Five-class Density Histogram and its Application in Short-term Heart Rate Variability

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Abstract

Histograms are commonly used to measure heart rate variability (HRV), particularly for measurements over a 24-hour period. In this study, a five-class density histogram (FCDH) is proposed to extend the application of histograms for short-term HRV evaluation. The cumulative density, an index derived from the FCDH, is compared with conventional time- and frequency-domain measures, namely (1) low-frequency power (LF); (2) high-frequency power (HF); (3) the power ratio (LF/HF); (4) triangular interpolation of NN intervals (TINN); and (5) the HRV triangular index (HRVi). A total of two hundred subjects participated in the HRV assessment. They came from four equal-sized groups: the healthy young (Young), the healthy old (Old), patients with coronary artery disease, and patients with congestive heart failure. After 7 days and 14 days, 46 subjects from the Young and Old groups were retested following the same protocol in order to examine the reliability of the FCDH. Results show significant differences between the four groups for the indices of cumulative density, LF, HF, TINN, and HRVi ($p < 0.001$), but not for LF/HF ($p = 0.269$). The cumulative density shows good-to-excellent interclass correlation (ICC) with an average ICC = 0.783 (95% confidence interval 0.676-0.864), which is higher than the average ICCs of LF (0.695), LF/HF (0.669), TINN (0.686), and HRVi (0.615), but lower than that of HF (0.893). The cumulative density derived from the FCDH is thus a valid and reliable method for short-term HRV assessment.

Keywords: Heart rate variability, Autonomic nervous system, Frequency-domain analysis, Histogram

1. Introduction

Hon and Lee found a diminished beat-to-beat variation in the fetal heart rate and treated it as an indicator of distress [1]. Since then, heart rate variability (HRV), a measurement of the beat-to-beat variations in the instantaneous heart rate or R-R intervals, has received a lot of research interest. HRV is regarded as an indicator of the health status of the autonomic nervous system [2-4]. Aberrant HRV is always associated with disorders of internal secretion or the cardiovascular system, such as coronary artery disease (CAD) [5,6] and congestive heart failure (CHF) [7,8]. Therefore, HRV plays an important role in the assessment of the cardiovascular system and overall health.

A number of methods are available for HRV calculation. They are generally categorized as time-domain, frequency-domain, and nonlinear methods [2-4]. The histogram, a geometrical time-domain representation of a frequency distribution, and the indices derived from it, such as the triangular interpolation of NN intervals (TINN) and the HRV triangular index (HRVi), are widely used for measuring long-term HRV [2-4]. For example, shape variance and a decreased variation were found in patients with CHF using 24-hour RR histograms [7,8].

The histogram is particularly suitable for long-term HRV due to its ease of implementation and relative insensitivity to the quality of the R-R interval series [2-3,9]. The major disadvantage of the histogram, however, is the exigency to the length of the series. In practice, recordings of at least 20 min, preferably 24 hours, should be used to ensure a valid histogram [2,3]. An excessively short series usually reduces the reliability of a histogram. Therefore, histograms are considered inappropriate for the assessment of short-term HRV.

In this study, a cumulative density based on a five-class density histogram (FCDH) is proposed as a quantitative index for HRV evaluation. The proposed index is particularly suitable to short-term (five to ten minutes) HRV, for which it has a higher reliability than those of widely used HRV measures.

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2. Materials and methods

2.1 Subject selection

Two hundred subjects aged between 18 and 80 years old participated in this study. Prior to any evaluation, each subject was given a detailed description of the objectives and requirements of the experiment. Following this discussion, an informed consent form was read and signed up by each subject before the test. Subjects had neither severe organ damage, psychiatric disorders, nor any participation in clinical trials in the past three months. The subjects fell into four equal-size groups: the healthy young (Young), the healthy old (Old), patients with CAD, and the patients with CHF. The criteria of age were under 35 years for the Young group and over the age of 45 for the Old group. No subject from either the Young or the Old group was found to have any abnormality by means of ultrasonic cardiograms (UCGs), blood lipid and glucose checks, and electrocardiograms (ECGs). Subjects in the CAD group were diagnosed based on the results of ECGs and UCGs by the chief physician of the Department of Cardiology in Qilu Hospital of Shandong University. Subjects in the CHF group were accord with classes II - III of the New York Heart Association (NYHA) Functional Classification and had a left ventricular ejection fraction of less than 0.50, as obtained from UCGs. The protocol was reviewed and approved by the Clinical Ethics Committee of Qilu Hospital of Shandong University.

2.2 Data acquisition

All tests took place in a quiet room at a controlled temperature of 22 ℃. Participants took no medications and smoked no cigarettes before the experiment. Participants were firstly asked to lie supine on a clinical bed for a 10-minute rest prior to the experiment. Standard limb lead II ECGs were recorded for 5 to 10 minutes using a cardiovascular system status monitor (CVFD-I) developed by the Institute of Biomedical Engineering, Shandong University, at a sampling frequency of 1000 Hz. A band-pass filter with a 0.05-125 Hz bandwidth was used for signal filtering. The R-peaks (t_i, r_i) of the ECG were extracted using the wavelet transform modulus maxima method [10]. Then, the R-R interval series were constituted from the R-peaks as: $z_i = t_{i+1}-t_i$. Due to possible artifacts in the original R-R interval series, preprocessing was employed to remove them; artifacts can lead to statistical bias in HRV analysis [11]. Time series *s*, with improved quality, was thus obtained. Subsequently, the FCDH was constructed and the index of cumulative density was obtained. Forty-six subjects from the Young and Old groups were retested following the same protocol after 7 and after 14 days, respectively, in order to examine the reliability of the method.

2.3 FCDH and cumulative density

After preprocessing, the FCDH is obtained from the time series *s*. The range of the new series s_{range} was calculated as:

$$s_{range} = s_{\max}-s_{\min} \quad (1)$$

where $s_{\max}$ and $s_{\min}$ are the maximum and the minimum of the series, respectively.

The left-step-length H_l and the right-step-length H_r are defined as:

$$H_l = [s_{median} - (s_{\min} + a)] \;/\; 5 \quad (2)$$

$$H_r = [(s_{\max} - a) - s_{median}] \;/\; 5 \quad (3)$$

where $a = 0.1 \times s_{range}$. Samples within ($s_{\min}$, $s_{\min} + a$) or ($s_{\max}$-a, $s_{\max}$) are discarded in order to decrease the stochastic fluctuation of the time series and to improve the reliability of the algorithm.

Suppose that s_i (i = 1, 2, … , M) is the point of the R-R interval series. The points of the time series are classified into five classes following the classification shown in Fig. 1. The criteria of the five classes are shown in Table 1.

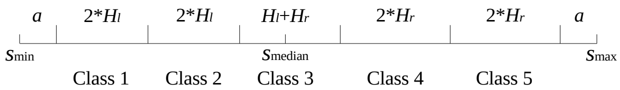

Figure 1. Schematic diagram of FCDH for R-R interval series.

Table 1. Conditions, ranges, and numbers for the five classes.

Class	Condition	Range	Number
Class 1	$s_{\min} + a \leqq s_i < s_{median}$-3*$H_l$	r_1 = 2*H_l	N_1
Class 2	s_{median}-3*$H_l \leqq s_i < s_{median}$-$H_l$	r_2 = 2*H_l	N_2
Class 3	s_{median}-$H_l \leqq s_i < s_{median}$+$H_r$	$r_3 = H_l + H_r$	N_3
Class 4	$s_{median} + H_r \leqq s_i < s_{median}$ + 3*H_r	r_4 = 2*H_r	N_4
Class 5	s_{median} + 3*$H_r \leqq s_i < s_{\max}$-a	r_5 = 2*H_r	N_5

The proportion of each class is defined as:

$$p_i = N_i / M, \quad i = 1, 2, \ldots, 5 \quad (4)$$

where N_i is the number of points in the i-th class and M is the length of the R-R interval series.

Then, the distribution density of each class is calculated as:

$$\rho_i = p_i / r_i, \; i = 1, 2, \ldots, 5 \quad (5)$$

where p_i is the proportion of the i-th class and r_i is the range of the corresponding class. The FCDH is plotted by showing ρ_i in the height, erected over each class.

A cumulative density is defined as the sum of the distribution densities of the five classes as:

$$\rho_c = \sum \rho_i, \; i = 1, 2, \ldots, 5 \quad (6)$$

2.4 Statistical analysis

All statistical analyses were performed using the Statistical Package for Social Sciences (V16, SPSS Inc., Chicago, IL, USA). Data were assessed for normality using the Kolmogorov-Smirnov test. Chi-squared tests were used to compare the data from different groups. A one-way analysis of variance (ANOVA) test was applied to test for differences between patients and control groups as well as between age groups. Multiple comparisons were applied using the least significant difference (LSD) method for data with homogeneous variances and Tamhane's T2 method for data with heterogeneous variances. A box plot was used to summarize the data in graphic form. The reliability of the algorithms was assessed by the interclass correlation coefficient (ICC). The reliability was considered to be moderate and high for ICC values of between 0.60 and 0.80 and above 0.80, respectively [12]. *p* values less than 0.05 were considered to be statistically significant.

3. Results and discussion

3.1 FCDH results

The characteristics of FCDH subjects are shown in Table 2. Figure 2(a) shows a histogram with an even distribution from a young healthy subject; Fig. 2(b) shows a concentrated distribution from a subject from the Old group. A more intensive centripetalism is shown in the distribution of a subject from the CAD group in Fig. 2(c). Fig. 2(d) shows a more concentrated distribution from a subject from the CHF group.

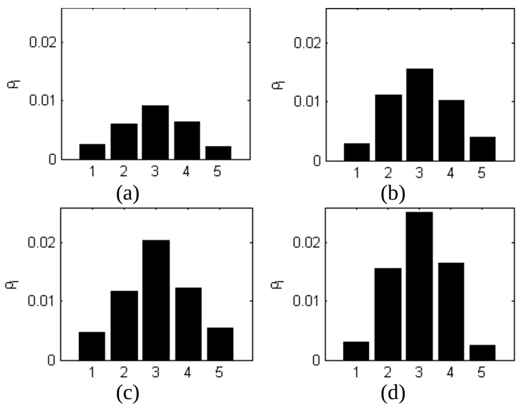

Figure 2. Typical FCDHs for individual subjects from (a) the Young group ($\rho_c = 0.026$), (b) the Old group ($\rho_c = 0.044$), (c) the CAD group ($\rho_c = 0.055$), and (d) the CHF group ($\rho_c = 0.063$).

Table 2. Subject characteristics.

Group	Young	Old	CAD	CHF
Age (years)	25 ± 5	56 ± 8	59 ± 9	60 ± 12
Sex (M/F)	31/19	24/26	24/26	33/17
Height (cm)	170 ± 7	165 ± 7	164 ± 7	166 ± 8
Weight (kg)	62 ± 10	66 ± 12	71 ± 11	69 ± 12
BMI (kg/m^2)	21.2 ± 2.5	24.0 ± 3.1	26.2 ± 3.6	24.9 ± 4.2
HR (beats/min)	68 ± 8	67 ± 8	68 ± 11	73 ± 11

Abbreviations: BMI: body mass index; HR: heart rate.

The cumulative density was compared with frequency-domain parameters (low-frequency power (LF: 0.04-0.15 Hz), high-frequency power (HF: 0.15-0.4 Hz), and their ratio (LF/HF)) and conventional histogram parameters (TINN and HRVi). The box plots shown in Fig. 3 show the statistical distribution of the cumulative density, the frequency-domain parameters, and the conventional histogram parameters for the Young, Old, CAD, and CHF groups. An increased cumulative density and decreased LF, HF, TINN, and HRVi were found for all four groups. The cumulative density of the four groups follows normal distributions ($p > 0.05$) and heterogeneous variance ($p < 0.001$). The frequency-domain parameters were log-transformed because of their non-normal distributions. After log-transformation, the variance of HF was heterogeneous ($p = 0.012$) and those of LF ($p = 0.111$) and LF/HF ($p = 0.969$) were homogeneous. The conventional histogram parameters were calculated for the series with normal distribution and homogeneous variance. Results of the ANOVA test are shown in Table 3. Significant differences among the four groups were found in the cumulative density, LF, HF, TINN, and HRVi ($p < 0.001$), but not for LF/HF ($p = 0.269$).

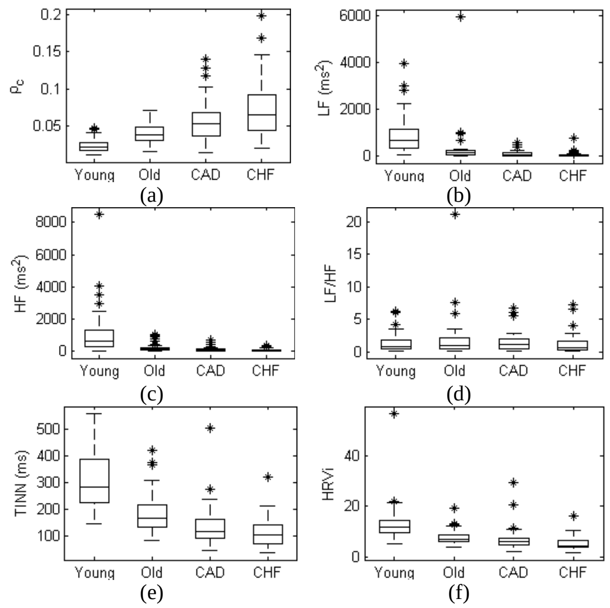

Figure 3. Box plots for (a) cumulative density, (b-d) frequency-domain parameters, and (e-f) conventional histogram parameters for the four groups.

Table 3. Cumulative density, frequency-domain parameters, and conventional histogram parameters for the four groups.

	Young	Old	CAD	CHF	F test
ρ_c ^{abcde}	0.0238 ± 0.0087	0.0406 ± 0.0129	0.0566 ± 0.0268	0.0732 ± 0.0376	$p < 0.001$
LF (ln)^{abcdef}	6.37 ± 0.95	5.03 ± 1.02	4.14 ± 1.06	3.16 ± 1.32	$p < 0.001$
HF (ln)^{abcde}	6.40 ± 1.11	4.94 ± 0.99	4.14 ± 1.24	3.50 ± 1.41	$p < 0.001$
LF/HF (ln)	-0.03 ± 0.93	0.08 ± 1.00	-0.01 ± 0.97	-0.29 ± 1.02	$p = 0.269$
TINN (ms) ^{abcde}	306.32 ± 111.14	183.16 ± 74.83	138.42 ± 74.36	108.7 ± 52.36	$p < 0.001$
HRVi ^{abce}	13.21 ± 7.37	7.82 ± 2.75	6.85 ± 4.36	5.37 ± 2.52	$p < 0.001$

Note: [a] Significant difference between the Young and Old. [b] Significant difference between the Young and CAD.
[c] Significant difference between the Young and CHF. [d] Significant difference between the Old and CAD.
[e] Significant difference between the Old and CHF. [f] Significant difference between the CAD and CHF.

Table 4. Interclass reliability coefficient (ICC) values for the cumulative density, frequency-domain parameters, and conventional histogram parameters across the three test sessions.

	Test 1	Test 2	Test 3	F test	ICC (95% CI)
ρ_c	0.034 ± 0.012	0.032 ± 0.013	0.032 ± 0.012	$p = 0.677$	0.783(0.676 - 0.864)
LF (ln)	5.35 ± 0.82	5.59 ± 1.13	5.63 ± 1.02	$p = 0.359$	0.695(0.559 - 0.804)
HF (ln)	5.54 ± 1.04	5.65 ± 1.17	5.68 ± 1.15	$p = 0.829$	0.893(0.833 - 0.935)
LF/HF (ln)	-0.18 ± 0.80	-0.07 ± 0.88	-0.06 ± 0.94	$p = 0.746$	0.669(0.527 - 0.786)
TINN (ms)	211.30 ± 77.76	232.43 ± 95.13	233.07 ± 89.92	$p = 0.404$	0.686(0.547 - 0.798)
HRVi	9.54 ± 2.99	9.64 ± 3.95	9.57 ± 3.11	$p = 0.989$	0.615(0.460 - 0.748)

These findings reflect the dynamic balance between the sympathetic and parasympathetic nervous systems controlled by the autonomic nervous system (ANS). A healthy balance between the sympathetic and parasympathetic nervous systems produces an ongoing oscillation, an orderly increase and decrease in the heart rate [2,4]. However, an abnormal balance can lead to a diminished variability that is usually associated with ageing and illness. Both the parasympathetic and the sympathetic activities decline during ageing, but the former usually declines faster than the latter [13]. In contrast, the patients with CAD and CHF have lower parasympathetic activity but higher sympathetic activity, which leads to decreased HRV, both time-and frequency-domain parameters [5-8,14,15]. The proposed method allows HRV imbalances to be detected from the density distribution of R-R intervals. It is thus a valid method for HRV assessment for both young and old healthy populations and for patients with CAD or CHF.

3.2 Test-retest reliability

In order to examine the test-retest reliability of the algorithm, 46 healthy subjects who participated in the first test were retested following the same protocol after 7 days and 14 days, respectively. The subjects were 20 females and 26 males (age 43 ± 16 years; height: 168 ± 8 cm; weight: 64 ± 11 kg; BMI: 22.5 ± 3.0 kg/m^2; HR: 67 ± 8 beats/min). All data were in normal ranges.

All the cumulative densities in the three tests followed normal distributions ($p > 0.05$) and homogeneous variance ($p = 0.918$). The TINN and HRVi also met the requirements of normal distribution ($p > 0.05$) and homogeneous variance ($p > 0.05$). The box plot in Fig. 4 shows the distribution of the cumulative density, the frequency-domain parameters, and the conventional histogram parameters across the three tests. They have similar distributions. More detailed information about the three tests is shown in Table 4. The LF, HF, and LF/HF were log-transformed. Data after transformation shows homogeneous variance ($p > 0.05$). No significant difference was found among the three tests in all the parameters. A good-to-excellent reliability was found in the test-retest analysis of cumulative density, with an ICC = 0.783 (95% confidence interval: 0.676-0.864), which is higher than those of LF (ICC = 0.695), LF/HF (ICC = 0.669), TINN (ICC = 0.686), and HRVi (ICC = 0.615), but lower than that of HF (ICC = 0.893).

In addition to the validity test, the reliability of HRV measurement should be examined before clinical application. Previous studies showed that time-domain parameters of HRV calculated from a long-term observation, such as over 24 hours, usually exhibit very high test-retest reliability, whereas those calculated from a series of a short period of time (e.g., less than 15 min), usually exhibit poor reliability [12], which is consistent with our results of TINN and HRVi. These findings indicate that the traditional time-domain parameters have acceptable reliability only for long-term HRV analysis. There are inconsistent assessement results of frequency-domain parameters: some show that these parameters are reliable [16,17] but some show otherwise [12,18]. This inconsistency may result from the differences in experimental protocols used, the participants involved, the data collection method, or the preprocessing algorithm. In this study, for the series recorded for 5 to 10 min, the proposed method has good-to-excellent test-retest reliability with an ICC = 0.783 (95% confidence interval: 0.676-0.864), which is similar to the reliabilities of previous time-domain methods for long-term HRV assessment [12]. The cumulative density has better reliability than those of LF, LF/HF, TINN, and HRVi.

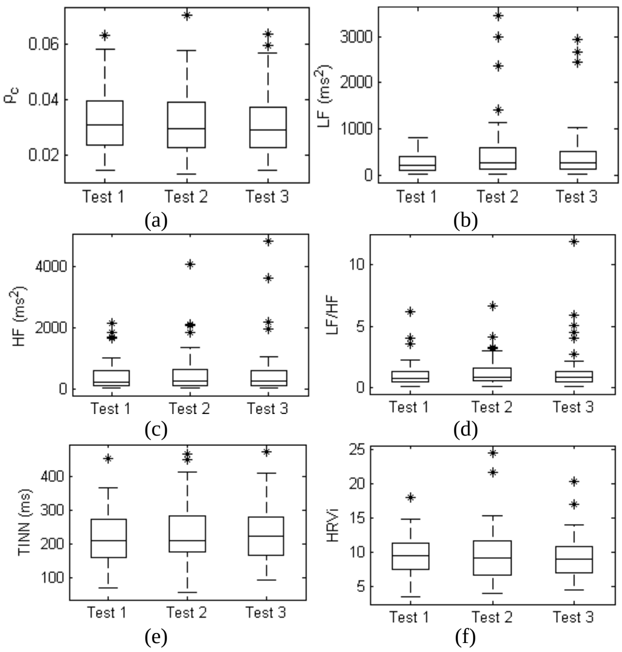

Figure 4. Box plots for (a) cumulative density, (b-d) frequency-domain parameters, and (e-f) conventional histogram parameters for the three tests of reliability.

4. Conclusion

This work examined the validity and reliability of a five-class density histogram for the non-invasive assessment of HRV. The results indicate that the FCDH is an effective, reliable, and simple method that is suitable to short-term HRV assessment. The validity of the algorithm will be further examined using a larger healthy population as well as patients with various cardiovascular diseases.

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References

[1] E. Hon and S. Lee, "Electronic evaluation of the fetal heart rate. VIII. Patterns preceding fetal death, further observations," *Am. J. Obstet. Gynecol.*, 87: 814-826, 1963.

[2] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, "Heart rate variability: standards of measurement, physiological interpretation and clinical use," *Circulation*, 93: 1043-1065, 1996.

[3] Y. Gang and M. Malik, "Heart Rate Variability: Measurements and Risk Stratification," in: I. Gussak, C. Antzelevitch, A. A. M. Wilde, P. A. Friedman, M. J. Ackerman and W.-K. Shen (Ed.), *Electrical Diseases of the Heart*, London: Springer, 365-378, 2008.

[4] A. Rajendra, J. Paul, N. Kannathal, C. Lim and J. Suri, "Heart rate variability: a review," *Med. Biol. Eng. Comput.*, 44: 1031-1051, 2006.

[5] J. Hayano, Y. Sakakibara, M. Yamada, N. Ohte, T. Fujinami, K. Yokoyama, Y. Watanabe and K. Takata, "Decreased magnitude of heart rate spectral components in coronary artery disease. Its relation to angiographic severity," *Circulation*, 81: 1217-1224, 1990.

[6] P. Rautaharju, C. Kooperberg, J. Larson and A. Lacroix, "Electrocardiographic abnormalities that predict coronary heart disease events and mortality in postmenopausal women: the Women's Health Initiative," *Circulation*, 113: 473-480, 2006.

[7] G. Casolo, E. Balli, T. Taddei, J. Amuhasi and C. Gori, "Decreased spontaneous heart rate variability in congestive heart failure," *Am. J. Cardiol.*, 64: 1162-1167, 1989.

[8] T. Stefenelli, J. Bergler-Klein, S. Globits, R. Pacher and D. Glogar, "Heart rate behaviour at different stages of congestive heart failure," *Eur. Heart J.*, 13: 902-907, 1992.

[9] M. Malik, R. Xia, O. Odemuyiwa, A. Staunton, J. Poloniecki and A. Camm, "Influence of the recognition artefact in automatic analysis of long-term electrocardiograms on time-domain measurement of heart rate variability," *Med. Biol. Eng. Comput.*, 31: 539-544, 1993.

[10] J. Martínez, R. Almeida, S. Olmos, A. Rocha and P. Laguna, "A wavelet-based ECG delineator: evaluation on standard databases," *IEEE Trans. Biomed. Eng.*, 51: 570-581, 2004.

[11] L. Li, J. Yang, C. Liu, B. Li and C. Liu, "An impulse rejection filter based on moving window for artifact removal in RR interval series," *J. Optoelectron. Laser*, 21: 1426-1430, 2010.

[12] M. Pitzalis, F. Mastropasqua, F. Massari, C. Forleo, M. Di Maggio, A. Passantino, R. Colombo, M. Di Biase and P. Rizzon, "Short- and long-term reproducibility of time and frequency domain heart rate variability measurements in normal subjects," *Cardiovasc. Res.*, 32: 226-233, 1996.

[13] K. Umetani, D. Singer, R. Mccraty and M. Atkinson, "Twenty-four hour time domain heart rate variability and heart rate: relations to age and gender over nine decades," *J. Am. Coll. Cardiol.*, 31: 593-601, 1998.

[14] J. Sanderson, "Heart rate variability in heart failure," *Heart Fail. Rev.*, 2: 235-244, 1998.

[15] S. Lucreziotti, A. Gavazzi, L. Scelsi, C. Inserra, C. Klersy, C. Campana, S. Ghio, E. Vanoli and L. Tavazzi, "Five-minute recording of heart rate variability in severe chronic heart failure: correlates with right ventricular function and prognostic implications," *Am. Heart J.*, 139: 1088-1095, 2000.

[16] G. Parati, S. Omboni, A. Villani, F. Glavina, P. Castiglioni, M. Di Rienzo and G. Mancia, "Reproducibility of beat-by-beat blood pressure and heart rate variability," *Blood Press. Monit.*, 6: 217-220, 2001.

[17] L. Cloarec-Blanchard, C. Funck-Brentano, M. Lipski, P. Jaillon and I. Macquin-Mavier, "Repeatability of spectral components of short-term blood pressure and heart rate variability during acute sympathetic activation in healthy young male subjects," *Clin. Sci.*, 93: 21-28, 1997.

[18] S. Lord, R. Senior, M. Das, A. Whittam, A. Murray and J. Mccomb, "Low-frequency heart rate variability: reproducibility in cardiac transplant recipients and normal subjects," *Clin. Sci.*, 100: 43-46, 2001.