

Heart Rate Variability in Patients with Coronary Artery Disease*

관상동맥질환 환자의 심박동변이도

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Abstract · This study is based on previous information regarding reduced cardiac vagal activity in patients with coronary artery disease(CAD), on reduced variance(SDNN : standard deviation of all normal RR intervals), low-frequency power(LF), and the complexity of heart rate variability(HRV) in patients with chronic heart failure(CHF), and on the normalized high-frequency power of HRV is the highest in the right lateral decubitus position among 3 recumbent postures in patients with CAD. However, nothing is known about the nonlinear dynamics of HRV for the 3 recumbent postures in patients with CAD. To investigate the linear and non-linear characteristics of HRV in patients with CAD, 29 patients as CAD group and 23 patients as control group were studied. Electrocardiogram(ECG) with lead II channel was measured on these patients for 3 recumbent postures in random order. The HRV from ECG was analyzed with linear method(for time and frequency domains) and nonlinear method. The lower the high-frequency power in normalized unit(nHF) in the supine or left lateral decubitus position, the higher the increase in nHF when the position was changed from supine or left lateral decubitus to right lateral decubitus. Among the 3 recumbent postures in patients with severe CAD, the right lateral decubitus position was observed to induce the highest vagal modulation, the lowest sympathetic modulation, and the highest complexity of human physiology system.

Key words Heart rate variability(HRV), Time and frequency domains, Complexity, Coronary artery disease (CAD), Recumbent posture

* Selected as an excellent paper in 2004 Korea-Japan Joint Symposium on Emotion & Sensibility.

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요약 : 본 연구는 관상동맥 질환(coronary artery disease : CAD) 환자의 심장 부교감신경 활성화가 감소하고, 만성 심부전(chronic heart failure : CHF) 환자의 심박동변이도(heart rate variability : HRV)에서 정상적 RR 간격의 분산(SDNN : standard deviation of all normal RR intervals)과 저주파수 대역의 전력스펙트럼(low-frequency power : LF), 그리고 복잡성이 감소하며, CAD 환자의 우측으로 누운 자세에서 HRV의 규격화된 고주파수대역의 전력스펙트럼(normalized high-frequency power : nHF)가 3가지 누운 자세 중에서 가장 높다는 사전 정보에 근거하였다. 세 가지 누운 자세에 대한 HRV의 비선형 특징은 알려진 바가 없으므로, 본 연구에서는 관상동맥질환 환자들을 대상으로 누운 자세에서 HRV의 선형과 비선형특성을 조사하였다. 이 목적을 위하여, 관상동맥질환군 29명과 통제군 23명을 대상으로 세 가지 누운 자세에서 심전도의 Lead II 채널을 측정된 뒤, 심전도로부터 심박동변이도의 선형특성(시간영역과 주파수영역)과 비선형특성을 분석하였다. 똑바로 누운 자세 또는 좌측으로 누운 자세에서 심박동변이도의 nHF가 더 작을수록, 이 자세들로부터 우측으로 누운 자세로 전환할 때 nHF가 더욱 증가하였다. 중증의 관상동맥질환 환자의 세 가지 누운 자세 중에서, 우측으로 누운 자세는 심장부교감신경계의 활성도를 가장 높게, 심장교감신경계의 활성도는 가장 낮게, 그리고 생체시스템의 복잡성은 가장 높게 유도함을 확인하였다.

주제어 : 심박동변이도, 시간 및 주파수 영역, 복잡성, 관상동맥질환, 누운 자세

1. Introduction

One of the most interesting non-invasive diagnostic methods increasingly used in medicine is analysis of heart rate variability(HRV) [5, 12]. It has been reported that HRV is related to autonomic nerve activity and is used as a clinical tool to diagnose cardiac autonomic function in both health and disease [14]. In patients with coronary artery disease(CAD), reduction of the cardiac vagal activity evaluated by spectral HRV analysis was found to correlate with the angiographic severity [6]. The reduction of variance(SDNN : standard deviation of all normal RR intervals) and low-frequency power(LF 0.04-0.15 Hz) of HRV seem related to an increase in chronic heart failure(CHF) [3]. The LF of HRV is decreased or absent in CHF patients with advanced disease and is related to the progression of the heart failure. The complexity of HRV seems reduced in CHF. In particular, the approximate entropy

(ApEn) [11], a measure of complexity, is lower in CHF patients than in controls. Patients with CHF were reported to prefer the right lateral decubitous position during sleeping, which attenuates sympathetic tone presumably due to an increase in cardiac output [8, 9, 10]. The normalized high-frequency power of HRV(nHF) is the highest in the right lateral decubitus position among 3 recumbent postures in patients with CAD [6]. Moreover, the mortality risk from acute myocardial infarction is lower in patients with higher vagal modulation [1, 6]. However, there have not been reported on non-linear characteristics of HRV for recumbent postures in patients with CAD.

Therefore, we intended to find the linear and non-linear characteristics of HRV depending on 3 recumbent postures in patients with CAD.

2. Method

For 74 patients with mild to severe CAD, who

have stenosis of luminal narrowing) 50% were recruited as the CAD group, the others were classified as the control group. They were instructed not to drink caffeinated beverages for more than 12 hours before ECG signals recording. This signals were recorded at Einthoven's Lead-II channel(right arm electrode : negative pole, left leg electrode : positive pole, right leg electrode : ground) with electrocardiograph(Model EKG-3000, Bionet Inc, Korea) during 5 minutes for each 3 recumbent postures with random order; supine, right lateral decubitus, and left lateral decubitus positions. Before recording ECG signals, patient took 5 minute rest for each recumbent posture to prohibit transient response of autonomic nervous system due to changing recumbent posture. Including 20 minutes needed in attaching and removing electrodes, about 50 minutes took for each patient in this study.

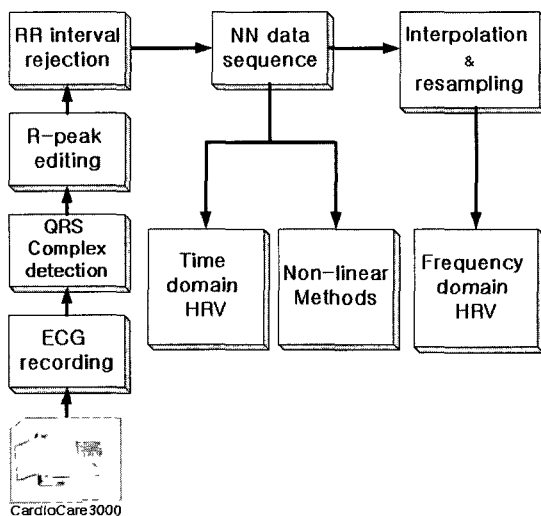


Figure 1. Flow chart of recording and processing the ECG signal in order to obtain data for HRV analysis[ECG = electrocardiogram, QRS complex = QRS waves in ECG, NN data = normal RR data after ejecting ectopic beats; HRV = heart rate variability]

The analog signals measured were converted to digital signals with sampling frequency of 500 Hz and resolution of $4.88 \mu\text{V/LSB}$. The HRV derived from the ECG was analyzed with time domain, frequency domain, and non-linear methods (see Figure 1). For statistical analysis, 29 patients in CAD group and 23 patients in control group were finally selected from the 74 patients. Informed consent was obtained for the patients before experiment.

3. Results and Discussions

For CAD group, the approximate entropy(ApEn) as a non-linear measure of HRV was higher in the right lateral decubitus position than in the supine position significantly($p=0.026$). This means that the complexity of the cardiovascular system is higher in the right lateral decubitus position than that of the supine position. In general, the complexity of cardiovascular system for healthy subjects is higher than that of the patients [4, 13, 15]. Miyamoto et al. demonstrated that patients with CHF during sleeping preferred the right lateral decubitus position, in which the imbalance of cardiac autonomic nervous activity was attenuated [10]. Therefore, the right lateral decubitus position is beneficial to those in patients with CAD or CHF.

There was a tendency that total power(TP : ≤ 0.4 Hz), very low-frequency power(VLF : ≤ 0.04 Hz)), and low-frequency power(LF : $0.04-0.15$ Hz) were lower in the right lateral decubitus position than in the supine position($p < 0.1$). There was a tendency that nHF(high frequency power(HF : $0.15-0.4$ Hz) in normalized unit($=100 \times \text{HF}/(\text{TP}-\text{VLF})$) was higher in the right lateral

decubitus position than in the supine position ($p=0.054$) and in the left lateral decubitus position ($p=0.057$), whereas $nLF(LF$ power in normalized unit ($=100 \times LF/(TP-VLF)$) was lower in the right lateral decubitus position than in the supine position ($p=0.054$) and in the left lateral decubitus position ($p=0.057$) (see Table 1). When the position was changed from supine or left lateral decubitus to right lateral decubitus, the percentage of change in nHF power in the severe CAD group was greater than that of the control group. The lower the nHF in the supine or left lateral decubitus position, the higher the increase in nHF when the position was changed from supine or left lateral decubitus to right lateral decubitus. The more severe the stenosis, the higher the increase in nHF when the position was changed from supine or left lateral decubitus to right lateral decubitus (see Figure 2). The percentage of change in nHF from supine to right lateral decubitus position $nHF(R/S)$ and that of from left to right lateral decubitus position $nHF(R/L)$ are defined as follows (see Equations (1) and (2))

$$nHF(R/S) = \frac{nHF(R) - nHF(S)}{nHF(S)} \times 100\% \quad (1)$$

$$nHF(R/L) = \frac{nHF(R) - nHF(L)}{nHF(L)} \times 100\% \quad (2)$$

, where $nHF(S)$, $nHF(R)$, and $nHF(L)$ are the normalized power of HF in supine, right lateral, and left lateral decubitus positions, respectively [6]. Because both vagal and sympathetic modulations in CAD group were significantly different from those of control group in both supine and the left lateral decubitus positions,

but not in the right lateral decubitus position, the right lateral decubitus position seemed to be capable of normalizing the autonomic nervous activity of patients with CAD toward normal.

Several mechanisms were suggested for the enhancement of vagal modulation and the suppression of sympathetic modulation when the right lateral decubitus position was assumed in patients with severe CAD or CHF [7, 10]. However, they were inconsistent in venous return. Miyamoto et al. postulated that the position of the heart is higher in the right lateral decubitus position, which results in decreased venous return [10]. However, Kuo et al. postulated that the lower positioning of the right atrium in the right lateral decubitus position facilitates greater venous return and higher right and left sided filling pressures, resulting in greater cardiac output [7]. At present research, we suggest a possible mechanism as follows: The position of the heart is higher in the right lateral decubitus position compared with the supine or left lateral decubitus position. This causes easy pumping of the blood from the heart to the rest of the body, which results in the increased cardiac output, while causes difficult in venous return. First, the increased cardiac output may induce the blood pressure rises both in carotid and in aorta, which results in both carotid sinus reflex and aortic reflex to increase the cardiac vagal nerve activity via cardioinhibitory center in the medulla oblongata. Second, the decreased venous return reduce the blood pressure in the venae cavae, which cause Bainbridge reflex to decrease the sympathetic activity via cardioacceleratory center in the medulla oblongata [2].

Table 1. HRV parameters for 3 recumbent postures

Parametres		Supine	Right Lateral	Left Lateral	
Control group (n=23)					
Time domain	SDNN(ms)	26.7 ± 10.4	24.5 ± 11.1	22.7 ± 10.4	
	SDSD (ms)	5.3 ± 2.3	5.4 ± 2.6	4.7 ± 1.9	
Frequency domain	TP (ms ²)	305.0 ± 240.1	273.9 ± 204.0	258.2 ± 200.6	
	VLF (ms ²)	143.0 ± 86.7	152.4 ± 125.3	142.8 ± 138.5	
	LF (ms ²)	108.1 ± 170.1	62.7 ± 63.4	71.3 ± 65.1	
	HF (ms ²)	54.0 ± 51.7	58.7 ± 57.1	44.2 ± 37.1	
	LF/HF	2.5 ± 2.5	1.4 ± 1.2	2.6 ± 3.7	
	nLF (nu)	59.4 ± 22.1	51.5 ± 18.0	59.4 ± 20.4	
	nHF (nu)	40.6 ± 22.1	48.5 ± 18.0	40.6 ± 20.4	
	Nonlinear	ApEn	0.59 ± 0.1	0.64 ± 0.1	0.62 ± 0.1
	CAD group (n=29)				
Time domain	SDNN(ms)	26.9 ± 11.4	22.3 ± 7.2	24.5 ± 8.3	
	SDSD (ms)	5.3 ± 2.3	5.3 ± 2.1	4.9 ± 1.6	
Frequency domain	TP (ms ²)	413.8 ± 514.5	253.6 ± 158.0	316.4 ± 206.8	
	VLF (ms ²)	268.8 ± 424.3	142.5 ± 116.2	202.9 ± 171.6	
	LF (ms ²)	85.4 ± 95.9	52.0 ± 63.5	65.8 ± 55.6	
	HF (ms ²)	59.6 ± 57.2	59.1 ± 42.0	47.6 ± 33.9	
	LF/HF	2.5 ± 4.3	1.4 ± 2.1	2.0 ± 2.3	
	nLF (nu)	54.7 ± 22.8	43.4 ± 21.5	54.6 ± 21.8	
	nHF (nu)	45.3 ± 22.8	56.6 ± 21.5	45.4 ± 21.8	
	Nonlinear	ApEn	0.59 ± 0.1*	0.64 ± 0.1*	0.60 ± 0.1

* p < 0.05

[SDNN = standard deviation of all NN intervals, NN intervals = normal RR intervals in electrocardiogram, SDSD = standard

deviation of differences between adjacent NN intervals, TP = total power, VLF = power in very low frequency range, LF = power in low frequency range, nLF = LF power in normalized unit(=100×LF/(TP-VLF)), HF = power in high frequency range, nHF = HF power in normalized unit(=100×HF/(TP-VLF)); nu = normalized unit, ApEn = approximate entropy][14].

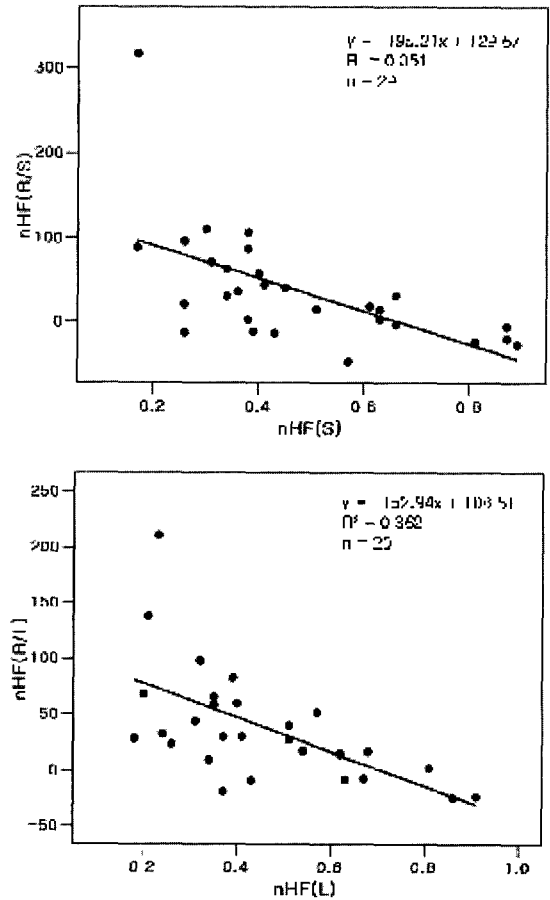


Figure 2. Effect of changing recumbent postures on HRV (CAD group).

[nHF(L) normalized high-frequency power during left lateral recumbent posture, nHF(S) normalized high-frequency power during supine position, nHF(R/S) = percentage of change in normalized high-frequency power when the posture was changed from supine to right lateral recumbent, nHF(R/L) = percentage of change in normalized high-frequency power when the posture was changed from left to right lateral recumbent, CAD = coronary artery disease].

4. Conclusions

Not only nLF, nHF, or LF/HF as a measure of linear characteristics but also ApEn as a measure of nonlinear characteristics of HRV can give an additional insight in studying physiological dynamics of RR interval time series. Among the 3 recumbent postures in patients with severe CAD, the right lateral decubitus position induce the highest vagal modulation, the lowest sympathetic modulation, and the highest complexity of human physiology system. The more severe the stenosis, the higher the increase in nHF when the position be changed from supine or left lateral decubitus to right lateral decubitus. The right lateral decubitus position is beneficial in patients with CAD.

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- 원고접수 · 2005. 1. 17.
수정접수 · 2005. 1. 24.
게재확정 · 2005. 1. 25.