Power spectral analysis of heart rate variability and autonomic nervous system activity measured directly in healthy dogs and dogs with tachycardia-induced heart failure

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BACKGROUND Heart rate variability (HRV), calculated in the frequency or time domain, decreases in congestive heart failure (CHF). In HRV power spectral analysis, the low-frequency (LF) component diminishes in patients with CHF and the decrease is related to an increased risk of sudden death.

OBJECTIVE Our aim was to clarify the nature of HRV power spectral analysis in normal and CHF dogs.

METHODS Using an implanted radiotransmitter, we directly studied integrated left stellate ganglion nerve activity (iSGNA), integrated vagal nerve activity (iVNA), and electrocardiographic tracings before and after pacing-induced CHF in 6 ambulatory dogs. In a short-term power spectral analysis of HRV, we measured power spectral density during high, medium, and low sympathetic and vagal nerve activity. We analyzed 38 data segments characterized by the same autonomic nerve activity patterns at baseline and after pacing-induced CHF.

RESULTS As compared with baseline, the spectral variables during CHF showed decreased total power ($P = .002$), LF power ($P < .0001$), and the LF/high frequency (HF) ratio ($P = .005$) and increased iVNA and iSGNA ($P < .0001$ for both). Only at baseline, iSGNA correlated positively with LF power ($P < .05$, $r = 0.314$). Under the same condition iVNA correlated positively with the HF component expressed as normalized units ($P < .05$, $r = 0.394$) and negatively with the LF component expressed both as absolute power ($P < .05$, $r = -0.464$) and normalized units ($P < .05$, $r = -0.425$).

CONCLUSION The spectral variables (LF power and the LF/HF ratio) and direct variables measuring sympathetic nerve activity (iSGNA) correlate at baseline but not during CHF. At baseline, the vagal activity (iVNA) is associated with an increase in HFnu and a decrease in LFnu. These data indicate that the reduction in LF power and LF/HF ratio observed in heart failure dogs are likely to reflect a diminished sinus node responsiveness to autonomic modulation or an abnormal baroreflex function rather than an increased sympathetic activity.

KEYWORDS Autonomic nervous system; Power spectral analysis; Heart rate variability; Congestive heart failure; Vagal nerve activity; Sympathetic nerve activity; Sudden death

(Heart Rhythm 2009;6:546–552)

Introduction

Neurohumoral activation in congestive heart failure (CHF) is thought to be important in the mechanisms of sudden cardiac death (SCD) and malignant ventricular arrhythmias. For more than 3 decades, power spectral analysis of heart rate variability (HRV), an indirect technique for assessing autonomic modulation of the cardiovascular signals, has been used as a noninvasive clinical tool for measuring autonomic nervous system (ANS) activity. In recent years, the HRV variables have acquired growing importance in stratifying the risk of SCD[1–3] and in serving as a clinical marker of CHF severity.[4,5] Among the HRV variables, in healthy subjects, low-frequency (LF) power (between 0.04 Hz and 0.15 Hz), especially as expressed in the normalized form, and the ratio between LF power and high-frequency (HF) power (LF/HF), increase during sympathetic stress (for example orthostatic testing).[6] Conversely, during CHF no correlation is found between these spectral variables and increased sympathetic activity.[5] In patients with CHF, how-

This study was supported in part by National Institutes of Health grants P01 HL78931, R01 HL78932, 71140, International Research Fund for Subsidy of Kyushu University and International Research Funds for Subsidy of Fukuoka University School of Medicine Alumni (M.O.), by an American Heart Association Established Investigator Award (S.F.L.), and by Medtronic-Zipes Endowments (P.S.C.). This manuscript was processed by a guest editor. The authors thank Lei Lin, Jian Tan, and Stephanie Plummer for their assistance. **Address reprint requests and correspondence:** Dr. Gianfranco Piccirillo, Dipartimento di Scienze dell'Invecchiamento, I Clinica Medica, Policlinico Umberto I, Viale del Policlinico, 00161, Rome, Italy. E-mail address: gianfranco.piccirillo@uniroma1.it. (Received September 16, 2008; accepted January 2, 2009.)

1547-5271/$ -see front matter doi:10.1016/j.hrthm.2009.01.006

ever, decreased (rather than increased) LF power is associated with the risk of SCD[1–3] or progression of CHF.[4,5] Despite this behavior, the physiological meaning of LF power remains controversial. Most investigators agree that LF power, especially when expressed in the normalized form, is a marker of sympathetic activity at the sinus node. Others, in earlier and more recent studies, have questioned this interpretation, favoring LF power as a marker of baroreceptor activity.[7,8] Hence the LF power reduction during CHF is variously interpreted from study to study either as a paradoxical response to spectral sympathetic hyperactivity or as a CHF-induced reduction in baroreceptor activity.

We recently developed methods to record ANS activity in ambulatory dogs before and after the induction of CHF by rapid pacing.[9] The results showed that during CHF, integrated left stellate ganglion nerve activity (iSGNA) and integrated vagal nerve activity- (iVNA) both increased. The purpose of the present study was to compare short-period power spectra analysis in selected data recording epochs with known direct ANS activity in normal and CHF condition.

Materials and methods

Surgical preparation and electrical recording

The data analyzed came from a previous study conducted in 6 female dogs.[9] The surgical procedures and the temporal relationship between cardiac arrhythmia and ANS activity have been reported in detail elsewhere.[9,10] In brief, a pacing lead was implanted in the right ventricular apex and connected to an Itrel neurostimulator (Medtronic, Minneapolis, Minnesota) in a subcutaneous pocket. We then implanted a Data Sciences International (DSI, St. Paul, MN) D70-EEE transmitter with 3 bipolar recording channels for simultaneous recording of SGNA, VNA from the left thoracic vagal nerve located above the aortic arch, and subcutaneous electrocardiogram. After implantation, the Itrel stimulator was initially turned off for 2 weeks to allow the dogs to recover from surgery and to obtain baseline recordings. The stimulator was then programmed to pace at 150 beats/min for 3 days, at 200 beats/min for 3 days, and then at 250 beats/min for 3 weeks to induce CHF. The pacemaker was then turned off to allow an additional 2 weeks of ambulatory monitoring and recording during CHF. All of the recordings obtained during CHF were obtained within the first week. All dogs underwent echocardiography and venous blood sampling to determine serum N-terminal brain natriuretic peptide (NT-proBNP) concentrations at baseline and after rapid pacing.

Direct measurement of autonomic nervous activity

Data were recorded real-time at a sampling rate of 1,000 samples per second per channel, then analyzed off-line. The software used has been described elsewhere.[9,10] In summary, to analyze long-term trends in the large segmented data files effectively, a custom-designed program was developed using Labview software to automatically import, filter, and analyze the DSI transmitter data for ANS activities and heart rates. The software determined the activation cycle lengths (RR intervals) automatically derived from electrocardiogram (ECG), based on a Hilbert transform algorithm.[11] The data from stellate ganglion (channel 1) and vagal nerve (channel 2) were high-pass (200 Hz) filtered and rectified over a fixed time segment. The nerve activity was then integrated (Figure 1). The inter-beat intervals (IBIs) were also calculated, resampled at 4 Hz, and after detrending, were used to calculate the HRV variables. Because IBIs shorter than 200 ms were usually caused by either ectopic beats, artifacts, or rhythm disturbances, they

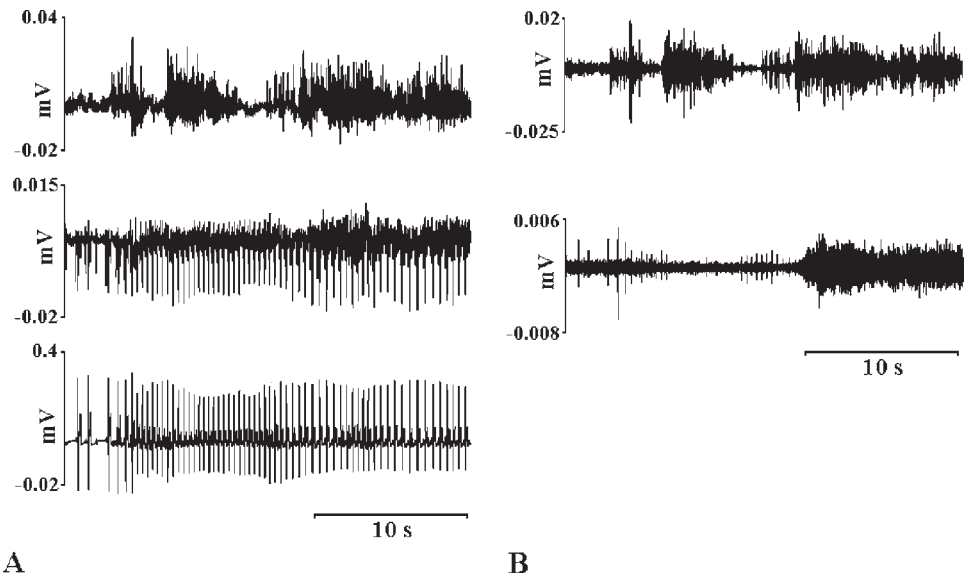

Figure 1 Simultaneous stellate ganglion nerve activity (SGNA) and vagal nerve activity (VNA) during severe congestive heart failure (CHF). Upper panel: SGNA, middle panel VNA, lower panel electrocardiographic (ECG) trace. On the left, raw recording **(A)**, and on the right filtered recording to eliminate ECG contamination **(B)**.