Active Standing Test Provokes Different Effects on the Variability of Diastolic and Systolic Electromechanical Subintervals

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Abstract

We compared the effects of the active standing test (AST) on the variability of systolic (SRS), and diastolic (DSR) subintervals in 24 volunteers. The time courses of the low-frequency (LF_{RR}, LF_{SRS}, and LF_{DSR}) and high-frequency powers (HF_{RR}, HF_{SRS}, HF_{DSR}) of RR, SRS, and DSR series were computed using a time-frequency distribution. While the time courses of RR and DSR series displayed a sudden fall, SRS series showed a minuscule increase. Correlation of RR intervals with DSR, and SRS were 0.996±0.004, and -0.313±0.29, respectively. LF_{RR} and LF_{DSR} showed overshoots, with coherence of 0.996±0.003, correlation of 0.995±0.007, and LF_{DSR}/LF_{RR} of 1.10±0.07. LF_{SRS} displayed very small overshoots, with LF_{SRS}-LF_{RR} coherence of 0.71±0.11, correlation of 0.64±0.22, and LF_{SRS}/LF_{RR} of 0.02±0.01. HF_{RR} and HF_{DSR} fell abruptly, with coherence of 0.993±0.007, correlation of 0.996±0.005, and HF_{DSR}/HF_{RR} of 1.21±0.13. HF_{SRS} showed a small increment, with HF_{SRS}–HF_{RR} coherence of 0.67±0.13, correlation of 0.01±0.54, and HF_{SRS}/HF_{RR} of 0.02±0.01. Our findings support that the autonomic modulation of AST is exerted mainly on the DSR subinterval, with minimal impact on the SRS subinterval. The greater variability of DSR than RR in the low and high frequencies results from the combined modulatory effects of respiratory and vascular factors.

1. Introduction

The left ventricular (LV) systolic time (ST_{LV}) and diastolic time (DT_{LV}) have been obtained from ECG and phonocardiogram recordings. ST_{LV} is the period from the R wave peak to the second heart sound (R-S2), while DT_{LV} is its complement, S2-R. The use of these LV times has been useful in the cardiological practice. Thus, the analysis of DT_{LV} has significantly improved the overall diagnostic value of the exercise tolerance test in myocardial ischemia [1]. ST_{LV} has been divided into the pre-ejection period and ejection time, which are used for the evaluation of LV function, with significant diagnostic and prognostic value in heart failure [2].

The conventional mode for measuring pulse transit time (PTT) is as the pulse arrival time, computed using ECG and the photoplethysmographic pulse waveform. It is used in clinical settings to assess arterial stiffness. It has been reported that the rising low-frequency (LF) component of PTT series variability (LF_{PTT}) may indicate an increase in sympathetic activity induced by sleep apnea [3].

The active standing test (AST) is a well-known maneuver that triggers an increase in sympathetic activity and vagal withdrawal. It is commonly used in clinical settings to assess baroreflex-induced cardiovascular autonomic activity. However, the time courses of RR intervals have only been characterized during the first 30 seconds of AST [4]. Moreover, the time courses of the LF and high-frequency (HF) powers of RR series variability (LF_{RR} and HF_{RR}) in AST have not been well-documented.

Our approach involves dividing the RR intervals into the systolic (SRS) and diastolic (DSR) electromechanical subintervals, by determining the timing of the systolic point (S) in the arterial pressure (AP) waveform, and then comparing the LF and HF powers of the variabilities of the SRS, DSR, and RR time series in response to the sympathoexcitatory maneuver AST.

We assessed and compared the effects of AST on the time courses of RR, SRS, DSR series and their corresponding LF (LF_{RR}, LF_{SRS}, LF_{DSR}) and HF (HF_{RR}, HF_{SRS}, HF_{DSR}) components. These were estimated using the pseudo-Wigner-Ville time-frequency distribution (TFD). Also, correlation and coherences between time series and spectral dynamics were obtained.

We hypothesize that the sympathetic modulatory effect of AST is much greater in DSR than in SRS, based on the notion that the autonomic modulation is exerted on the diastolic depolarization slope of the sinoatrial node [5] and that the small variability of the SRS, that includes PTT, is produced by arterial factors.

2. Methods

2.1. Subjects

Twenty-four healthy, nonsmoking, and sedentary volunteers, 13 men and 11 women, participated. Their

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mean age, height, and weight were 22.2±2.2 years, 167±8 cm, and 69.1±10.4 kg, respectively. Their written informed consent was requested to participate. This study was approved by the ethics committee of our university.

2.2. Protocol

During the first visit to the laboratory, the subjects' health status and anthropometric variables were assessed. During the second visit, the experimental stage was carried out. Subjects underwent 1-min control, 1-min AST, and 2-min recovery stages. To perform AST, the subjects rapidly stood up from the supine position, remained standing for a minute, and returned to the supine position to end the maneuver. Throughout the entire session ECG, noninvasive AP, and respiratory signals were recorded.

2.3. Signal recording and acquisition

ECG was detected at the thoracic bipolar lead CM5 using a bioelectric amplifier (Biopac Systems). Noninvasive AP was measured by Finapres (Ohmeda). The respiratory signal was obtained by an inductance transducer (Respitrace). All signals were digitized at a sampling rate of 1 kHz via an acquisition and display system (Biopac Systems).

2.4. Data processing

Fiducial points of ECG (R wave peak) and AP (S peak) recordings were detected to construct the RR, systolic pressure (SBP), and diastolic pressure (DBP) time series. The SRS subinterval was measured as the time from the occurrence of the R wave to the corresponding SBP, and the DSR as the complementary time, i.e. as the period from the SBP to the next R wave. The time series were cubic-spline interpolated, resampled at 4 Hz, and detrended by the smoothness priors method.

Auto- and cross-time-frequency spectra of RR, SRS, and DSR were estimated with the smoothed pseudo-Wigner-Villé TFD. We extracted the instantaneous LF_{RR}, LF_{SRS}, and LF_{DSR}, and the corresponding HF_{RR}, HF_{SRS}, HF_{DSR} from the first moment of their TFD in the standard HRV LF and HF bands. Correlations, coherences, and ratios between the spectral indexes of SRS and DSR vs. RR were also obtained. The ensemble averages of the individual indexes dynamics were obtained to highlight any patterned responses. Also, indexes' time courses were divided into 15-s epochs for statistical purposes.

2.4. Statistical analysis

Differences between the control and mean epoch values of each variable and between epoch values of the different variables were tested by ANOVA for repeated measures. Post-hoc pairwise comparisons were performed by the Tukey test. Indexes dynamics were used to compute linear regressions and correlations vs. RR intervals. Statistical significance was accepted at $p<0.05$.

3. Results

During AST, the response patterns of the indexes' time-courses showed the following changes, all significant ($p<0.001$) relative to their baseline.

At the onset of AST, RR and DSR series fell abruptly, recovered partially, and presented a minor fall at the end, followed by an overshoot in recovery (Fig. 1). SRS series showed a minuscule increase that recovered and a tiny decrease after the maneuver.

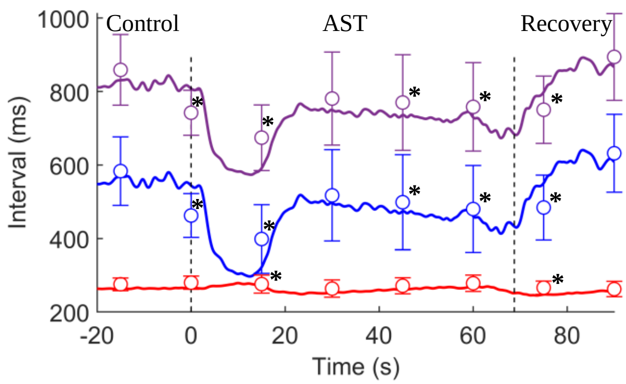

Fig. 1. Ensemble averages of the time courses of RR (purple), SRS (red), and DSR (blue) intervals time series during control, AST, and recovery. *p<0.01 vs. control

DSR subintervals were directly proportional to RR intervals, with a mean correlation of 0.996±0.004, while SRS subintervals presented poor inverse proportionality with RR, with mean r=-0.313±0.29 (Fig. 2).

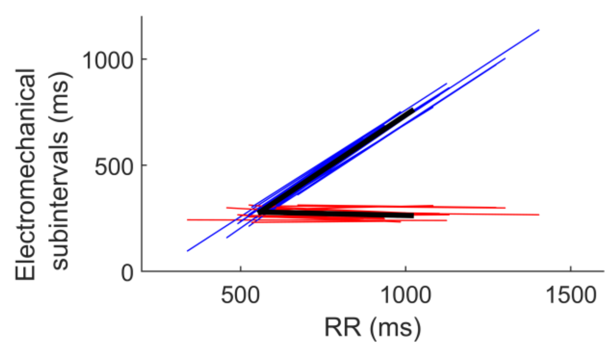

Fig. 2. Mean linear regressions (thick black lines) computed from the individual regressions between SRS and RR (red) and between DSR and RR (blue).

LF_{RR} and LF_{DSR} overshoot at the beginning and the end of AST (Fig. 3 A-B). LF_{DSR}-LF_{RR} relation presented a mean coherence of 0.996±0.003 (Fig. 3D) and a mean correlation of 0.995±0.007. LF_{DSR} power was greater than LF_{RR} ($p<0.001$), with an LF_{DSR}/LF_{RR} ratio of 1.10±0.07 (Fig. 3E). LF_{SRS} displayed very small overshoots at the beginning and the end of AST (Fig. 3C). LF_{SRS}-LF_{RR} relation presented a mean coherence of 0.71±0.11 (Fig. 3D) and a mean correlation of 0.64±0.22. LF_{SRS} was much less than LF_{RR} ($p<0.001$), with a mean LF_{SRS}/LF_{RR} ratio of 0.02±0.01 (Fig. 3E).

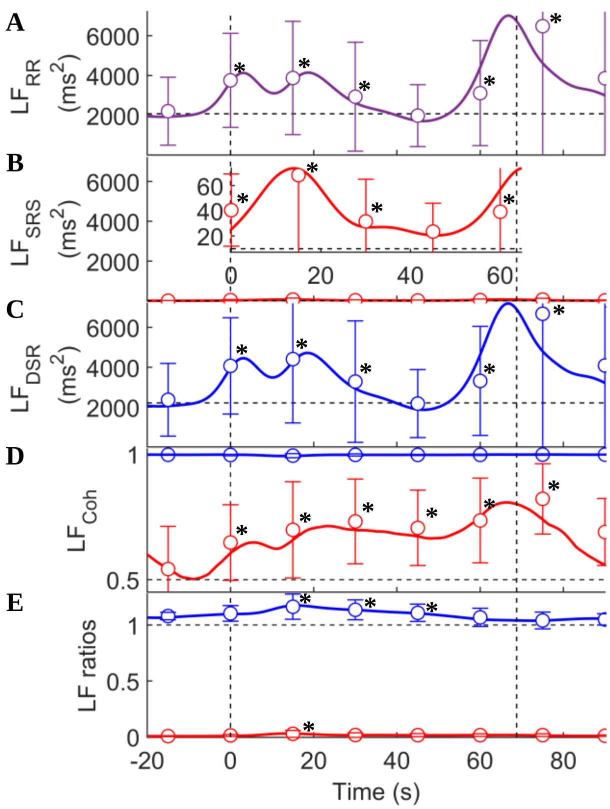

Fig. 3. Ensemble averages of the time courses of A) LF_{RR}, B) LF_{SRS}, C) LF_{DSR}, D) LF_{SRS}-LF_{RR} coherence (red), and LF_{DSR}-LF_{RR} coherence (blue), E) LF_{SRS}/LF_{RR} (red) and LF_{DSR}/LF_{RR} (blue) ratios during control, AST, and recovery. Insert in B) depicts LF_{SRS} at 100x scale zoom. *p<0.01 vs. control

HF_{RR} and HF_{DSR} fell suddenly and remained reduced until the end of AST, followed by an overshoot during recovery (Fig. 4 A-B). HF_{DSR}-HF_{RR} relation presented a mean coherence of 0.993±0.007 (Fig. 4D) and a mean correlation of 0.996±005. HF_{DSR} power was greater than HF_{RR}, with a mean HF_{DSR}/HF_{RR} ratio of 1.21±0.13 (Fig. 4E). HF_{SRS} displayed a small increment at the beginning of AST, sustained until the end (Fig. 4C). HF_{SRS}-HF_{RR} relation presented a mean coherence of 0.670±0.130 (Fig. 4D) and a mean correlation of 0.011±0.54. HF_{SRS} power was much less than HF_{RR} ($p<0.001$), with a mean HF_{SRS}/HF_{RR} ratio of 0.02±0.01 (Fig. 4E).

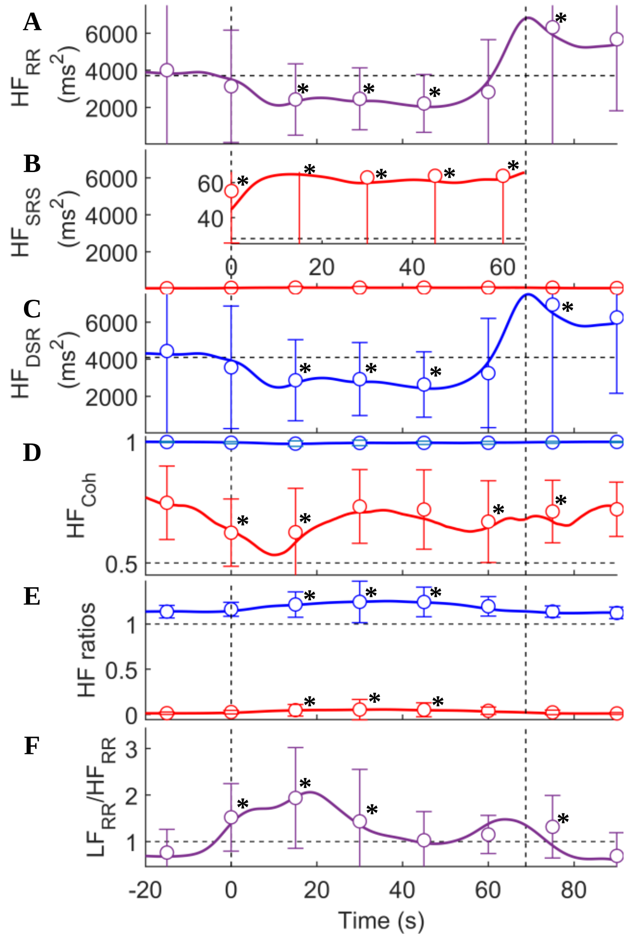

Fig. 4. Ensemble averages of the time courses of A) HF_{RR}, B) HF_{SRS}, C) HF_{DSR}, D) HF_{SRS}-HF_{RR} coherence (red) and HF_{DSR}-HF_{RR} coherence (blue), E) HF_{SRS}/HF_{RR} (red) and HF_{DSR}/HF_{RR} (blue), and F) LF_{RR}/HF_{RR} ratios during control, AST, and recovery. Insert in B) depicts HF_{SRS} at 100x scale zoom. *p<0.01 vs. control

4. Discussion

This study documents that AST induces sympathetic modulation mainly in the DSR series, with minimal effect in the SRS series. Our main findings are as follows: At the beginning and end of AST there is a shortening in the highly correlated RR and DSR interval series, and a minuscule effect on the SRS series. The onset and the end of AST induce overshoots in the LF_{RR} and LF_{DSR}, and depression of HF_{RR} and HF_{DSR} dynamics. The patterns over time of both types of indicators in both frequency bands are very similar, strongly correlated, and highly coherent with each other. Conversely, the autonomic modulation on the time courses of LF_{SRS} and HF_{SRS} is minuscule.

AST causes a significant shortening of RR time courses within the first 10 seconds, followed by a gradual recovery [4]. Our study adds to this known response by documenting that, when the subject returns to the supine position to end the AST, a second shortening occurs (Fig. 1). The relationships of the RR series with the DSR and SRS subintervals clearly indicate that while the DSR subinterval accurately mirrors RR changes (very strong correlation), SRS maintains a certain constancy (Fig. 2). These relationships resemble the reported relationships of RR series with DT_{LV} and ST_{LV} [6].

The time courses of sympathetic and vagal activity in response to AST has not been consistently characterized. Our findings document overshoots of sympathetic activity and decreases in vagal activity at the start and end of the maneuver, which revert in the recovery. Throughout the AST maneuver, there is a clear prevalence of sympathetic activity, as indicated by the increased LF_{RR}/HF_{RR} ratio time course (Fig. 4F). The increase in sympathetic outflow at the start of AST is much greater than at the end (Fig. 4F).

In heart transplant recipients, small beat-to-beat fluctuations in DT_{LV} series and respiratory-related oscillations in ST_{LV} series have been observed [6]. Therefore, in the absence of autonomic modulation, the variability of DT_{LV} is largely diminished. The effects of heart disease on ST_{LV} and DT_{LV}, measured from ECG and phonocardiogram recordings, have been well-documented [1,2]. This justifies the importance of studying these subintervals by estimating them from recordings that facilitate their beat-to-beat monitoring, such as peripheral pulse recordings. However, the SRS subinterval overestimates the duration of ST_{LV} measured as the R-S2 interval, because it includes the PTT. The DSR subinterval underestimates the duration of DT_{LV} by a similar amount.

Partitioning RR intervals into the SRS and DSR subintervals, based on the timing of the S point in the peripheral pulse recording (AP waveform), along with AST and TFD spectral analysis, enables the comparison of the effects of the maneuver on the variability over time of these subintervals in the LF and HF bands, which, according to the findings of the present study, are influenced by cardiac and arterial factors. The LF_{DSR} and HF_{DSR} time courses closely resemble the dynamics of the LF_{RR} and HF_{RR} components. There are high correlations and coherences between them (Fig. 3C and 4C), mainly because they are affected by the same autonomic modulation. During AST, approximately 85% of the fluctuations of the DSR interval is produced by autonomic modulation, while the remaining 15% is attributed to arterial factors. This interpretation is supported by the LF_{DSR}/LF_{RR} and HF_{DSR}/HF_{RR} ratios, which are both greater than 1, 1.10±0.07 and 1.21±0.13, respectively.

The minuscule effects elicited by AST on the SRS series (Fig. 1) and on the LF_{SRS} and HF_{SRS} components (Fig. 3B and 4B) suggest that the SRS subinterval is not influenced by autonomic modulation, unlike its complement DSR (Fig. 3C and 4C). The increases in both LF_{SRS} and HF_{SRS} time courses observed in the current study are significant in comparison to their baseline but minuscule in comparison to those of RR and DSR, as shown by the LF_{SRS}/LF_{RR} and HF_{SRS}/HF_{RR} ratios (Fig. 3E and 4E). These increases are possibly caused by mechanical respiratory and arterial mechanisms. This supports our explanation that the autonomic modulation of RR series only occurs in the DSR subinterval, ruling out any autonomic modulation in the SRS interval. Further support for our explanation comes from studies that have shown that the small variability in the LF and HF bands of R-T periods, comprised in ST_{LV}, is not provoked by autonomic modulation [7]. Therefore, our interpretation differs from the reported autonomic sympathetic origin ascribed to the increase in LF_{PTT} [3].

Our findings support that: 1) since the modulatory effects of sympathetic increase and vagal reduction caused by AST on the RR series are faithfully reproduced by the DSR variability, and the effects on SRS variability are minuscule, the autonomic modulation occurs exclusively on the diastolic subinterval. 2) The greater variability in LF and HF bands of the DSR subinterval compared to that of the RR interval is due to the addition of the modulatory effects of respiratory and arterial factors.

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