Tracking Central Hypovolemia with Heart Period Variability (HPV) in Humans: Implications for Patient Monitoring

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ABSTRACT

Objective: To ascertain the utility of HPV metrics in tracking central blood volume during simulated hemorrhage in humans. Methods: One hundred six (62M/44 F) healthy, non-smoking volunteers were instrumented for measurement of ECG and beat-by-beat finger arterial pressure. Stroke volume (SV) was estimated from the arterial pulse wave and used to reflect central blood volume. Progressive lower body negative pressure (LBNP) was applied as a simulation of hemorrhage until the onset of impending hemodynamic decompensation (SBP<70 mmHg and/or presyncopal symptoms). HPV was assessed with analysis of R-to-R intervals using time, frequency and complexity metrics. To ascertain whether HPV metrics could track individual responses to central hypovolemia, between change scores at successive LBNP stages with percentage change in SV were performed. Results: Application of increasing LBNP progressively reduced R-R intervals and SV. Group means of each HPV metric also changed progressively during LBNP and were strongly correlated (amalgamated r≥0.87) with SV. Cross-correlation analysis revealed that none of the HPV metrics showed strong individual correlations with SV (r≤0.49) across successive LBNP levels. Conclusion: While group mean values for HPV metrics are well-correlated with SV changes during central hypovolemia, these metrics do not reliably track individual SV responses during LBNP. HPV parameters therefore may not be useful in monitoring hemorrhagic injuries in individual patients.

BACKGROUND

- Heart period variability (HPV) indices have been proposed for use in assisting triage decisions in hemorrhaging trauma patients (1-5)
  - HPV metrics distinguish between prehospital trauma patients who:
    - Live *vs.* die (1-4)
    - Receive a life-saving intervention *vs.* those that do not (5)
  - HPV metrics change with progressive blood loss in:
    - Hemorrhaged animals (6, 7)
    - Humans exposed to central hypovolemia via lower body negative pressure (LBNP) (1)
- All previous proposals of HPV utility for patient monitoring have been solely based on analysis of average group responses to hypovolemia
- The subsequent step of determining individual responses to hypovolemia has not yet been performed, but is necessary for further assessment of clinical utility

HYPOTHESIS

Group means of HPV metrics are strongly correlated with mean progressive reductions in central blood volume during LBNP, but there is also high inter-individual variability in these responses

METHODS

- Subjects: 101 healthy humans (58 M/43 F; height, 173 ± 1 cm; weight, 76 ± 2 kg; age, 28 ± 1 yrs (mean ± SE))
- Progressive LBNP leading to hemodynamic decompensation (i.e., precipitous fall in BP and/or onset of presyncopal symptoms)
- Measurements:
  - Finometer® → arterial BP, stroke volume (SV)
  - Lead II ECG → heart rate (HR), R-to-R interval (RRI)
- Data from last 3 minutes of baseline and each LBNP level analyzed off-line
- HPV Metrics Analyzed:
  - *LINEAR - Time Domain*: RRI standard deviation (RRISD); RRI root mean squared standard deviation (RMSSD); % adjacent RRI that vary by at least 50 ms (pNN50); Poincaré plot descriptors standard deviation 1 and standard deviation 2 (SD1; SD2); complex demodulation LF and HF (CDM LF; CDM HF)
  - *LINEAR - Frequency Domain*: RRI low frequency power (RRI LF; 0.04-0.15 Hz) and RRI high frequency power (RRI HF; 0.15-0.4 Hz)
  - *NONLINEAR*: Sample entropy (SampEn); Lempel-Ziv entropy (LZEn); fractal dimensions by curve length (FD-L); fractal dimensions by dispersion analysis (FD-DA); stationarity (StatAv); symbol dynamics entropy (SymDyn); detrended fluctuation analysis (DFA Long)

RESULTS

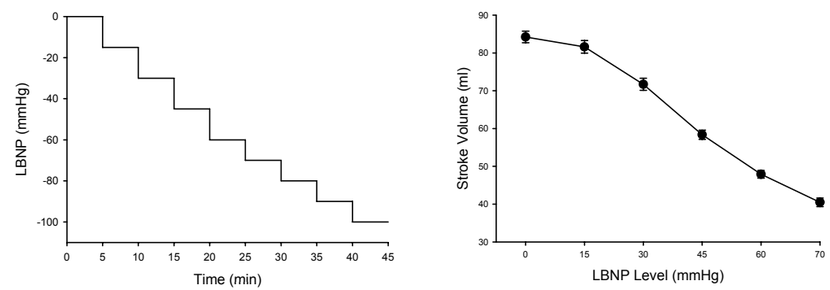

Figure 1. LBNP experimental protocol (left) and resultant stroke volume changes (right).

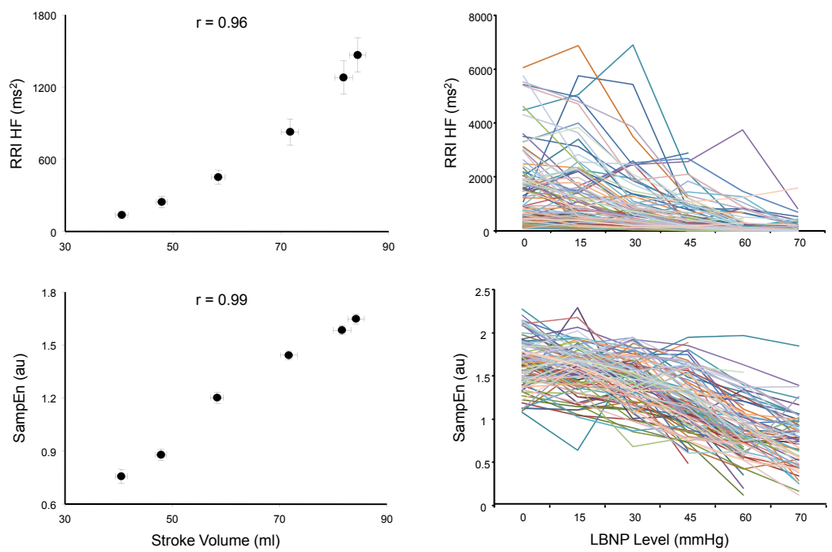

Figure 2. Examples of data analysis methods using RRI HF (top panels) and SampEn (bottom panels). Left panels show relationships between group means of each HPV metric and stroke volume during LBNP. Right panels show individual trajectories for each of the 101 subjects.

Table 1. Correlations of change scores at successive LBNP stages with percentage change in SV (i.e. Lag 1 differences cross correlations).

	LBNP Stage				
Metric	**0 to -15 (n=101)**	**-15 to -30 (n=101)**	**-30 to -45 (n=101)**	**-45 to -60 (n=82)**	**-60 to -70 (n=49)**
RRI	.31	.52	.62	.30	.30
RRISD	.02	.00	.11	.10	.22
$RMSSD_{ln}$	.18	.25	.35	-.02	.49
$pNN50_{sqrt}$	.13	.22	.41	.27	.07
$SD1_{sqrt}$	.14	.08	.34	.25	.41
SD2	-.02	-.02	.08	.11	.34
SD2/SD1	-.29	-.24	-.19	.08	-.28
CDM HF	.19	.09	.24	.30	.35
CDM LF	-.02	-.13	.10	.04	.44
RRI HF_{ln}	.12	.18	.17	.15	.49
RRI LF_{ln}	-.08	-.19	.03	-.03	.43
SampEn	.04	.25	.24	.19	.03
LZEn	.09	.24	.01	.07	.21
FD-L	.04	.05	.13	.01	.34
FD-DA	.14	-.09	.04	.26	.27
StatAv	-.13	.00	-.26	-.20	-.31
SymDyn	.09	.19	.17	.12	.15
DFA Long	-.09	.05	-.19	-.20	-.30

CONCLUSIONS

- Group means of each HPV metric accurately tracked changes in SV during central hypovolemia induced by LBNP (r ≥ 0.87)
- High inter- and intra-individual variability in responses of HPV metrics derived from RRI precluded reliable determination of the severity of hypovolemia at the individual level (r≤ 0.49)
- Our data indicate that use of HPV metrics to monitor trauma patients during the early dynamic phase of hemorrhagic injury may not be useful

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