General Hospital Psychiatry 53 (2018) 59–64

Contents lists available at ScienceDirect

General Hospital Psychiatry

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

Longitudinal associations of burnout with heart rate variability in patients following acute coronary syndrome: A one-year follow-up study

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ARTICLE INFO

Keywords:
Burnout
Heart rate variability
Acute coronary syndrome

ABSTRACT

Objective: To investigate longitudinal associations of burnout with heart rate variability (HRV) in patients after their first acute coronary syndrome (ACS).

Methods: Two hundred eight patients participated in this one-year follow-up study. On the day before discharge, their personal burnout level was assessed by the Copenhagen Burnout Inventory. HRV signals were collected at four time points: the day before discharge, one month, six month and one year after discharge. HRV was measured by 24-h ambulatory electrocardiography and analyzed in time and frequency domains. Generalized estimating equations were applied to analyze the associations of burnout at baseline with longitudinal tracking of HRV during follow-up.

Results: After adjusting for relevant confounding factors, high burnout at baseline was significantly associated with low SDNN, a time domain measure of HRV [regression coefficient = −0.087, 95% CI = (−0.136, −0.038) by an increase per SD in burnout score, $p = 0.001$]. Also, baseline burnout was inversely associated with five frequency domain measures, i.e., HF [coefficient = −0.179, 95% CI = (−0.352, −0.006), $p = 0.043$], LF [coefficient = −0.171, 95% CI = (−0.319, −0.023), $p = 0.024$], VLF [coefficient = −0.367, 95% CI = (−0.483, −0.250), $p < 0.001$], ULF [coefficient = −0.268, 95% CI = (−0.351, −0.184), $p < 0.001$], and TP [coefficient = −0.283, 95% CI = (−0.340, −0.165), $p < 0.001$].

Conclusion: Personal burnout is longitudinally associated with decreased HRV during one-year period among patients after first ACS.

1. Introduction

For survivors of coronary heart disease (CHD), the burden of recurrent coronary events and cardiovascular mortality remains high [1]. Among several established risk factors, psychosocial factors have received special attention in the past decades, given their unique contribution to the prognosis of first CHD [2,3]. In particular, a growing body of evidence on prognostic value of depression for CHD patients suggested that depression after CHD could increase the risk of poor clinical outcomes, such as all-cause mortality (1.2–2.2 folded) and cardiovascular events (1.1–1.6 folded) [4,5]. However, research on other psychosocial factors has also accumulated notable evidence in recent years, burnout is such a case. Mainly being characterized as exhaustion, burnout is an affective response to stressors within and beyond occupational settings [6]. For instance, according to a couple of systematic reviews, burnout/exhaustion has been found to be associated with the risk of initial CHD by 53% [7,8]. Regarding the recurrent CHD / mortality, several studies examined the role of burnout/exhaustion [9–13]. In patients with CHD, burnout/exhaustion has been showed to be associated with a 2-fold increased risk of recurrence of cardiac events [14].

Yet, the bio-physiological mechanism between psychosocial factors and CHD is not fully understood. One of the well-accepted explanations focuses on the autonomic nervous system [15]. Heart rate variability (HRV) measures the variation in the time interval between heartbeats, which is a reflection of autonomic nervous system activity in relationship with other physiology processes, such as respiration and baroreflex sensitivity [16]. Large number of studies have demonstrated that

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https://doi.org/10.1016/j.genhosppsych.2018.05.008
Received 5 April 2018; Received in revised form 23 May 2018; Accepted 24 May 2018

decreased HRV is associated with elevated risk of developing CHD among healthy population [17], as well as increased risk of recurrent events and mortality in patients after myocardial infarction, heart failure, ischemic and idiopathic cardiomyopathy [18–20]. The interrelationships among depression, decreased HRV, and CHD have been accumulatively observed [21–23]. Unfortunately, research on burnout and HRV is still quite scarce, even though HRV has been suggested as one biomarker of burnout [24]. To date, one study reported significant associations between burnout and HRV in healthy individuals [25]. Four studies compared HRV between CHD patients with burnout and healthy controls, of which two did not find any differences [26,27], whereas the other two reported reduced HRV in the burnout patients [28,29].

To the best of our knowledge, no study has investigated the relationship between burnout and HRV in CHD patients; also, all of the above mentioned five studies on burnout and HRV were with cross-sectional design [25–29]. In order to fill this research gap, we conducted a hospital-based longitudinal study among patients with first acute coronary syndrome (ACS), with hypothesis that personal burnout at baseline would affect HRV trajectory during the year after ACS. Previously, we have found that burnout was prospectively associated with poor physical performance and low quality of life [30]. In this study, we aimed to explore the longitudinal associations of burnout with HRV in a sample of ACS patients as an attempt to provide scientific evidence to explain HRV-related mechanism between burnout and CHD.

2. Methods

2.1. Study subjects

The details of this study have been described elsewhere [30]. In summary, this was a hospital-based longitudinal study with a one-year follow-up period. The study subjects were patients with their first ACS, who were admitted into the coronary intensive care unit, 1st Affiliated Hospital of Kunming Medical University, China, during March 2013 to April 2014. ACS was defined as ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), or unstable angina (UA) [31,32]. The protocol of this research project was approved by the Ethics Committee of Kunming Medical University (Kunming, China), and the Yale University Human Investigation Committee (New Haven, USA). The written informed consent was obtained from each participant, and this study was carried out in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

2.2. Collection of socio-demographic and medical data

Research staff administered a questionnaire survey to collect participants' personal data (age, sex, medical history, family history of cardiovascular disease, smoking status, alcohol consumption, education level, occupation, etc.). Data on physical exam and laboratory values (Killip class, serum biochemistry, etc.) on admission were collected through review of the medical record.

2.3. Assessment of burnout

All participants were interviewed to assess their burnout level on the day before discharge, using the personal burnout subscale of Copenhagen Burnout Inventory (CBI) [33]. The subscale on personal burnout measures the degree of physical and psychological exhaustion/fatigue of the respondents. The items of this scale do not refer to occupational factors and can be answered by all respondents regardless of employment status. The Chinese version of CBI has been developed with satisfactory reliability and validity [34]. The Cronbach's alpha coefficient for the 6-item CBI personal burnout subscale was 0.74 in our study. The potential score range of CBI is 0 to 100, high scores indicating high levels of burnout [33]. Given that there is no solid clinical cut-off point so far to define high or low burnout, the continuous values of personal burnout were used for the analyses.

In addition, depression as another psychosocial factor was also measured at the same time using the depression subscale from the Hospital Anxiety and Depression Scale (HADS), being largely composed of reflections of the state of anhedonia (i.e., loss of interest and lack of enjoyment) [35]. This instrument has been successfully applied into Chinese CHD patients [36]. The Cronbach's alpha coefficient for the 7-item HADS-depression subscale was 0.76 in our study. The depression is ranged from 0 to 21, with high scores indicating high levels of depressive symptoms [35].

2.4. Measurement of HRV

HRV was repeatedly measured four times: the day before discharge, one month, half a year and one year after discharge, respectively. All participants underwent Holter monitoring, which began between 08:00–09:00 in the morning and lasted 24 h. The continuous electrocardiograph (ECG) signal of 24 h was recorded using 12-channel Holter system provided by Biomedical Systems of the United States. After the recording, the analog ECG signal was converted to digital signal and analyzed by the BMS Century 3000 HRV analysis software package (version 2.0). The analysis system automatically identified sinus heartbeat, excluded the RR interval before and after the premature beat, and all the RR intervals which were 20% longer than their previous RR interval, so that obtained all normal RR intervals of 24 h. A time domain measure, i.e. the standard deviation of all normal RR intervals (SDNN), was calculated. Then the normal RR interval of 24 h was changed into the heart rate power spectrum by fast Fourier transform, and five frequency domain measures were calculated: [1] high frequency (HF 0.15–0.40 Hz) power; [2] low frequency (LF 0.04–0.15 Hz) power; [3] very low frequency (VLF 0.0033 to 0.04 Hz) power; [4] ultra low frequency (ULF $<$ 0.0033 Hz) power; [5] total power (TP $\leq$ 0.40 Hz) [16]. The measures of these six HRV parameters were then transformed to their natural logarithm, i.e., ln(SDNN), ln(TP), ln(HF), ln(LF), ln(VLF), and ln(ULF), due to skewed distribution.

2.5. Statistical analyses

Continuous variables were presented as means ± standard deviations (SDs), and relative frequencies were used to summarize categorical variables. Linear correlation was applied to analyze the inter-relationships between each continuous variable and HRV measures at baseline. Mean values for HRV measures at baseline according to categorical variables were analyzed by *t*-test or one-way analysis of variance. Due the fact that HRV data during the one-year follow-up were collected four times, generalized estimating equation (GEE) was used to analyze this type of data with repeated measures, taking change over time into account [37]. The results were shown as regression coefficients of the HRV parameters induced by an increase per SD in burnout score at baseline (continuous measure) and their 95% confidential intervals (CIs). Two-step stepwise regression models were performed. Firstly, all univariable associations between every independent variable and HRV measures during the one-year follow-up were calculated. Secondly, variables with $p < 0.20$ in the univariable analyses were included in the multivariable analysis; in this step, the value of $p < 0.05$ (two-sided) was considered as significant. The statistical analyses were performed using the Stata 10 statistical package.

3. Results

3.1. Baseline characteristics of study subjects

Of the 208 patients who participated in this study, 151 were male