Age Related Changes in Variability of Short-Term Heart Rate and Diastolic Period

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Abstract

Previous studies have proved that the heart rate variability (HRV) is preferentially expressed in cardiac diastolic period variability (DPV). Does that mean that DPV analysis should act as an alternative approach for characterizing the autonomic regulation? And do they behave in accordance with each other in all subjects with various ages?

Our aim was thus to assess the age related changes in: 1) HRV and DPV through frequency domain analysis, and 2) the interactions between HRV and DPV in a nonlinear coupling analysis framework. Totally 60 healthy subjects were enrolled. Results showed that both LF and HF powers of DPV decreased with the increasing of age (both $p<0.001$), which behaved generally in the same way with HRV. However, their coupling, especially in terms of short-range correlations ($p<0.01$), decreased significantly with aging, which suggests that the interactions between HRV and DPV might provide additional valuable information for characterizing the autonomic regulation in aged individuals.

1. Introduction

The heart rate variability (HRV) has served as a non-invasive method for characterizing the autonomic regulation [1]. Capable of obtaining an almost immediate test result, short-term HRV analysis well meets the increasing clinical needs for personal healthcare, remote monitoring, etc. [2].

HRV refers to the beat-to-beat fluctuations in heart period, which is often represented by the consecutive RR intervals from the electrocardiogram (ECG) data. Since the cardiac contracts and relaxes quasi-periodically, one cardiac cycle, exactly one RR interval in ECG, can be divided into two complementary electromechanical intervals which indicate the duration of the cardiac systolic and diastolic phases, respectively. Due to HRV, these two periods should also vary from beat to beat. We have observed the phenomena in a previous study and named them cardiac systolic period variability (SPV) and diastolic period variability (DPV). Meanwhile, we have proved that HRV is expressed preferentially in DPV while the systolic period stays relatively constant with a tiny variability [3]. Similar conclusion was also presented independently soon after our research by Carrasco-Sosa and Guillén-Mandujano [4].

It is generally accepted that the overall HRV decreases progressively with aging, indicating by analysis in both time/frequency domain and state space [2, 5-8]. However, little is known about how DPV varies with aging. Additionally, there should be close interactions between HRV and DPV as it seems in [3, 4] that the diastolic period is more flexible to shorten and lengthen, which is consequently responsible for the adjustments of heart rate. The possible age related changes in the interactions between them thus need further elucidation.

Therefore, the aim of this study was to assess the age related changes in: 1) HRV and DPV, and 2) the interactions between HRV and DPV.

2. Methods

2.1. Subjects

Sixty healthy subjects aged between 23 and 72 (28 men and 32 women) were enrolled. Their characteristics are presented in Table 1. Before participation, the written informed consent was requested. This study has obtained full approval from the Clinical Ethics Committee of the Qilu Hospital of Shandong University.

2.2. Protocol

Measurements were undertaken in a quiet, temperature controlled clinical measurement room (25 ± 3 °C) at Qilu Hospital of Shandong University, by a Cardiovascular Function Detection device (CV FD—I) produced by Huiyironggong Technology Co., Ltd., Jinan, China. Before the formal signal recording, each subject lay

Table 1. Subjects characteristics.

Variables	Values
No.	60 (28/32)
Age (years)	50 ± 14
BMI (kg/m^2)	23 ± 3
HR (beats/min)	67 ± 8
SBP (mmHg)	110 ± 12
DBP (mmHg)	75 ± 8

BMI body mass index, *DBP* diastolic blood pressure, *HR* heart rate, *No*. number, *SBP* systolic blood pressure. Data are expressed as number (male/female) or mean ± SD.

supine on a measurement bed for a 10 min rest period to allow cardiovascular stabilization. ECG electrodes were attached to the right wrist and the right and left ankles to acquire a standard limb lead-II ECG. A piezoresistive sensor was attached to the left wrist to acquire the radial artery pressure waveforms (RAPW). Subjects were told to breathe regularly and gently during the measurement.

2.3. Signal acquisition and preprocessing

For each subject, the ECG and RAPW signals were recorded synchronously at a sampling rate of 1 kHz for 5 min. R-wave peaks from ECG and the systolic feet and dicrotic notches from RAPW were detected automatically and then visually inspected. The raw HRV and DPV series were obtained from the consecutive R-R intervals and intervals between the dicrotic notches and the following systolic feet, respectively. Before other processes, anomalous intervals due to ectopic beats or poor signal quality were visually identified and removed. Only series with less than 10% of anomalous intervals were finally accepted.

2.4. Frequency domain analysis

Detrend was applied to the raw HRV and DPV series based on a smoothness priori approach (SPA) [9]. They were then evenly sampled with a frequency of 4 Hz by spline interpolation. The corresponding power spectra of them were finally computed using a Burg method with the order of 16.

For both spectra of HRV and DPV, they were integrated in two frequency bands, from 0.04 to 0.15 Hz to obtain the power of low frequency (LF) band and from 0.15 to 0.4 Hz to compute the power of high frequency (HF) component (units: ln ms^2). To facilitate the following depiction, we denoted power of LF, HF of HRV and LF, HF of DPV by LF_{RR}, HF_{RR}, LF_{DT}, and HF_{DT}, respectively. At last, ratio between power of the corresponding LF and HF band was obtained and denoted as LF/HF_{RR} and LF/HF_{DT}.

2.5. Coupling between HRV and DPV

To investigate the coupling between HRV and DPV, we introduced a newly-developed entropy-based method —multiscale multivariate sample entropy (MMSE) [10]. MMSE is a generalized form of multiscale entropy to the multivariate case, so as to provide coupling analysis of real-world systems [11]. Following is a brief description of MMSE.

For sequences $\{y_{k,j}\}, k=1,2,\mathrm{L}\ , p,\ j=1,2,\mathrm{L}\ , N$ and a scale ε, coarse grain each series by $x_{k,i}^{\varepsilon}=\frac{1}{\varepsilon}\sum_{i=(j-1)\varepsilon+1}^{j\varepsilon} y_{k,j}$, $1\le j\le \lfloor N/\varepsilon \rfloor$.

Form $X_m^{\varepsilon}(i)=\{x_{1,i}^{\varepsilon}, x_{1,i+1}^{\varepsilon},\mathrm{L}\ , x_{1,i+(m_1-1)}^{\varepsilon}, x_{2,i}^{\varepsilon},\mathrm{L}\ , x_{2,i+(m_2-1)}^{\varepsilon}, \mathrm{L}\ , x_{p,i}^{\varepsilon},\mathrm{L}\ , x_{p,i+(m_p-1)}^{\varepsilon}\}=\{z_i^{\varepsilon}, z_{i+1}^{\varepsilon},\mathrm{L}\ , z_{i+m-1}^{\varepsilon}\}$ for each ε, where $m=\sum_{k=1}^{p} m_k$, $i=1,2,\mathrm{L}\ , N^{\varepsilon}-n$, $n=\max\{\mathbf{M}\}$, $\mathbf{M}=\{m_1,m_2,\mathrm{L}\ ,m_p\}$ and $N^{\varepsilon}=\lfloor N/\varepsilon \rfloor$. The distance between two vectors is defined as: $d\{X_m^{\varepsilon}(i), X_m^{\varepsilon}(j)\}=\max_{l=1}^{m}\{|z_{i+l-1}^{\varepsilon}-z_{j+l-1}^{\varepsilon}|\}$.

Denote $B_i^{\varepsilon,m}(r)$ the average number of j that $d[X_m^{\varepsilon}(i), X_m^{\varepsilon}(j)]\le r, j\ne i$ (rigid criterion). Extend the dimensionality from m_k to m_k+1 and thus $p\times(N^{\varepsilon}-n)$ vectors $X_{m+1}^{\varepsilon}(i)$ are obtained. Calculate $B_i^{\varepsilon,m+1}(r)$ as the average number of j that $d[X_{m+1}^{\varepsilon}(i), X_{m+1}^{\varepsilon}(j)]\le r, j\ne i$. Then MMSE is defined by:

$$\mathrm{MMSE}(\varepsilon)=-\ln\frac{\frac{1}{p(N^{\varepsilon}-n)}\sum_{i=1}^{p(N^{\varepsilon}-n)} B_i^{\varepsilon,m+1}(r)}{\frac{1}{N^{\varepsilon}-n}\sum_{i=1}^{N^{\varepsilon}-n} B_i^{\varepsilon,m}(r)}.$$

Raw HRV and DPV series after anomalous removal were used for this analysis. They were normalized by the corresponding SD first. Lengths of HRV and DPV in this study were around 300. To improve the stability for manipulating such short series, we substituted a Gaussian membership function for the rigid criterion [12]. Parameter $\mathbf{M}$ was set at [2, 2], r at 0.12 and $\varepsilon=5$.

2.6. Statistical analysis

Linear regressions were performed using the SPSS software (v. 20.0, IBM, USA) to determine the effect of age on the frequency and coupling parameters. Statistical significance was accepted at $p<0.01$.

3. Results

Totally 54 subjects were accepted, 6 were excluded because of ectopic beats (1 man and 1 woman aged at 63 and 56) and poor signal quality (2 men and 2 women aged at 61, 61, 55 and 48).

Regression analysis showed that for both HRV and DPV, the LF and HF power (LF_{RR}, HF_{RR}, LF_{DT}, HF_{DT}) had a significantly inverse relationship with age (all $p<0.001$), while LF/HF_{RR} and LF/HF_{DT} had no relationship ($p=0.89$ and 0.91). MMSE at the first 2 scales (MMSE1) was significantly inversely related to age (both $p<0.01$), MMSE3 was slightly related ($p<0.05$) while at larger scales (4 and 5) it had no relationship to age ($p=0.14$ and 0.38). Figure 1 shows the frequency domain parameters and coupling parameters as functions of age.

4. Discussion and conclusion

Losses in both LF power and HF power of HRV in aged subjects have showed in this study. Our results support the previous studies [2, 6, 7]. However, the ratio of LF power and HF power (LF/HF) of HRV remained unchanged as shown in Figure 1. It is generally

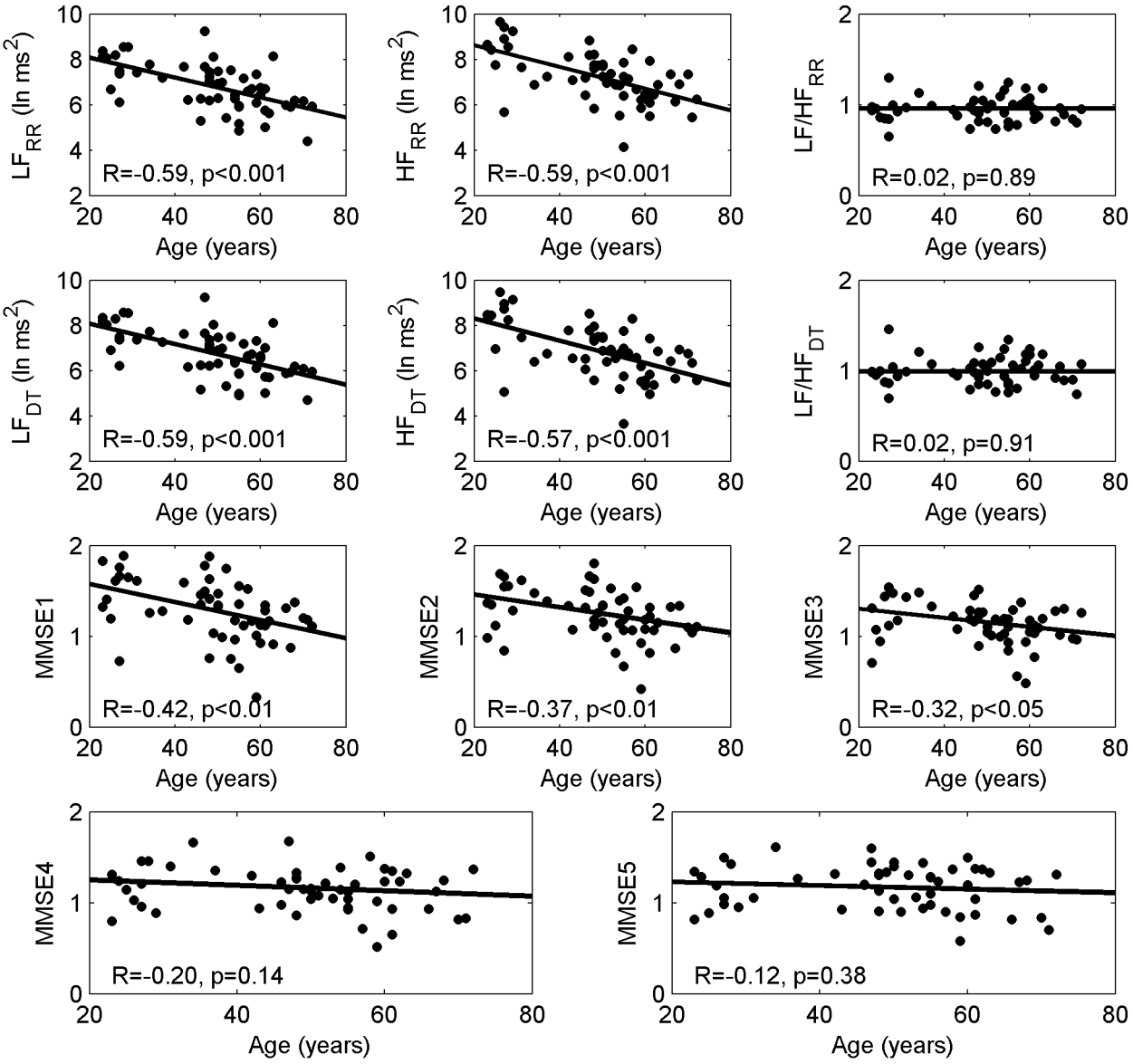

Figure 1. Frequency domain parameters (LF_{RR}, HF_{RR}, LF_{DT}, HF_{DT}, LF/HF_{RR} and LF/HF_{DT}) and coupling parameters (MMSE1 to MMSE5) as functions of age. The regression lines with p values and R values are also shown.

controversial of LF/HF in published studies: Greiser *et al* showed an inverse relationship with aging (1779 subjects aged between 45 and 83) [8] while Voss *et al* published an increasing trend (1906 subjects aged between 25 and 74) [2]. The unchanged LF/HF in our study is possibly partly because of the relatively small data set in our study. Also, it might be due to an ethnicity difference in subjects among different studies as Choi *et al* has showed [7].

For the unknown DPV, similar behavior to HRV was showed as in Figure 1: both the LF power and the HF power decreased significantly with the increasing of age; no significant relationship between LF/HF and aging was detected. Actually at the first sight, the scatter plots of DPV and HRV in Figure 1 seems to have no obvious difference. The results also confirmed that HRV is mainly reflected by DPV as shown in two previous studies [3, 4].

One marked finding of our study is that the coupling between HRV and DPV decreased significantly (MMSE1 and MMSE2, in terms of short-range correlations) or slightly (MMSE3) with the increasing of age, while in terms of long-range correlations (MMSE4 and MMSE5) it showed no relationship with aging. Although frequency domain analysis had already confirmed that DPV behaved in accordance with HRV, their interactions indeed changed with aging. It seems that these changes in the interactions between each other are too tiny to be captured by conventionally linear approaches. Analysis in the state space thus should be an important nonlinear tool.

Meanwhile, the decreasing trend was less significant in MMSE3 and no significant relationship with aging was showed in MMSE4 and MMSE5. It might mean that aging is more associated with the short-range correlations, which should be a reflection of the interactions between high frequency bands of HRV and DPV. Thus the significant decrease of MMSE1 and MMSE2 presumably indicated a loss of cardiorespiratory coupling in older individuals. In addition, the different behavior of MMSE in larger scales might provide a clue to the mechanism of aging. Besides, the different mechanism of cardiovascular disease might also be captured in such analysis, which will be showed through our future exploration.

To summarize, we found that aging was significantly associated with the decreasing of both LF and HF powers in both HRV and DPV. Although DPV behaved in the same way in frequency domain with aging, their short-range correlations showed a marked decrease. Future studies will focus on the coupling of HRV and DPV in subjects with different cardiovascular diseases.

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References

[1] Stein PK, Bosner MS, Kleiger RE, Conger BM. Heart rate variability: A measure of cardiac autonomic tone. Am Heart J 1994;127:1376-81.

[2] Voss A, Heitmann A, Schroeder R, Peters A, Perz S. Short-term heart rate variability—age dependence in healthy subjects. Physiol Meas 2012;33:1289-311.

[3] Liu CY, Liu CC, Li LP, Zhang QG, Li B. Systolic and diastolic time interval variability analysis and their relations with heart rate variability. 3rd International Conference on Bioinformatics and Biomedical Engineering. Beijing, China: IEEE; 2009. 1-4.

[4] Carrasco-Sosa S, Guillen-Mandujano A. Variability of the systolic and diastolic electromechanical periods in healthy subjects. Computing in Cardiology 2010: 133-6.

[5] Yeragani VK, Sobolewski E, Kay J, Jampala VC, Igel G. Effect of age on long-term heart rate variability. Cardiovasc Res 1997;35:35-42.

[6] Vigo DE, Guinjoan SM, Scaramal M, Nicola Siri L, Cardinali DP. Wavelet transform shows age-related changes of heart rate variability within independent frequency components. Auton Neurosci 2005;123:94-100.

[7] Choi J-B, Hong S, Nelesen R, Bardwell WA, Natarajan L, Schubert C, Dimsdale JE. Age and Ethnicity Differences in Short-Term Heart-Rate Variability. Psychosom Med 2006;68:421-6.

[8] Greiser K, Kluttig A, Schumann B, Swenne C, Kors J, Kuss O, Haerting J, Schmidt H, Thiery J, Werdan K. Cardiovascular diseases, risk factors and short-term heart rate variability in an elderly general population: the CARLA study 2002–2006. Eur J Epidemiol 2009;24:123-42.

[9] Tarvainen MP, Ranta-aho PO, Karjalainen PA. An advanced detrending method with application to HRV analysis. IEEE Trans Biomed Eng 2002;49:172-5.

[10] Ahmed MU, Mandic DP. Multivariate multiscale entropy: A tool for complexity analysis of multichannel data. Phys Rev E 2011;84:061918.

[11] Li P, Liu CY, Wang XP, Li LP, Yang L, Chen YC, Liu CC. Testing pattern synchronization in coupled systems through different entropy-based measures. Med Biol Eng Comput 2013;51:581-91.

[12] Li P, Liu CY, Li LP, Ji LZ, Yu SY, Liu CC. Multiscale multivariate fuzzy entropy analysis. Acta Phys Sin 2013;62:120512.

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