Variability of Left Ventricular Ejection and Diastolic Times Obtained from Impedance Cardiography: A Comparison with Heart Rate Variability

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Abstract

Our aim was to compare the spectral measures of heart rate variability (HRV) with those of the variability of: impedance heart periods (IHPV), ejection time (ETV) and diastolic time (DTV), computed from the impedance cardiography (ICG) traces obtained from 17 healthy volunteers during four 5-min steady-state conditions that elicit different vagal activity levels. From the time-frequency spectra of RR intervals (RR), impedance heart period (IHP), IHP-RR difference, ejection time (ET) and diastolic time (DT) series, their corresponding high frequency (HF_{RR}, HF_{IHP-RR}) and low frequency powers (LF_{RR}, LF_{IHP-RR}) were computed. Time-frequency coherences of HF_{RR} and LF_{RR} with the respective components of the other series were obtained. Coherences and correlations of HRV spectral measures with those of IHPV and DTV were very strong and much greater ($p<0.01$) than with those of ETV. HF_{IHP-RR} power was much greater ($p<0.005$) than LF_{IHP-RR} in all maneuvers. Although HRV determines most IHPV, the latter contains additional respiratory modulation that limits their interchangeability. Intra-beat variability is documented by DTV, a surrogate of HRV and therefore susceptible to autonomic modulation, and by ETV, which is much reduced and less responsive to modulation.

1. Introduction

One of the first noninvasive procedures developed to assess cardiac function was the measurement of left ventricular systolic time intervals, currently used in clinical practice because of its significant diagnostic and prognostic value in heart disease [1]. Diastolic time (DT) has been related to the performance of subendocardial perfusion [2] and left ventricular ejection time (ET) has been employed for detecting left ventricular systolic dysfunction [3]. Moreover, the latter participates in the computation of the left ventricle stroke volume measured by impedance cardiography (ICG) [4].

The variability of ET (ETV) and DT (DTV) has been poorly studied. Some knowledge has been obtained from time domain analysis of 15-s periods of ET and DT series, measured from aortic pressure waves in heart transplant recipients [5]. It has been recently reported that the spectra of electromechanical diastolic times obtained from ECG and arterial pressure wave traces are very similar to HRV spectra [6]. Even though ET and DT have been widely used for evaluating left ventricular function, the comparison between their spectra and those of R-R interval series (RR) at different levels of autonomic activity has not been documented. Therefore, our aim was to compare the time-frequency spectral measures of HRV with those of impedance heart periods variability (IHPV), ETV and DTV, computed from ICG traces in four maneuvers that elicit different vagal activity levels.

2. Methods

2.1. Subjects

Seventeen healthy, normotensive and sedentary subjects, 11 men and 6 women, were studied. Mean age, height and weight were 21.8±2.4 years, 165±8 cm and 60±8 kg respectively. Their written informed consent was requested to participate. The present study was approved by the ethics committee of our university.

2.2. Protocol

Volunteers visited the laboratory twice. The first time their health status and anthropometric variables were evaluated, and in the second visit the experimental stage was carried out. The 5-min supposedly steady-state conditions employed to induce specific changes in cardiac autonomic activity [7] were: supine position (SP), considered the control condition; standing position (S), which elicits a sympathetic activity increase; controlled breathing (CB) at 0.2 Hz that augments vagal modulation, and a single bout of 100W cycling exercise (E), which provokes substantial vagal withdrawal. ECG and ICG were recorded during each condition.

2.3. Signal recording and acquisition

ECG was detected from the CM5 bipolar lead and a bioelectric amplifier (Biopac Systems). ICG was recorded from four aluminum band electrodes, two placed around the neck and two around the thorax [8], attached to an impedance plethysgmograph and a differentiator (Nihon Kohden). ECG and ICG were digitized at a sampling rate of 1kHz via an acquisition and display system (Biopac Systems).

2.4. Data processing

From ICG first derivative traces, the fiducial points B, corresponding to aortic valve opening, and X, indicating aortic closing [8], were automatically detected. IHP was computed as B-to-B period, ET as B-to-X time interval and DT as X-to-B time interval. In a beat-to-beat format, the detection of the characteristic points was overseen by an expert and corrected when needed. RR series were beat-by-beat subtracted from IHP to form IHP-RR series. All series were cubic-spline interpolated, resampled at 4 Hz and detrended. Time-frequency spectra of RR, IHP, IHP-RR difference, ET and DT series were estimated via the smoothed pseudo-Wigner-Ville distribution and integrated in the standard low (LF) and high frequency (HF) bands to compute their corresponding high frequency (HF_{RR}, HF_{IHP}, HF_{IHP-RR}, HF_{ET}, HF_{DT}) and low frequency powers (LF_{RR}, LF_{IHP}, LF_{IHP-RR}, LF_{ET}, LF_{DT}). Time-frequency coherences of LF_{RR} and HF_{RR} with the respective components of the other periods were obtained. Coherences greater than 0.5 were considered significant. Instantaneous dynamics of the indexes were segmented into 50-s epochs and integrated to obtain a mean value per epoch.

2.5. Statistical analysis

Data are expressed as means ± SD. Indexes differences among the four maneuvers were tested by ANOVA for repeated measures. Post-hoc pairwise comparisons were performed by the Tukey test. Intra-condition comparison between ETV and DTV indexes was performed using Student's paired t test. Individual mean values of the 50-s epochs of the indexes dynamics in the four maneuvers were used to compute linear regressions and correlations between the measures of HRV and of ICG-derived periods. Statistical significance was accepted at $p<0.05$.

3. Results

Maneuvers elicited similar changes in mean LF_{RR}, LF_{IHP} and LF_{DT}: with respect to SP they did not change in CB ($p>0.05$), increased in S ($p<0.02$) and decreased in E ($p<0.001$). LF_{ET} and HF_{ET} powers were different from SP ($p<0.05$) only in E (Table 1). HF_{RR}, HF_{IHP} and HF_{DT} powers changed similarly throughout the conditions: in relation to SP condition they increased in CB ($p<0.01$), decreased in S ($p<0.01$) and were minimal in E ($p<0.001$). The SD of all intervals was large (Table 1).

Table 1. Means ± SD of the epochs mean values of LF and HF powers of RR, IHP, DT and ET series during the four maneuvers. N=16.

		SP	CB	S	E
LF	RR	1998±1303	1742±839	2807±2347*	30±25*
(ms^2)	IHP	1983±1241	1740±859	2844±2391*	31±25*
	DT	1743±1105	1440±725	2053±2130*	47±25*
	ET	35±15†	30±14†	35±18†	12±8*†
HF	RR	3987±4137	9800±5192*	1057±803*	29±26*
(ms^2)	IHP	3886±3742	9925±5547*	1149±863*	89±40*
	DT	2550±2529	7031±3452*	778±640*	35±20*
	ET	71±38†	86±71†	48±45†	22±18*

*p<0.01 vs. SP condition
†p<0.01 ET vs. DT powers

Correlation coefficients and slopes of the LF_{RR}-LF_{IHP} relation were greater than 0.98 in the four maneuvers (Table 2). The HF_{RR}-HF_{IHP} relation exhibited similar behavior, with correlations and slopes greater than 0.95 in all maneuvers but E, where both decreased ($p<0.01$). Coherences of LF_{RR}-LF_{IHP} and HF_{RR}-HF_{IHP} relations were greater than 0.92 in the four maneuvers (Table 2).

Table 2. Mean values ± SD of coherences (C), correlations (r) and slopes (m) of the relations of LF_{RR} and HF_{RR} powers with the respective LF and HF powers of IHP, ET and DT series in the 4 maneuvers. N=16.

		SP	CB	S	E
C_{LF}	IHP	1.00±0.00	0.99±0.02	1.00±0.00	0.99±0.02
	DT	0.99±0.01	0.99±0.01	0.99±0.00	0.92±0.06
	ET	0.72±0.08†	0.66±0.09†	0.81±0.05†	0.71±0.05†
r_{LF}	IHP	1.00±0.01	0.99±0.01	1.00±0.00	0.99±0.01
	DT	0.98±0.02	0.98±0.01	0.99±0.01	0.81±0.17*
	ET	0.15±0.30†	0.11±0.33†	0.36±0.25†	0.20±0.27†
m_{LF}	IHP	0.98±0.04	0.99±0.04	1.00±0.02	1.02±0.05
	DT	0.89±0.05	0.91±0.07	0.83±0.07	1.07±0.40
	ET	0.00±0.01†	0.00±0.01†	0.01±0.01†	0.12±0.22*†
C_{HF}	IHP	0.99±0.01	1.00±0.00	0.99±0.01	0.92±0.04
	DT	0.99±0.02	1.00±0.00	0.99±0.01	0.84±0.06*
	ET	0.82±0.06†	0.88±0.06†	0.79±0.11†	0.79±0.09†
r_{HF}	IHP	0.97±0.04	0.98±0.02	0.95±0.07	0.23±0.34*
	DT	0.95±0.04	0.97±0.04	0.94±0.05	0.36±0.41*
	ET	0.14±0.46†	0.00±0.32†	0.17±0.34†	0.13±0.34†
m_{HF}	IHP	0.98±0.20	0.97±0.14	0.96±0.14	0.44±0.74*
	DT	1.02±0.13	1.04±0.20	0.98±0.18	0.42±0.93*
	ET	0.07±0.96†	0.55±0.95†	0.21±0.87†	0.42±1.43†

*p<0.01 vs. SP condition
†p<0.001 ET vs. DT relations

While LF_{IHP-RR} power was very small in the four maneuvers, HF_{IHP-RR} power was greater ($p<0.001$) in all maneuvers (Fig. 1).

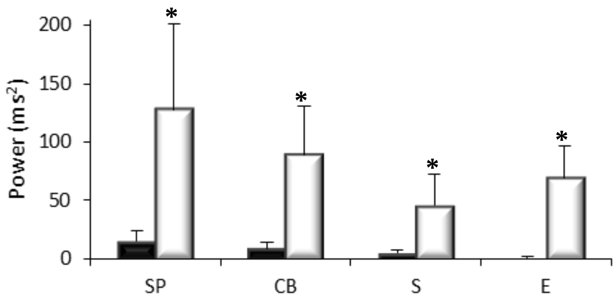

Figure 1. Means ± SD of the LF_{IHP-RR} (black bars) and HF_{IHP-RR} (white bars) mean values in the four conditions.
* $p<0.01$ LF_{IHP-RR} *vs.* HF_{IHP-RR}

Analogously to HRV spectra, powers of DTV and ETV spectra were distributed in the standard LF and HF bands. LF_{DT} and HF_{DT} powers changed similarly to LF_{RR} and HF_{RR} in SP, CB and S conditions. The TFDs of ET series did not show characteristic changes throughout the maneuvers and presented much lower powers than those of DT series, except in E (Fig. 2). Instantaneous powers of ET and DT series, estimated by TFDs, presented strikingly large fluctuations during supposedly stationary maneuvers (Fig. 2).

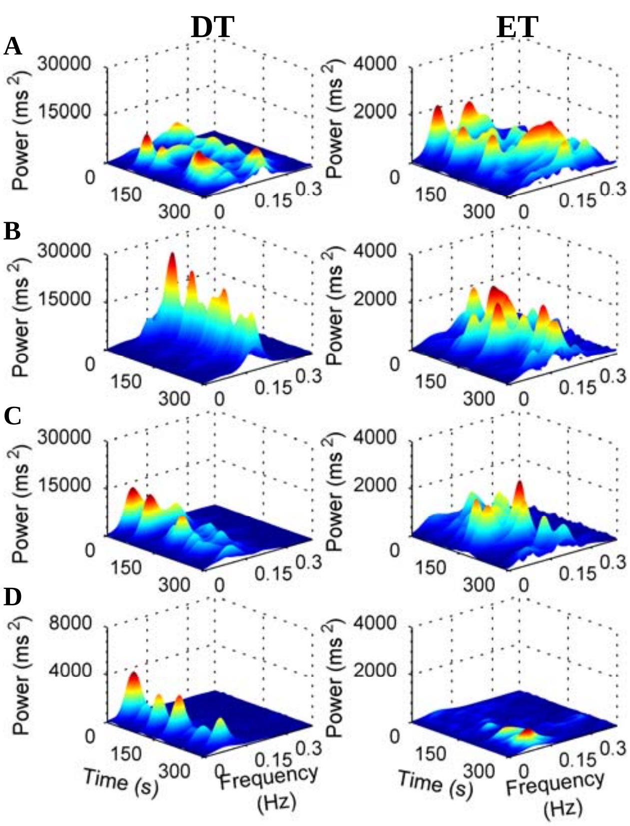

Figure 2. Representative example of the TFDs of DT series (left column) and ET series (right column) in (A) SP, (B) CB, (C) S and (D) E conditions.

Both LF_{DT} and HF_{DT} powers were much greater than LF_{ET} and HF_{ET} ($p<0.001$) in all maneuvers but E, where differences were smaller (Table 1).

Coherences, correlations and slopes of the LF_{RR}-LF_{DT} and HF_{RR}-HF_{DT} relations were greater than 0.83 in SP, CB and S. In E condition, correlations and coherences decreased ($p<0.01$) in the two frequency bands (Table 2). Correlations of the LF_{RR}-LF_{ET} and HF_{RR}-HF_{ET} relations were less than 0.36 in the four conditions with slopes ranging from 0 to 0.55 (Table 2, Fig. 3).

Figure 3 depicts the differences between the regressions of the spectral measures of HRV with those of DTV and ETV. Slopes of DTV regressions are close to identity in both frequency bands during SP, CB and S. On the left column, the flat slopes of the LF_{RR}-LF_{ET} regressions can be observed. On the right column, the great dispersion of the HF_{RR}-HF_{ET} regressions in SP, CB and S, and the similar dispersion in E is clearly seen.

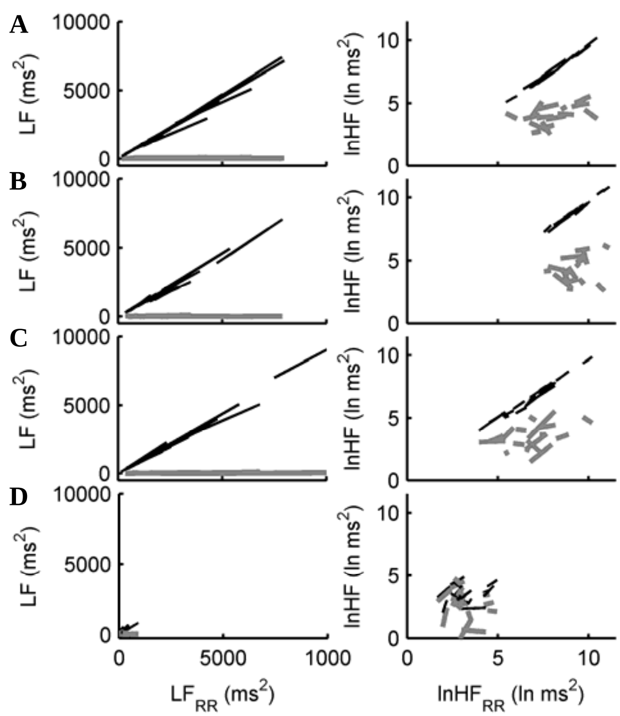

Figure 3. Individual regressions between LF_{RR} (left column) and HF_{RR} (right column) with the respective components of DT (black lines) and ET (grey lines) in (A) SP, (B) CB, (C) S and (D) E maneuvers.

4. Discussion

Our main findings are: (1) coherences and correlations of LF_{RR} and HF_{RR} with the corresponding IHPV components were very strong, indicating the close parallelism between the variability responses of both types of series to the four maneuvers. However, IHP-RR differences, small in the LF band but significantly larger in the HF band, document the greater respiratory modulation of IHP in the four maneuvers, outstanding in E condition. (2) DTV time-frequency spectra are similar to those of HRV in the four maneuvers and different from those of ETV. Coherences and correlations of LF_{RR} and HF_{RR} with LF_{DT} and HF_{DT} are high and greater than those with LF_{ET} and HF_{ET} in all maneuvers. Except in E, LF_{DT} and HF_{DT} power are much greater than LF_{ET} and HF_{ET}, an observation that establish the great similarity between DTV and HRV as well as the much reduced modulation of ET series.

ETV and DTV have been poorly studied. In heart transplant recipients, small beat-to-beat fluctuations in DT series and respiratory-related fluctuations in ET series have been observed [5]. Therefore, in absence of autonomic modulation, the variability of these time intervals is largely diminished. The findings of the present study support that, in individuals with preserved autonomic function, DTV is subject to autonomic modulation but ETV not so much. These findings are in agreement with those found in systolic and diastolic electromechanical intervals obtained from ECG and arterial pressure traces in healthy subjects [6].

Our findings provide some evidence regarding the following functional properties of the autonomic-cardiovascular system: (1) Instantaneous values of LF and HF powers of the studied periods and times present large fluctuations during supposedly steady-state maneuvers. By assuming that time series are non-stationary and using TFD to perform spectral estimation, the problems associated to attaining and testing steady-state series are avoided. (2) The large data dispersion of the spectral measures documents the characteristic high inter-subject cardiovascular-autonomic variability. (3) Maneuvers provoke systematic inter-subject HRV, IHPV and DTV spectral measures responses. (4) Changes in HF power are the main source of the inter-beat variability of RR and IHP series. However, the significant HF_{IHP-RR} power found in the four maneuvers suggests that IHP series undergo additional respiratory modulation due to a direct mechanical effect. (5) Intra-beat variability is documented by DTV and ETV, which present spectral components in the same frequency bands as HRV but with differential autonomic modulation. DT and RR series present similar variability, which indicates that they are the intervals susceptible to autonomic modulation. In contrast, the minimal variability showed by ET series supports their low responsiveness to autonomic modulation.

HRV time-frequency spectra computed from RR series were used as reference to compare to both inter-beat variability (RR vs. IHP series) and intra-beat variability (RR vs. DT and ET series). IHP series obtained from ICG traces are not interchangeable with RR series, because the former present differences depending on the frequency band and on the maneuver, in particular the greater additional respiratory modulation of mechanical origin, conspicuous in E condition. These results discourage the use of heart periods extracted from cardiovascular signals other than ECG as surrogates for RR series for spectral analysis of HRV.

In conclusion, although HRV determines most IHPV, the latter contains additional respiratory modulation that limits their interchangeability, especially in maneuver E. Intra-beat variability is documented by DTV and ETV. The similarity between DTV, IHPV and HRV, indicates that DT is the portion of the cardiac cycle where autonomic modulation preferentially occurs, contrasting with the much reduced ETV, required for the appropriate timing of systolic processes. HRV autonomic modulation permeates all the cardiovascular variables with two inter-beat rhythms, which are fully transmitted to the intra-beat DT series and, to a lesser extent, to the ET series.

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