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Circadian Rhythms of Spectral Components of Heart Rate Variability

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Abstract—**Circadian rhythms of heart rate variability have been widely studied in recent years. However, most previous reports described such rhythms in terms of normalized units of the low- and high-frequency (LF and HF) spectral components. In this study, we analyzed circadian rhythms of spectral components in absolute units and found unexpected results in normal subjects as well as coronary heart disease (CHD) and congestive heart failure (CHF) patient groups. The results indicate that the notion of sympathovagal balance needs to be re-evaluated.**

I. INTRODUCTION

IN 1981, Akselrod and his colleagues proposed that heart rate variability (HRV), as revealed by power spectral analysis, might be a useful quantitative probe of autonomic control in the cardiovascular system (Akselrod, 1981). According to their analysis, there are three main peaks - high, low and very low frequency components – in the power spectrum of HRV time series. The high-frequency (HF) component is modulated by parasympathetic nervous system, and low-frequency (LF) component is modulated by both sympathetic and parasympathetic nervous systems. Since then, linear analyses either in time or frequency domains of HRV have been applied to investigate cardiac diseases, as well as other diseases with neurological disorder (Task Force, 1996). With the increasing interest in HRV, the interpretation of its spectral components has received much attention. As a first approximation, Malliani et al. proposed that LF and HF represent the sympathovagal balance because "*In most physiological conditions, the activation of either sympathetic or vagal outflow is accompanied by the inhibition of the other*" (Malliani, 1991, 1999). The underlying assumption is that LF and HF are modulated by sympathetic and parasympathetic nervous activity, respectively. This hypothesis was suggested by a mathematical model of DeBoer et al. (1987), in which LF was modeled by a band-pass filter with 0.1 Hz frequency describing sympathetic memories.

On the other hand, the circadian rhythm of HRV may be indicative of changes in sympathovagal balance. Furlan (1990) reported the 24-hr recording of LF and HF components of HRV and blood pressure variability (BPV) for ambulant subjects and concluded that the day-night changes of these components are markers of sympathovagal balance. However, they only showed these components in normalized units for HRV. A similar approach was reported by Huikuri (1994).

In this work we analyzed the circadian rhythms of HRV in both normalized and absolute units of the power spectrum for healthy, coronary heart disease (CHD) and congestive heart failure (CHF) subjects. In contrast to previous studies using normalized units, we found that the absolute powers of LF and HF components did not exhibit reciprocal changes. Therefore, the interpretation of the spectral components of HRV needs to be re-evaluated.

II. METHODOLOGY

A. Data acquisition

The data of healthy subjects (n=8) and CHF (n=8) patients were obtained from Physionet (Goldberger, 2000), and the data of coronary heart disease (CHD, n=10) were recorded in our laboratory. Sample rates of 24-hr Holter recordings were 128-250 Hz.

B. Linear analysis

Autoregression model and its power spectrum density (equation 1 and 2) were applied to analyze the linear characteristics of 24-hr heartbeat recordings. The 24-hr heartbeats were divided into 120 segments for spectral analysis and all spectra were plotted in a mesh type.

$$y_n^{lin} = a_0 + a_1 y_{n-1} + \cdots + a_k y_{n-k} + \varepsilon \tag{1}$$

$$X(\omega) = \frac{\varepsilon}{\left| 1 + \sum_{m=1}^{k} a_m e^{jm\omega} \right|^2} \tag{2}$$

Spectral components LF and HF were evaluated as integration of power spectral density at the following frequency

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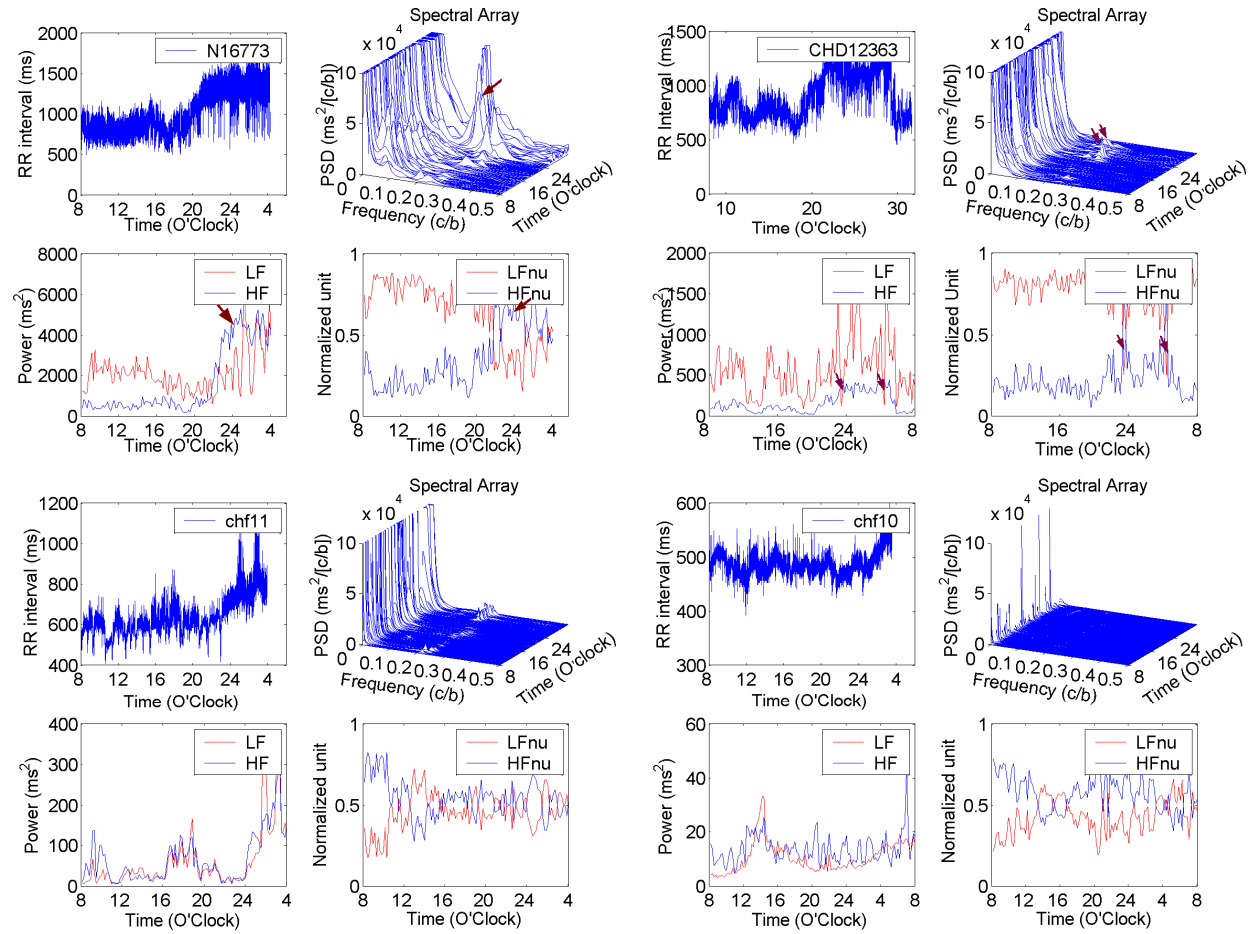

Fig. 1. Representative HRV in time and frequency domains, LF and HF in absolute and normalized units. N16773 was normal subjects; CHD 11937 was a patient with coronary heart disease; CHF10 and CHF11 were patients with congestive heart failure.

bands: very low frequency (VLF, <0.03 cycle/beat), low frequency (LF, 0.03-0.14 cycle/beat) and high frequency (HF, 0.14-0.4 cycle/beat). Normalized components of LFnu and HFnu were defined as:

$$LFnu = \frac{LF}{LF + HF}$$
$$HFnu = \frac{HF}{LF + HF} \quad (3)$$

III. RESULTS

Figure 1 shows some representative plots of HRV in the time and frequency domains, with LF and HF in both absolute and normalized units. In time domain, the heart rates were decreased at night for all subjects as expected. There were HF components for normal and CHD patient only at night but not during daytime. Occasionally, tiny peaks of HF could be observed in siesta as in the plot of patient CHD 11937. Variations of heart rate in CHF patients were much lower than in normal and CHD subjects as revealed by the ordinates of the spectral array. There were reciprocal changes in LFnu and HFnu symmetrical about the 50% line for all subjects, as per their definitions. Normal and CHD subjects showed circadian rhythms in LFnu and HFnu, while CHF patients did not. In contrast, when plotted in absolute units both LF and HF increased at night except for patient CHF11. Thus, in absolute values LF and HF did not change reciprocally. Interestingly, the duration in which HF exceeded LF at night for normal subject and CHD patient was coincident with those of the HF peaks (designated by arrows). There were two types of variation of LF and HF in the CHF group. One is indicated in CHF11 with concomitant changes in LF and HF, and the other is indicated in CHF10, in which LF appeared to be low-pass filtered and lost quick response.

The LF/HF ratio is a widely used index of sympathovagal balance. Figure 2 shows the LF/HF for three individuals. For both normal subject and CHF patient the LF/HF ratio exhibited circadian rhythm with LF dominance diurnally and HF dominance nocturnally. For the CHF patient, LF/HF was around 1 suggesting that neither LF nor HF was dominant all the time.

Figure 3 shows the circadian variations of the

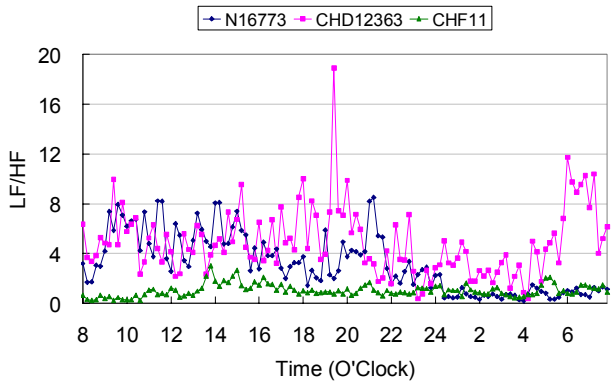

Fig. 2. The LF/HF ratio in individuals of healthy, CHD and CHF patients. Circadian rhythm exhibited in normal subject and CHD patient, but not in CHF patient.

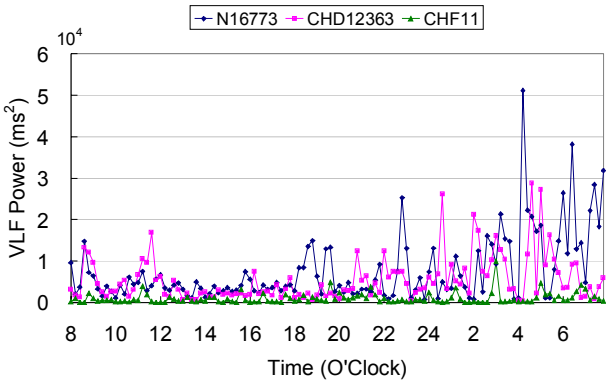

Fig. 3. VLF power in healthy subject, CHD and CHD patients. Nocturnal VLF was larger than diurnal ones in normal and CHD patient. Whereas circadian rhythm did not exhibit in CHF patient.

very-low-frequency (VLF) component of HRV. VLF had large values from 22 pm to 9 am for normal subject, but from 0 am to 6 am for CHD patients. No circadian rhythm can be seen in CHF patients.

IV. DISCUSSION

The LF and HF spectral components of HRV have received a lot of attention as markers of sympathetic and parasympathetic activities, respectively. The most important evidence supporting sympathovagal balance is the circadian rhythm of spectral components of HRV. Although absolute units (ms^2) of spectral components have been used to evaluate the prognosis of CHF (Guzzetti, 2005) recently, in previous studies only normalized units were used to describe sympathovagal balance of HRV spectral components. The present results showed that the LF and HF components did not change reciprocally in absolute units. Thus the interpretation of LF and HF, and hence the perspective of sympathovagal balance, need to be re-evaluated.

Originally, the HF component was considered to be modulated by parasympathetic activity, while LF was modulated by both sympathetic and parasympathetic activities as reported by Akselrod (1981). If we return to this notion, i.e. LF component is composed of both sympathetic and vagal contents while HF component is influenced by only parasympathetic content, the results may be interpreted more easily. For example, if we consider that LF includes parasympathetic activity, the large value of LF at night is reasonable because vagal activity increases nocturnally. Similarly, the concomitant variations of LF and HF components in CHF patients may be explained as exhausted sympathetic function, which will be discuss below.

CHD and CHF are hemodynamic diseases in themselves. CHD, also known as ischemic heart disease, is indicated when the blood supply to the myocardium is insufficient for its needs. Myocardial infarction caused by the fissuring of atherosclerotic plaques has been demonstrated to affect autonomic function (La Rovere, 1998). Congestive heart failure (CHF) is said to have occurred when the heart is no longer able to maintain the circulation to the tissues for normal metabolism, e.g., as a result of damaged cardiac muscles. Physiologically, the varying demand of cardiac output is regulated by neurohumoral systems through inotropic, chronotropic and dromotropic effects of the myocardium. For instance, during daytime or performing exercises, physical activities will lead to excitation of sympathetic tone and inhibition of parasympathetic tone to elevate heart rate and blood pressure. Therefore, a reduction of cardiac contractility in CHD or CHF is compensated by an increase in filling pressure via neurohumoral systems in order to restore cardiac output. It is well known that the sympathetic nervous system acts on the myocardium with positive inotropism, chronotropism and dromotropism. Thus it plays an important role in the compensation of cardiac contractility, and peripheral vasoconstriction/venoconstriction to elevate system blood pressure and to fulfill the demand of cardiac output.

However, in our results, the absolute values of LF power did not increase, but decreased for CHD and CHF patients. Especially, LF power during diurnal hours in CHD was much lower than the healthy subject. It seems that the excitation of the sympathetic nervous system in CHD was depressed, and the sympathetic activity was exhausted in CHF. This result is similar to the result of LF loss in CHF reported by Van de Borne et. al. (1997) although they insisted that sympathetic activity was still excited in CHF patients for high level of muscle sympathetic nervous activity. LF/HF is an index of sympathovagal balance. Figure 2 shows that LF/HF was increased nocturnally in CHD, but was reduced in the CHF patient with no circadian rhythms. Therefore it may be imbalanced between parasympathetic and sympathetic branches in CHD, but impairment of both branches of the autonomic nervous system in CHF. This impairment leads to insufficient compensation, even decompensation, in hemodynamics.

Reciprocal change of sympathovagal balance is attributed

mainly to close-loop barorereflex. Really, increase of blood pressure will lead inhibition of sympathetic efferent and excitation of vagal efferent, resulting in bradycardia to reduce cardiac output. However, baroreceptor reflex is affected by physiological factors. For example, defence reaction inhibits, while vasopressin facilitates baroreflex. Therefore, unlike at rest or in sleep, baroreceptor reflex is not the only factor to determine cardiovascular regulation. Defence reaction is initially defined as the response when an animal faces an enemy; now it is extended to behaviors with sympathetic hyper-activity, such as mental arithmetic and the stress of daily urban life (Schenberg, 1993). The signal inducing defence reaction is not within the closed loop of baroreceptor reflex, but is descended from higher level of cardiovascular center, such as mid-brain or cerebral cortex. The effect of defence reaction is tachycardia and increase of blood pressure. Therefore in open-loop cardiovascular regulation reciprocal change of sympathovagal balance is not the only option. Both concomitant and reciprocal alterations of LF and HF of HRV are possible.

The perspective of sympathovagal balance has been challenged by Eckberg (1997) who argued that "*the construct of sympathovagal balance imposes attributes on physiological regulatory mechanisms that they do not possess*". In addition to open-loop control, pre-synaptic interaction of sympathetic and vagal efferents may be another factor to interfere with reciprocal changes of LF and HF, because pre-synaptic interaction changes their drives to cardiac pacemaker. Thus, sympathetic efferent could be significant influenced by vagal efferent even before reaching cardiac pacemaker. Pre-synaptic interaction introduces nonlinearity in cardiac-autonomic regulation which cannot be accounted for by linear interpretation of HRV spectral components. Probably this is the reason why there is confusion in interpreting various experiment results. Although pre-synaptic interaction has not been quantified up to now, it may give an available interpretation of cardiac response to autonomic efferents. Pyetan and Akselrod (2003) suggested a mathematical model to elucidate the nonlinear interaction of cardiac sympathetic and vagal efferents and concluded that sympathetic activity plays some role in modulating RSA. Therefore, the relationship between autonomic function and spectral components of HRV still needs further discussion.

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