disease (COPD) is still responsible for over 9000 hospital admissions, and the mean duration of hospital stay for COPD acute exacerbation (AECOPD) patients is about 11 days, in the United Kingdom.¹ The national inpatient burden of AECOPD is considerable.² The risk of mortality for AECOPD patients in the hospital

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and one year after discharge were 8% and 23% respectively.³ Traditionally, emergency physicians decide whether to discharge or admit a patient with AECOPD, from the emergency room, based on clinical symptoms/signs such as relief from dyspnea, absence of wheezing, and degree of respiratory distress. If the patients do not respond adequately to treatment, hospitalization is recommended. Objective tests, like as arterial blood gas (ABG) and the pulmonary function test, can help clinical physicians determine disease severity^{4–6}; however, they cannot aid in determining if patients should be admitted. In addition, spirometric measurements are not sensitive enough to detect relief from dyspnea over the course of an ED visit.⁷ Hence, non-invasive and novel measures that enable the risk-stratification of AECOPD patients' response to treatment are highly desirable for ED physicians.

Some specific spectral components of heart rate variability (HRV) are considered to be associated with the autonomic modulation of the heart. In a previously conducted study, the increase in total power, low frequency (LF) component, and low LF/high frequency (HF) ratio (LF/HF ratio) pointed to the fact that intermittent hypoxic training increased the response of the autonomic nervous system, predominantly through increased sympathetic activity.⁸ The indexes of HRV appear to reflect severity and may have prognostic value in COPD patients.⁹ Patients with AECOPD have increased HRV parameters than those with stable COPD.¹⁰ However, it has not been reported if the indexes of HRV enable the identification of AECOPD patients who do not respond adequately to treatment. The aim of the present study was to noninvasively evaluate cardiac autonomic modulation in patients with COPD, during acute exacerbation. We hypothesized that AECOPD patients, without adequate response to treatment, would demonstrate impaired cardiac autonomic regulation.

2. Methods

2.1. Definition of COPD and AECOPD

Patients were diagnosed as having COPD according to the internationally accepted criteria determined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD).¹¹ The spirometric criterion for airflow limitation remains a post-bronchodilator fixed ratio of FEV1/FVC <0.70. Patients were then divided into the mild (GOLD stage 1), moderate (GOLD stage 2), severe (GOLD stage 3), and very severe (GOLD stage 4) groups, according to the predicted FEV1. AECOPD was defined by the symptoms of increased dyspnea and sputum volume with or without purulent sputum, coughing or wheezing.¹²

2.2. Study setting and population

We enrolled 33 consecutive patients who presented to the emergency department (ED) of Taipei Veterans General Hospital, Taiwan. The inclusion criteria were: a physician's diagnosis of COPD; presence of moderate (GOLD stage 2) to severe (GOLD stage 3) COPD; presentation to the ED for

AECOPD treatment; age >50 year; and ability to provide informed consent. Exclusion criteria were: presence of mild (GOLD stage 1) and very severe (GOLD stage 4); not being able to perform spirometry; presence of decompensated congestive heart failure; history of lung cancer or surgery; presence of diabetic neuropathy; presence of an implanted cardiac pacemaker; frequent occurrence of atrial fibrillation; and premature atrial or ventricular contractions or other forms of arrhythmia. These patients were not on any medication other than those required for control of COPD control, such as inhaled bronchodilators (salbutamol and ipratropium bromide) and corticosteroids (budesonide, beclomethasone or fluticasone). Patients taking methylxanthines were excluded.

Institutional review board in Veterans General Hospital Taipei approved the protocol (VGHIRB No.: 97-07-20A), and written informed consent was obtained from all patients.

2.3. Treatment

Treatment comprised a combination of bronchodilators, corticosteroids, antibiotics if necessary, controlled oxygenation, and non-invasive or, if required, invasive ventilation. An inhaled short-acting beta₂-agonist (salbutamol) and anticholinergic (ipratropium) were given upon arrival to the ED, followed by 6-h intervals, when additional dosages were given, on a pro re nata basis. Intravenous methylprednisolone (31.25 mg) was given upon presentation to the ED, followed by 31.25 mg once or twice daily. Methylxanthines was not used as they may interfere with HRV. An empiric antibiotic was administered to patients with at least two of the following symptoms: increased dyspnea, sputum purulence or sputum volume. Oxygen was delivered in a controlled manner to achieve a maximal oxygen saturation (90%–92%).

2.4. Assessment and hospital admission

The factors taken into consideration for hospital admission included a marked increase in the intensity of symptoms, onset of new physical signs, altered mental status, signs of respiratory failure, hemodynamic instability and a failure to respond to treatment after 24 h of ED observation.

2.5. Physiological parameters and processing of electrocardiogram signals

Arterial blood oxygen saturation (SpO₂) was recorded using an NPB-40 Handheld Pulse Oximeter (Nellcor Puritan Bennett Inc, Pleasanton, California). The HRV of all the participants was measured upon arrival at the ED before medical treatment, after 1 h of treatment, and 24-h after treatment. The detailed procedures used for HRV analysis have been described in other articles.¹³ A precordial electrocardiogram (ECG) was taken and recorded for 5 min, with the participants in a semi-recumbent posture. Electrocardiogram signals were recorded using an analog-to-digital converter with a sampling rate of 256 Hz. The digitized ECG signals were analyzed online and were simultaneously stored on a hard disk for

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