CORRELATION BETWEEN SHORT-TERM HEART RATE VARIABILITY INDICES AND HEART RATE, BLOOD PRESSURE INDICES, PRESSOR REACTIVITY TO ISOMETRIC HANDGRIP IN HEALTHY YOUNG MALE SUBJECTS

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Abstract : The purpose of the present study was to determine whether readily measured blood pressure (BP) indices and responses to autonomic reflex tests could be used as surrogates of short-term heart rate variability (HRV), which is an established marker of autonomic regulation of SA node. Therefore, we examined the correlation between short-term HRV and heart rate (HR), BP indices viz. systolic pressure, diastolic pressure, pulse pressure (PP), and rate-pressure product (RPP), during supine rest and head-up tilt in 17 young healthy normotensive subjects, aged 19.8 ± 1 yr (mean $\pm$ SD). Three classic autonomic indices viz. Valsalva ratio, HR response to deep breathing and pressor response to isometric handgrip were also determined. We noted two interesting and statistically significant ($P<0.05$ in both cases) correlations viz. i) a positive correlation ($r = 0.6$) between change in RPP during tilt and change in low frequency (LF) RR spectral power expressed in normalized units (LF nu) during tilt, and ii) a negative correlation ($r = -0.6$) between change in PP during isometric handgrip and LF nu during tilt. The possible physiologic significance of these and other correlations is discussed in this paper. In conclusion, the presence of a statistically significant correlation between RPP, PP and spectral measures of short-term HRV supports a simplistic approach to autonomic assessment, in that, easily measurable BP indices could be used as surrogates of HRV when it is not feasible to determine HRV indices directly. However, the same have to be tested in healthy subjects belonging to various age groups and in patients with conditions known to be associated with autonomic dysregulation.

Key words : autonomic function   RR variability
                     rate-pressure product   isometric handgrip

INTRODUCTION

Cardiovascular autonomic function is increasingly evaluated with frequency-domain measures of short-term heart rate variability (HRV) because it reflects the frequency specific modulation of SA node by the two limbs of the autonomic nervous

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system (1–3). Studies of baroreflex physiology (4) and HRV in hypertensives (5) suggest that HRV is inversely correlated with blood pressure (BP). The purpose of this study was to test whether readily measured BP indices and responses to classic autonomic reflex tests could be used as surrogates of short-term HRV. Therefore, we examined the correlation between measures of short-term HRV and heart rate (HR), BP indices viz. systolic pressure (SP), diastolic pressure (DP), pulse pressure (PP), mean pressure (MP), and rate-pressure product (RPP), during supine rest and head-up tilt in 17 young healthy normotensive subjects. Apart from spectral indices of HRV, we determined the correlation between Valsalva ratio (VR) – a complex global index of sympathetic and parasympathetic effects (6, 7) and heart rate response to deep breathing (I - E HR difference) – a reliable index of vagal modulation of RR intervals (6–8), with HR and BP indices. The pressor response to sustained isometric handgrip (IHG) was taken as an index of sympathetic modulation of BP (6–8). We report here some interesting and statistically significant correlations that exist between short-term HRV indices and autonomic responses to head-up tilt and IHG in the group of subjects examined in the present study.

MATERIALS AND METHODS

Twenty seven male subjects aged 19.8 ± 1 yr (mean $\pm$ SD) were recruited for the study after a brief history and physical examination. The mean $\pm$ SD weight, height and body mass index (BMI) of the subjects were 53.8 ± 8.2 Kg, 1.67 ± 0.05 m, and 19.7 ± 2.5 Kg/m^2 respectively. None of them

had a significant medical history and their physical examination was normal. Autonomic reflex tests were carried out in the mornings, 1–2 h after a light breakfast and after familiarizing the subjects with the testing procedures. Subjects refrained from smoking and caffeinated drinks on the morning of the tests. None of the subjects were taking any medication at the time of testing. The Institute Ethics Committee approved the study protocol. All subjects gave written informed consent.

Baseline BP and HR were measured after 5 min of rest in the supine position on the tilt table. BP was measured with an oscillometric device (Colin Press-Mate, Model BP 8800, Colin Corporation Inc., Japan). For assessing the response to tilt, we used a manually operated tilt table with footplate support and the subject was strapped to the tilt table by safety restraints. After 5 min rest in the supine position, subjects were tilted 80° head-up for 5 min. BP was recorded immediately, 2 min and 5 min after tilt. The subject was then made to lie down comfortably on a couch, rest for 5 min and after that, instructed to breathe slowly and deeply, at six breaths per min. The HR response to deep breathing (I – E HR difference) was expressed as the average of the differences between the maximum HR and the minimum HR during deep breathing at six breaths per minute for one minute (6–8). The subjects were asked to perform the Valsalva maneuver in the sitting position by blowing into a mouthpiece attached to a manometer and maintaining an expiratory pressure of 40 mm Hg for 15 seconds. Valsalva ratio (VR) was calculated as the maximum RR interval immediately following

the strain divided by minimum RR interval during the strain (6–8). IHG was done by asking subjects to maintain 30% of maximum voluntary contraction pressure using a handgrip dynamometer for one and a half minutes. The difference between DP just before the release of handgrip and the baseline DP was noted as the pressor response to the test (7). RPP was calculated as SP $\times$ HR $\times$ 10^{-2} and expressed in units of mm Hg $\times$ beats per min $\times$ 10^{-2}.

Heart rate variability analysis) : A chest lead ECG was recorded throughout supine rest, head-up tilt, deep breathing and Valsalva maneuver using the BIOPAC MP 100 system (BIOPAC Inc., USA). Beat-to-beat variations in instantaneous HR were derived offline using a rate-detector algorithm (Acknowledge 3.7.3 software, BIOPAC Inc., USA). For computing HRV indices during supine rest and tilt, recommendations of the Task Force on HRV were followed (3). Briefly, a 5-min ECG was acquired at a sampling rate of 1000 Hz during supine rest and during tilt, with the subjects breathing normally at 12–18 per min. RR intervals were plotted using the BIOPAC Acknowledge 3.7.1 software. An RR series was extracted using a rate-detector algorithm after exclusion of artifacts and ectopics. A stationary 256 second RR series was chosen for analysis. In the time domain, the standard deviation of normal-to-normal RR intervals (SDNN) was taken as an index of overall HRV. The RR series was resampled at 4 Hz, the mean and trend removed, a Hann window applied and the 1024 data point series transformed by fast Fourier transformation. Low frequency (LF) and high frequency (HF) spectral powers

were determined by integrating the power spectrum between 0.04 and 0.15 Hz and 0.15 and 0.4 Hz respectively. Total power was calculated by integrating the spectrum between 0.004 and 0.4 Hz and includes very low frequency, LF and HF components. Spectral powers are expressed in absolute units of milliseconds squared. LF and HF powers are also expressed in normalized units as described previously (3).

Statistical analysis : Unless otherwise noted, data are expressed as mean $\pm$ SD. Since correlation was tested, the range of values of various parameters that were used is mentioned in Table I. Spectral powers are presented as median (interquartile range). Changes in parameters during tilt or handgrip were compared using Student's paired t-test for normally distributed data and Wilcoxon-matched pairs test for skewed data. Correlation between normally distributed indices was determined using the Pearson correlation coefficient. Correlation between various indices and RR interval spectral powers was tested using Spearman's rank correlation test. A two tailed P value less than 0.05 was considered significant.

RESULTS

Results are given in Tables I – IV. Resting BP, HR, I – E HR difference, VR and pressor response to IHG, are given in Table I. The mean RR and HRV indices at rest and during head-up tilt are given in Table II. HRV data during supine rest as well as head-up tilt were available only for 17 subjects. Thus, the correlations between resting HR, BP indices and HRV indices

TABLE I : Resting cardiovascular parameters, Valsalva ratio, heart rate (HR) response to deep breathing (I – E HR difference), and pressor response to isometric handgrip (IHG).

Parameter	Mean ± SD	Range (min – max)
Systolic pressure (mm Hg)	115±8	106–127
Diastolic pressure (mm Hg)	63±6	54–71
Pulse pressure (mm Hg)	51±5	40–61
Heart rate (beats per minute)	67±7	60–88
Rate-pressure product ($SP \times HR \times 10^{-2}$)	77±10	62–105
Valsalva ratio	2.1±0.5	1.3–3.25
I – E HR difference	29±7	15–36
Increase in diastolic pressure during IHG (mm Hg)	31±14	2–64
Change in pulse pressure during IHG (mm Hg)	6±15	-27–40

Data are for 27 subjects.

TABLE II : Mean RR and heart rate variability indices during supine rest and head-up tilt.

Parameter	Supine	Head-up-tilt	P value
Mean RR (ms)	817±100	721±92	<0.001
SDNN (ms)	48±20	50±13	NS
LF power (ms^2)	108 (52–236)	249 (166–513)	NS
HF power (ms^2)	157 (37–460)	54 (38–120)	<0.05
Total power (ms^2)	556 (189–1187)	563 (421–847)	NS
LF nu	46±18	79±16	<0.0001

Data from 17 subjects are expressed as mean±SD or median (interquartile range) whichever is appropriate.

SDNN: standard deviation of normal-to-normal RR intervals; LF and HF power : low frequency and high frequency RR spectral power respectively; LF nu : low frequency RR spectral power expressed in normalized units; NS : not significant.

given in Table III, and some interesting correlations given in Table IV were derived from 17 subjects. The correlation between HRV indices and BP and HR during supine rest is presented in the form of a correlation

TABLE III : Correlation matrix showing correlations between resting heart rate, blood pressure indices and short-term heart rate variability indices.

	Mean HR	SP	DP	PP	MP	RPP
SDNN	–0.6*	0.2	0	0.4	0.1	–0.5*
LF power	–0.4	0	0.1	0.5*	0.3	–0.3
HF power	–0.5*	0	–0.1	0.3	0	–0.4
LF+HF powers	–0.5*	0	–0.1	0.4	0.2	–0.4
Total power	–0.6*	0	–0.1	0.4	0.2	–0.5*
LF nu	0.3	0.3	0.4	0.1	0.4	0.5*
Valsalva ratio	0.1	–0.3	–0.3	–0.5	–0.3	–0.1
I – E HR difference	–0.2	0.1	0.2	–0.1	0.3	–0.2

Data (n = 17) are expressed as Pearson or Spearman correlation coefficient, whichever is appropriate.

*P<0.05

HR: heart rate; SP: systolic pressure; DP: diastolic pressure; PP: pulse pressure; MP: mean pressure; RPP: rate-pressure product; SDNN: standard deviation of normal-to-normal RR intervals; LF and HF powers: low frequency and high frequency RR spectral powers; LF nu: low frequency RR spectral power expressed in normalized units; I – E HR difference: Inspiration – expiration HR difference.

TABLE IV : Summary of other interesting correlations.

Parameter 1	Parameter 2	Pearson's correlation coefficient	P value
MP during supine rest	Tilt LF nu – rest LF nu	–0.4	0.09
MP after 5 min tilt	LF power at rest	0.4	0.08
MP ater 5 min tilt	LF nu at rest	0.4	0.08
MP ater 5 min tilt	Tilt LF nu – rest LF nu	–0.5	0.03
Δ RPP during tilt	Tilt LF nu – rest LF nu	0.6	0.01
Δ DP during IHG	LF nu tilt	0.4	0.1
Δ PP during IHG	LF nu tilt	–0.6	0.01
Valsalva ratio	Body mass index	–0.6	0.02

Data are given for 17 subjects.

Δ: change; MP: mean pressure; RPP: rate-pressure product; DP: diastolic pressure; IHG: isometric handgrip; LF power: low frequency spectral power; LF nu: low frequency spectral power in normalized units.

matrix in Table III. Change in RPP during tilt (Table IV) was derived as the difference between RPP after 2 minutes of tilt and resting RPP. Similarly, change in PP during IHG (Table IV) was derived as the difference between PP after one and a half minutes IHG and resting PP.

There was a statistically significant decrease in mean RR (P<0.001), HF power (P<0.05), and an increase in LF nu (P<0.0001) during head-up tilt (Table II). Statistically significant inverse correlations (P<0.05) were observed between SDNN, HF power, sum of LF and HF powers, total power, and mean HR at rest (Table III). There was no significant correlation between SP, DP and any of the HRV indices. There was no correlation between VR, I – E HR difference and HR or BP indices at rest or during tilt. We observed statistically significant (P<0.05) positive correlations between PP at rest and LF power, and between MP and LF power, LF nu at rest (Table III). A significant inverse correlation was noted between RPP and SDNN, and RPP and total power (P<0.05 for both) at rest (Table III).

DISCUSSION

It is worth noting that Valsalva ratio and I – E HR difference did not correlate with HR and BP indices whereas there were significant correlations between some HRV indices and HR, RPP as well as between HRV indices and autonomic responses to tilt and IHG. SDNN, which encompasses all components responsible for RR variability, is a simple time domain measure of overall HRV (3, 6). High frequency spectral power

reflects parasympathetic modulation of RR intervals at respiratory frequency (1–3, 9–11). LF power in absolute units of power quantifies baroreflex-mediated modulation of RR intervals in the 0.04–0.15 Hz range. Changes in sympathetic as well as vagal nerve traffic to the heart are thought to contribute to LF power (2, 3, 11). Total power, calculated as the sum of LF and HF powers is also an index of overall HRV (2). At least in physiologic states characterized by sympathetic excitation, low frequency spectral power expressed in normalized units of power (LF nu) has been shown to be a useful noninvasive index of sympathovagal balance (2, 12).

The decrease in mean RR, increase in LF nu, and decrease in HF power during head-up tilt (Table II) are well known concomitants of sympathetic excitation (2, 3, 12). Sympathetic excitation, which is associated with an increase in mean HR, reduces the magnitude of respiratory sinus arrhythmia (13). Also, greater the number of normal sinus beats in a given time period, lesser is the scope for modulation of RR intervals. RPP, which increases in states associated with sympathetic excitation, has been shown to correlate with myocardial oxygen consumption (14). Thus, the inverse correlation between RPP and SDNN, as well as RPP and total power is not surprising since sympathetic activation is known to result in an increase in HR, RPP and a decrease in overall HRV (3, 11, 13).

For a greater PP, loading of high-pressure baroreceptor afferents is greater and consequently, the reflex modulation of

RR interval is also higher. This is the basis for the positive correlation between PP and LF power during supine rest (Table III). However, the correlation between MP at rest and LF power was weak. This indicates that LF power is more closely related to stretch induced changes in firing of baroreceptor afferents rather than the tonic discharge in baroreceptor afferents in response to the prevailing MP.

LF nu is a widely used index of sympathovagal balance during head-up tilt (2, 12). A significant positive correlation between RPP during tilt and the change in LF nu (i.e. LF nu during tilt – LF nu during supine rest), given in Table IV, is possibly because of sympathetic excitation during head-up tilt. The physiologic significance of the positive correlation between the pressor response to isometric handgrip and LF nu during tilt, although not statistically significant (P = 0.1), may be the same. The pressor response to IHG is an index of sympathetic activation and vascular responsiveness to pressor stimuli (7). The inverse correlation between the increase in PP during IHG and LF nu during tilt has the same significance. The prominent increase in DP due to sympathetic augmentation of total peripheral resistance and accompanied by a baroreflex-mediated lowering of cardiac output causes PP to decrease during IHG. Thus, a greater decrement in PP during IHG would be

expected to be associated with higher LF nu. A significant negative correlation between VR, an index of sympathetic as well as parasympathetic modulation (6, 7) and BMI is not surprising since BMI and overall HRV are known to be inversely correlated (15).

In conclusion, the presence of a significant correlation between mean HR, pulse pressure, mean pressure, rate-pressure product changes during tilt, pulse pressure changes during isometric handgrip and spectral measures of short-term HRV, during the physiologic states examined, supports a simplistic approach to autonomic assessment, in that, mean HR and rate-pressure product could be used as surrogates of overall HRV and the pulse pressure change during isometric handgrip could be used as surrogate of LF nu when it is not feasible to determine HRV indices directly. However, observations need to be made in healthy subjects belonging to various age groups and in patients with conditions known to be associated with autonomic dysregulation.

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