



Original Contribution

Preoperative depressed mood and perioperative heart rate variability in patients with hepatic cancer^{☆,☆☆}



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Abstract

Study Objective: How perioperative heart rate variability (HRV) indices differ according to the anxiety or depressed mood of patients scheduled to undergo a major surgical procedure for cancer.

Design: Prospective observational study.

Setting: Operating room.

Patients: Forty-one male patients between 40 and 70 years of age with hepatocellular carcinoma were included in the final analysis.

Interventions: HRV was measured on the day before surgery (T1), impending anesthesia (T2), and after anesthetic induction (T3). Preoperative anxiety and depressed mood of all patients were evaluated using the State-Trait Anxiety Inventory and Self-Rating Depression Scale (SDS).

Measurements and Results: HRV was significantly different among T1, T2, and T3. At T2, high frequency (HF) (normalized units of HF [nuHF]) was decreased and low frequency (LF) (normalized units of LF) and LF/HF were increased compared with those at T1 and T3. In the subgroup analysis between high and low SDS groups, high SDS group showed significantly decreased nuHF ($P = .035$), increased nuLF ($P = .039$), and increased LF/HF ($P = .020$) compared to low SDS group at T1. However, these values at T2 and T3 were not different between 2 groups. In analysis within the groups, low SDS group showed significant differences in nuHF, nuLF, and LF/HF among T1, T2, and T3 ($P < .05$, respectively), but no changes in these values were observed in high SDS group among the 3 different time points.

Conclusions: HRV decreased significantly immediately before anesthesia and recovered to baseline with anesthetic induction. Preoperative, more depressed patients showed increased sympathetic tone at baseline and blunted response to impending anesthesia on the HRV measurements.

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1. Introduction

Preoperative anxiety has a prevalence of between 11% and 80%, depending on the assessment method [1,2]. Based on available physiological data, the event before impending anesthesia is the most stressful one from a patient perspective [3]. Several studies have shown that presurgical patients have increased self-reported anxiety scores [4-6]. These preoperative psychological stress can affect the stability of the autonomic nervous system (ANS) [1,2,7] and may complicate the perioperative course in the surgical patients undergoing general anesthesia, increasing morbidity and mortality, and therefore, it should be considered as an additional risk factor during preoperative evaluation [4-6,8].

Cancer patients experienced emotional changes including the anxiety and depressed mood. In 1 study, 77% patients with cancer recalled experiencing anxiety [7]. The anxiety may also be present in association with depressed mood, which is the most common emotional symptom in patients with cancer [7,9]. Therefore, we assumed that the patients waiting for cancer surgery may have higher preoperative anxiety than non-cancer patients and the increased anxiety in these patients might destroy the balance of ANS.

Heart rate variability (HRV) has been used as a simple, noninvasive method to evaluate the sympathovagal balance of the ANS at the sinoatrial level [8,10] and can be used as a monitoring tool in clinical conditions with altered ANS function [11,12]. Increased HRV indicates a well-controlled ANS that is able to respond to stressful events [13,14]. A decline in HRV, an autonomic imbalance associated with increased sympathetic activity and reduced vagal tone, has been strongly implicated in the pathophysiology of fatal arrhythmia, acute myocardial infarction, congestive heart failure, and sudden cardiac death [12,15-17].

There is a paucity of studies relating preoperative anxiety or depressed mood and perioperative HRV in cancer patients. Therefore, the aim of this study was to evaluate how perioperative HRV indices differ according to the anxiety or depressed mood of patients scheduled to undergo a major surgical procedure for cancer.

2. Materials and methods

2.1. Study design and subject selection

This prospective cohort study was approved by the institutional review board of our institution (ref: SMC 2012-08-043) and registered with Clinical Trials (ref: NCT02011074). After obtaining preoperative informed consent, 50 adult male patients undergoing elective surgery for hepatocellular carcinoma (HCC) from April 2013 to December 2013 were enrolled in the study. Only male patients, 40 to 70 years old, previously healthy or with mild systemic disease who underwent surgery in the morning were included [12]. Exclusion criteria were as

follows: history of a psychiatric disorder, autonomic nervous system dysfunction, or disease that can affect the ANS (eg, malignant hypertension, uncontrolled diabetes, arrhythmia, thyroid dysfunction). No premedication was offered to any of the patients. Anesthesia in the current study was induced with thiopental sodium 5 mg/kg and sevoflurane under 100% O₂ mask ventilation, followed by the muscle relaxant vecuronium 1 mg/kg to facilitate tracheal intubation. Patients' lungs were ventilated at a rate of 10 breaths per minute with sevoflurane and an oxygen/air mixture using positive pressure ventilation. To maintain anesthesia, standard monitoring of invasive arterial blood pressure, electrocardiogram, peripheral oxygen saturation, and bispectral index (BIS) were performed.

2.2. Psychological evaluation

Patients' psychological status was examined the day before surgery using 2 self-report questionnaires: the State-Trait Anxiety Inventory (STAI) [18] and the Self-Rating Depression Scale (SDS) [19]. STAI is widely used as a self-report anxiety assessment instrument. It comprises two 20-item scales that measure state and trait anxiety, respectively. The STAI is the criterion standard for assessing anxiety in adults and has been used with good validity and reliability [18]. In this investigation, we used the STAI to assess both the situational (state, STAI-S) and the baseline (trait, STAI-T) anxiety of the patients. Scores range from 20 to 80 for both scales, and higher scores represent higher anxiety. SDS was used to evaluate patients' depression [19,20]. SDS consists of 20 items that were constructed based on clinical diagnostic criteria and is commonly used to characterize depressive disorders. A high total score corresponds to the presence of more depressive symptoms (cutoff, 50 of 80).

2.3. HRV measurement

We assessed HRV at the following 3 study time points: on the day before surgery (T1), immediately before anesthesia (T2), and approximately 10 to 15 minutes after anesthetic induction (T3) when the BIS was between 40 and 60, end-tidal sevoflurane was 1.8% to 2.5%, and the patient had a stabilized hemodynamic status ($\pm 20\%$ of baseline heart rate [HR] and blood pressure). HRV was recorded for 150 seconds for each patient in the supine position. The electrocardiographic/HRV recordings performed were free of artifacts and dysrhythmias. In this study, we used HRV-Addon (LAXTHA, Inc, Daejeon, Korea) to measure components of HRV. HRV is measured by variation in beat-to-beat intervals and is usually analyzed using time and frequency domain methodologies. Frequency domain technique, which involves the use of a fast Fourier transform method, determines a spectrum with 2 major frequency bands: low frequency (LF) and high frequency (HF) [10]. The LF band mainly reflects sympathetic discharge of baroreceptor-mediated regulation. The HF band reflects modulation of parasympathetic nerve activity caused by respiratory

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