Variability of the Maximal Amplitudes of Impedance Cardiogram and of its First Derivative during Supine, Standing, Paced Breathing, and Exercise Maneuvers

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Abstract

Beat-to-beat variability of the maximal amplitudes of thoracic impedance (ΔZ_{max}) and of its first derivative (dZ/dt_{max}) remain unexplored. We examined the effects of four maneuvers eliciting different sympathetic activity levels on ΔZ_{max} and dZ/dt_{max} time-frequency spectral measures. Seventeen healthy subjects performed 5-min maneuvers: lying, controlled breathing, standing (S) and exercise (E). Time-frequency spectra of RR intervals (RR), ΔZ_{max}, dZ/dt_{max} and respiration (Res) time series were estimated to compute their low-frequency ($LF\Delta Z_{max}$, $LFdZ/dt_{max}$) and high-frequency powers (HF_{RR}, $HF\Delta Z_{max}$, $HFdZ/dt_{max}$, HF_{Res}) and the time-frequency coherences of HF_{Res} with $HF\Delta Z_{max}$ and $HFdZ/dt_{max}$. HF_{RR} and RR level decreased in S and E. $LF\Delta Z_{max}$ was negligible. $HF\Delta Z_{max}$ was maximal in E and showed significant coherences with HF_{Res}. $LFdZ/dt_{max}$ was maximal in E and decreased in S. $HFdZ/dt_{max}$ was much greater than $LFdZ/dt_{max}$ and showed significant coherences with HF_{Res}. Because $LFdZ/dt_{max}$ power is cardiac sympathetic activity and stroke volume dependent, it can be considered a noninvasive index of global left ventricular systolic function. $HFdZ/dt_{max}$ power is originated by thoracic volume changes. The mechanical respiratory effect is the main source of ΔZ_{max} and dZ/dt_{max} time series variability.

1. Introduction

The clinical utility of impedance cardiography (ICG) is controversial. For some authors, ICG favors diagnosis, medication titration and prognosis of cardiovascular disease, but for others its clinical use is limited due to the difficulty of getting stable, reliable and reproducible recordings [1, 2]. Still, ICG is a widely used methodology in research and clinical settings for the evaluation of cardiovascular function because it is simple, easy to apply, safe, noninvasive, and capable of beat-to-beat monitoring stroke volume (SV) and contractility [2, 3]. From amplitudes and time intervals of ICG waveform and of its first derivative, a multitude of parameters are derived, prominently the maximal amplitudes of impedance signal (ΔZ_{max}) and of its first derivative (dZ/dt_{max}). The latter participates in all the proposed equations for computing SV by ICG [3] and in the derivation of several myocardial contractility measures, such as the Heather Index [4]. However, the beat-to-beat variability of ΔZ_{max} and dZ/dt_{max} time series remains unexplored. Using an innovative methodology we tested if the levels and oscillations of ΔZ_{max} and dZ/dt_{max} series are affected by autonomic and/or respiratory states. Therefore, our aim was to examine, in healthy subjects, the effects of four maneuvers that elicit different sympathetic activity levels on the time-frequency spectral measures of ΔZ_{max} and dZ/dt_{max} time series.

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 conditions employed to induce specific changes in cardiac autonomic activity were: lying position (L), considered the control condition; controlled breathing (CB) at 0.2 Hz that augments vagal modulation; standing position (S), which elicits a sympathetic activity increase, and a single bout of 100W cycling exercise (E), which provokes substantial vagal withdrawal and sympathetic activation [5]. ECG, ICG, and respiration (Res) signals were recorded during each condition. Uniformity of the maneuvers performance was maintained as much as possible.

2.3. Signal recording and acquisition

ECG was detected from the CM5 bipolar lead and a bioelectric amplifier (Biopac Systems). ICG signal and its first derivative were recorded from four aluminum band electrodes, two placed around the neck and two around the thorax, connected to an impedance plethysmograph and a differentiator (Nihon Kohden). Res was registered with a stretching pneumograph (Nihon Kohden). All signals were digitized at a sampling rate of 1kHz via an acquisition and display system (Biopac Systems).

2.4. Data processing

Peak values of R wave, maxima and minima of Res and ICG signals, and B and C fiducial points of dZ/dt traces were automatically beat-to-beat detected to generate the respective R-R intervals (RR) and maximal amplitudes time series. The detection of the characteristic points was overseen by an expert and manually corrected when needed. All the time series were cubic-spline interpolated, resampled at 4 Hz and separated into trend (level or tone) and oscillations (variability) by the smoothness priors method [6] with a cutoff frequency of 0.03Hz. Trends were characterized by their mean value and SD. Time-frequency spectra of the variability of RR, ΔZ_{max}, dZ/dt_{max} and Res time series were estimated via the smoothed pseudo-Wigner-Ville time-frequency distribution (TFD) and integrated in the standard low-frequency (LF) and high-frequency (HF) bands to compute the high-frequency powers of RR (HF_{RR}), ΔZ_{max} ($HF\Delta Z_{max}$), dZ/dt_{max} ($HFdZ/dt_{max}$) and Res (HF_{Res}), and the low-frequency powers of ΔZ_{max} ($LF\Delta Z_{max}$) and dZ/dt_{max} ($LFdZ/dt_{max}$). Time-frequency coherences of HF_{Res} with $HF\Delta Z_{max}$ and $HFdZ/dt_{max}$ were obtained. Coherences greater than 0.5 were considered significant.

2.5. Statistical analysis

A logarithmic transformation was applied to HF_{RR} ($lnHF_{RR}$) because it presented a skewed distribution. Data of the variables dynamics were pooled and expressed as mean±SD. Inter-maneuver differences were tested by ANOVA for repeated measures. Post-hoc pairwise comparisons were performed by the Tukey test. Statistical significance was accepted at $p<0.05$.

3. Results

In relation to L (control condition), $lnHF_{RR}$ increased in CB and decreased progressively in S and in E (Fig. 1A), with significant differences among maneuvers ($p<0.001$). RR level (Fig. 1B) decreased in S ($p<0.001$) and was minimal in E condition ($p<0.001$). ΔZ_{max} series level was not different among the maneuvers (Fig. 1C), but its SD increased in E ($p<0.01$). In relation to L, dZ/dt_{max} series level increased ($p<0.01$) in E (Fig. 1D). SD of dZ/dt_{max} series level decreased in S ($p<0.02$) and was maximal ($p<0.02$) in E (Fig. 1E).

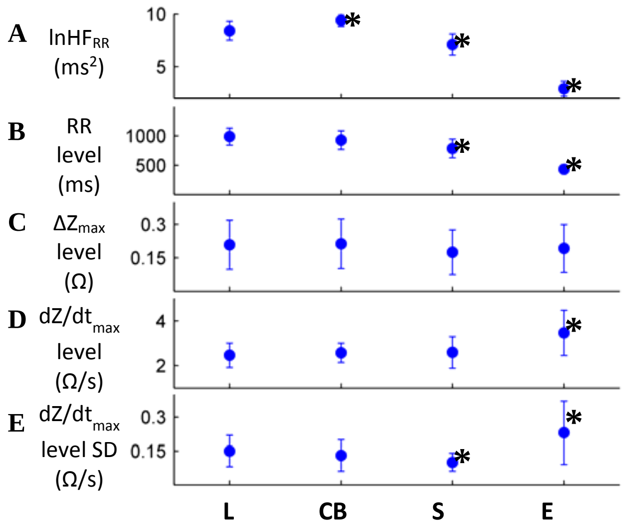

Figure 1. Mean ± SD of pooled data from dynamics of (A) $lnHF_{RR}$ power (B) RR level, (C) ΔZ_{max} level, (D) dZ/dt_{max} level and (E) SD of dZ/dt_{max} level during the 4 maneuvers. *$p<0.01$ vs. L (control condition).

The TFD of ΔZ_{max} series showed that their power is only distributed in the HF band, since no components are appreciable in the LF band. Additionally, $HF\Delta Z_{max}$ did not change throughout the maneuvers, except in E, and presented much lower powers than the TFD of dZ/dt_{max} series (Fig. 2). In contrast, power of dZ/dt_{max} TFD were distributed in both LF and HF bands, and were affected by the maneuvers, attaining their maximal value during E. Instantaneous powers of ΔZ_{max} and dZ/dt_{max} series presented large fluctuations in all maneuvers (Fig. 2).

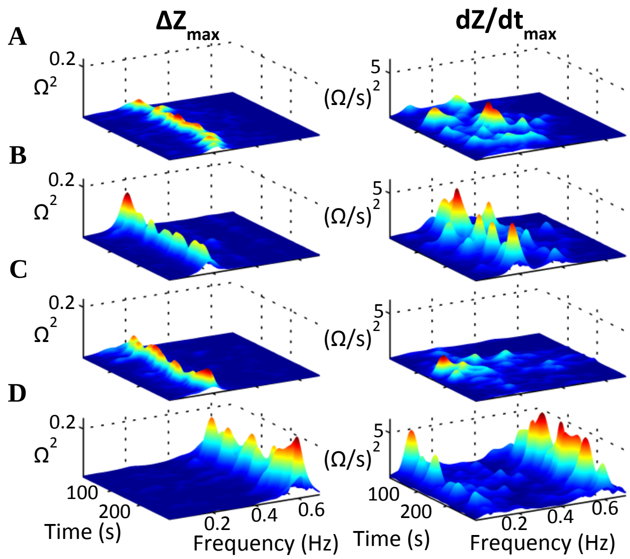

Figure 2. Representative example of the TFD of ΔZ_{max} (left column) and dZ/dt_{max} time series (right column) in (A) L, (B) CB, (C) S and (D) E conditions.

$LF\Delta Z_{max}$ power did not change significantly during the maneuvers (Fig. 3A) and was 20 times smaller than $HF\Delta Z_{max}$ power (Fig. 3B), which was maximal in E condition ($p<0.01$).

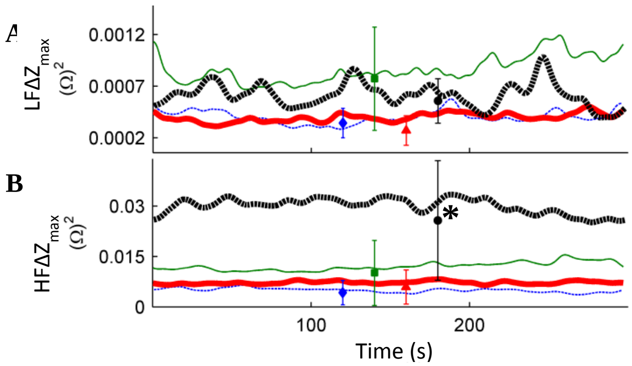

Figure 3. Ensemble averages of the dynamics and mean ± SD of pooled values of (A) $LF\Delta Z_{max}$ and (B) $HF\Delta Z_{max}$ during the four maneuvers: L (thin dotted line, ♦), CB (thin solid line, ■), S (thick solid line, ▲) and E (thick dotted line, ●) *$p<0.01$ vs. L control condition.

During the four supposedly stationary maneuvers $LFdZ/dt_{max}$ and $HFdZ/dt_{max}$ power dynamics presented important instantaneous fluctuations, visible even in their ensemble averages (Fig. 4). With respect to L, $LFdZ/dt_{max}$ decreased in S ($p<0.01$) and increased ($p<0.01$) in E (Fig. 4A). In relation to L, $HFdZ/dt_{max}$ power presented a large increment ($p<0.001$) in E and decreased ($p<0.01$) in S (Fig. 4B). $HFdZ/dt_{max}$ power was around 6 times larger than $LFdZ/dt_{max}$ in all maneuvers but E, during which the $HFdZ/dt_{max}$ to $LFdZ/dt_{max}$ ratio reached a value of 12.

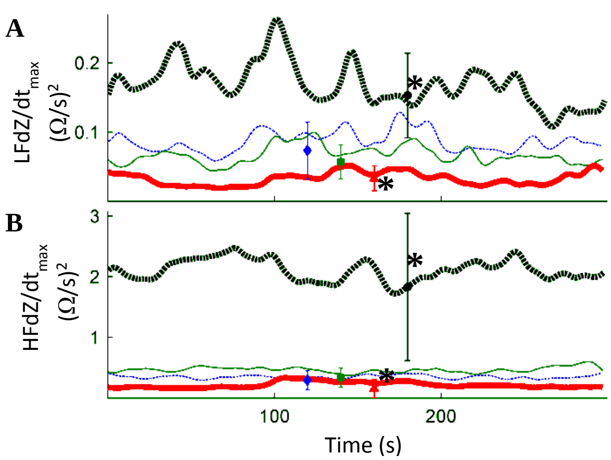

Figure 4. Ensemble averages of the dynamics and mean ± SD of pooled data of (A) $LFdZ/dt_{max}$ and (B) $HFdZ/dt_{max}$ during the four maneuvers: L (thin dotted line, ♦), CB (thin solid line, ■), S (thick solid line, ▲) and E (thick dotted line, ●) *$p<0.01$ vs. L control condition.

The averages of the individual pooled time-frequency coherences of HF_{Res} with $HF\Delta Z_{max}$ and with $HFdZ/dt_{max}$ were greater than 0.85 in all maneuvers (Fig. 5).

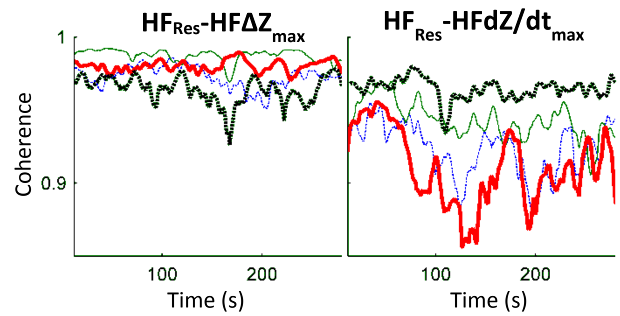

Figure 5. Ensemble averages of HF_{Res}-$HF\Delta Z_{max}$ (left panel) and HF_{Res}-$HFdZ/dt_{max}$ (right panel) time-frequency coherences obtained during: L (thin dotted line), CB (thin solid line), S (thick solid line) and E (thick dotted line)

4. Discussion

This study establishes that, in healthy subjects, both levels and spectral measures of ΔZ_{max} and dZ/dt_{max} time series are associated with cardiac sympathetic and/or respiratory activities, the latter being the major source of their variability. These notions are supported by the following findings: with respect to L condition, SD of ΔZ_{max} level and $HF\Delta Z_{max}$ power increased greatly in E and remained unchanged in CB and S, $HF\Delta Z_{max}$ with very high coherences with HF_{Res}; ΔZ_{max} level and $LF\Delta Z_{max}$ did not change through the maneuvers and its power was 20 times smaller than that of $HF\Delta Z_{max}$; SD of dZ/dt_{max} level and $LFdZ/dt_{max}$ power were smaller in S and much larger in E; $HFdZ/dt_{max}$ power showed large increments in E, with very high coherences with HF_{Res}.

Our methodology comprises the following strategies: 1) The analysis of the time series considers both their trend and variability, obtained by the smoothness priors method. The tone was evaluated by its mean and SD, and the variability by its TFD. 2) The use of a TFD, which allows to: a) better characterize the variability of the time series due to its ability to track the instantaneous power of non-stationary signals over time; b) avoid the difficult task of testing the stationarity of the signals [7]; and c) compute the time-frequency coherence between different signals by cross-spectral analysis to assess their degree of association over time. 3) The application of three provoking maneuvers, CB, S and E, to produce increasing levels of sympathetic and respiratory activities, and thus testing if the tone and variability of the cardiovascular time series are dependent on autonomic and respiratory mechanisms.

To our knowledge, this is the first study to perform spectral analysis of ΔZ_{max} and dZ/dt_{max} time series, and to establish that their level and $LFdZ/dt_{max}$ power present some association with cardiac sympathetic activity, and the mechanical respiratory origin of $HFdZ/dt_{max}$ power. It also adds evidence favoring our hypothetical generalization that the time series of all cardiovascular variables possess tone and variability that are associated with autonomic and/or respiratory states.

ΔZ_{max} occurs in the late ventricular ejection phase, and is probably associated with atrial filling, pulmonary and vena cava blood flows [8]. ΔZ_{max} time series do not exhibit significant beat-to-beat variability. $LF\Delta Z_{max}$ power is very little. $HF\Delta Z_{max}$ is 20-times greater and unresponsive to the maneuvers, except for its increase in E (Fig. 3B), condition that courses with a remarkable reduction of heart rate variability. These results suggest that ΔZ_{max} variability is not subject to autonomic modulation but only to the mechanical respiratory modulation exerted through changes in thoracic volume and in the central blood flows involved in ΔZ_{max} genesis.

dZ/dt_{max} is associated with the maximal changes in the volume of ascending aorta during the ventricular ejection phase [8]. It participates in all algorithms for computing SV by ICG, and has been employed as a noninvasive estimate of myocardial contractility by itself [9] or combined with other parameters, such as in the Heather index, which is the most validated contractility measure [4, 10]. The increase observed in dZ/dt_{max} series level during E agrees with that reported previously [10]. An interesting finding is that the SD of dZ/dt_{max} series level is modified by the maneuvers, especially by E (Fig. 1E), indicating that the tone also presents fluctuations dependent on the autonomic and/or respiratory state of the subject.

The TFD of dZ/dt_{max} series present spectral powers distributed in the standard frequency bands of heart rate variability, which are affected by the maneuvers (Fig. 2 and 4). In our supposedly stationary maneuvers, instantaneous powers of ΔZ_{max} and dZ/dt_{max} series showed important fluctuations over time in both frequency bands (Fig. 2 and 4), suggesting that all physiological signals are unavoidably non-stationary. The increment of $LFdZ/dt_{max}$ spectral power in E and its diminution in S condition (Fig. 4A) can be explained by its dependence on both the cardiac sympathetic activity and left ventricular preload–SV levels. In S, sympathetic activity is augmented, as supported by the observed reduction of RR level (a sympathetic tone index), and of $lnHF_{RR}$ power (a vagal outflow measure), but preload and SV level are reduced, as has been well documented [3]. In E condition, the sympathetic activity increment, documented by the great reduction of RR level and $lnHF_{RR}$ power (Fig. 1), and the well-known rise in preload–SV and cardiac contractility levels [10], all contribute to the increase of $LFdZ/dt_{max}$ power.

The high coherences between $HFdZ/dt_{max}$ and HF_{Res} observed in the four maneuvers (Fig. 5) and the maximal $HFdZ/dt_{max}$ power in E (Fig. 4B) suggest that this component is originated by the mechanical respiratory effect on thoracic volume and aortic blood flow. Res is the main source of the overall beat-to-beat variability of dZ/dt_{max} time series, as supported by the large ratio between $HFdZ/dt_{max}$ and $LFdZ/dt_{max}$ observed.

In conclusion, in healthy subjects, ΔZ_{max} series variability is minimal and of mechanical respiratory origin. $LFdZ/dt_{max}$ power is determined in part by cardiac sympathetic activity and in part by the preload–SV levels, as supported by its decrement in S and increment during E. Therefore, this component can be considered as an indicator of global left ventricular systolic function. $HFdZ/dt_{max}$ power is produced by the non-neurally mediated respiratory influence. Res is the major source of the overall beat-to-beat variability of ΔZ_{max} and dZ/dt_{max} time series.

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