ORIGINAL ARTICLE

The association of heart rate variability examined in supine and standing position with ambulatory blood pressure monitoring in anorexia nervosa

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Abstract

OBJECTIVE: To evaluate the association of heart rate variability (HRV) examined in supine and standing position with ambulatory blood pressure monitoring (ABPM) in patients with anorexia nervosa (AN).

METHODS: HRV in supine and standing position and ABPM were examined in 30 AN patients and 30 control subjects. The correlations between HRV and ABPM were evaluated.

RESULTS: The average age was 25±5 in AN patients and 25±4 years in controls (NS). LF (low frequency) power in AN patients and controls was comparable in supine position. LF power significantly increased during standing in controls, but no increment was detected in AN patients. The HF (high frequency) power was significantly increased in AN patients in supine position, but after standing was comparable with controls. The ratio LF/HF was lower both in supine and standing position in AN patients but the differences did not reach statistical significance. Blood pressure values in AN patients were comparable with controls in supine position but were significantly lower in standing position. Ambulatory blood pressure values were significantly lower in AN patients during active but not sleeping period. In standing position HF and LF powers positively and LF/HF negatively correlated with ABPM blood pressure values during active period in controls while in AN patients only LF power correlated with diastolic and mean blood pressures.

CONCLUSION: The lower ABPM values in AN patients during active period in comparison with control subjects may be explained by HRV changes, mainly by its impaired relations with blood pressure in standing position.

Abbreviations:

HRV	- heart rate variability
ABPM	- ambulatory blood pressure monitoring
BP	- blood pressure
BPs	- systolic blood pressure
BPd	- diastolic blood presure
BPm	- mean arterial blood pressure
HR	- heart rate
AN	- anorexia nervosa
HF	- high frequency
HF1	- high frewquency power in supine position
HF2	- high frequency power in standing position
LF	- low frequency
LF1	- low frequency power in supine position
LF2	- low frequency power in standing position
BMI	- body mass index
ms^2	- square miliseconds

INTRODUCTION

The natural history of anorexia nervosa is characterized by an increased cardiac mortality rate due to cardiovascular complications following the massive weight loss (Neumarker 1997; Casiero & Frishman 2006; Ono *et al.* 2009). The effect of severe caloric deprivation on heart size, myocardial mass, left ventricular function has been documented (Ulger *et al.* 2006; Galletta *et al.* 2005). The abnormalities of heart rate variability as well as variability of QT interval on electrocardiogram has been recognized in the previous studies and may be important for the development of cardiac complications (Koschke *et al.* 2010; Macias-Roblesa *et al.* 2009).

In the recent studies using ambulatory blood pressure monitoring (ABPM), lower blood pressure (BP) values and lack of circadian variation of BP in the anorexia nervosa (AN) patients were demonstrated. BP values were lower during active period but BP measured during sleep was not statistically different from those of control subjects (Cong *et al.* 2004; Oswiecimska *et al.* 2007; Awazu *et al.* 2000). In one of these studies 24 hours heart rate variability was examined together with ABPM (Cong *et al.* 2004). According to its results high frequency power (HF) is increased during whole 24 hours period and ratio of low frequency power (LF) to HF power is decreased in comparison with control subjects. However it does not explain why BP values are lower in active period and comparable with control subjects during sleep. During active period the patients frequently change the body position and majority of time are not in supine position contrary to sleeping period. In the literature there are only few reports about the effect of body position on HRV in patients with AN (Casu *et al.* 2002; Murialdo *et al.* 2007). Casu *et al.* (2002) found that HF components of spectral analysis did not significantly change when passing from clino- to ortostatism in the subjects with AN, but there were significant changes in controls. The changes in LF components were similar in both groups, but smaller in the subjects with AN. Contrary Murialdo *et al.* (2007) have shown mainly the impaired sympathetic activation after tilting in the patients with AN. In order to cast light on the contradictory results the aim of our study was to evaluate the changes of heart rate variability induced by body position (supine and standing) and its possible association with BP values during active and sleeping period measured by ABPM in comparison with control healthy subjects.

MATERIAL AND METHODS

The study was performed on 30 young women suffering from AN hospitalized due to acute phase of AN in Department of Medicine, University hospital, Prague-Motol, Czech republic. Control group consisted of thirty young women – nurses working in our hospital. Written informed consent was obtained from all the participants prior to entering the study. This study was approved by the Ethics Committee of University Hospital Motol, Prague and followed the Declaration of Helsinki.

The measurements of heart rate variability (HRV) were performed in the morning between 7.00 and 8.00 AM. No meal, drink or smoking was allowed before examination. After 10 minutes of rest the examination of HRV was recorded using telemetric system VariaCardio TF4 (Sima Media, Olomouc, Czech republic). Two 5 minutes periods were examined: the first one in the supine position, the second one in the standing position. In each period we evaluated HF and LF power. At the end of each period blood pressure was noninvasily measured in each patient and control person by monitor Dash 4000 (Marquette Hellige, Freiburg, Germany)

As soon as the examination of HRV was completed noninvasive 24-h ambulatory BP monitoring was performed by oscilometry with a portable automated Cardiette bp one (CardiLine, Milan, Italy) with calibration certification; simultaneous 24 hour heart rate monitoring was obtained. The unit was set to take reading every 30 minutes throughout 24 h. The following parameters were evaluated: daytime, nighttime and 24 hours systolic, mean and diastolic blood pressure and heart rate. Daytime and nighttime periods were based on the actual time of sleep reported by the patients. The patients recorded time when they went to bed at night as well as time when they got up in the morning. The percent sleep decline in BP was calculated by subtracting the sleep mean arterial pressure from the awake mean arterial blood pressure and dividing this value by awake mean arterial blood pressure.

Statistical analysis

Data are presented as means±SD. Data distribution was assessed using Kolmogorow-Smirnow test**.** The evaluation of basic continuous parameters and ABPM values was performed by t-test. Orthostatic changes of heart rate variability parameters and blood pressures were evaluated by ANOVA. Correlations between heart rate variability parameters with ABPM values were analyzed by Pearson linear correlation or Spearman test (for distribution different than normal). Statistical significance level was established on $p<0.05$. The statistical analyses were performed using the statistical software Stat graphic Centurion, version XV from Stat Point Inc (Herndon, Virginia, USA).

RESULTS

Basic characteristics of the patients with AN and control subjects are presented in Table 1. Duration of AN in our patients was 9±4 years.

The comparison of orthostatic changes of HRV components and blood pressures in the patients with AN as well as control subjects are summarized in Table 2.

The results of ABPM are summarized in Table 3. The sleep decline was 16.3±5.1% in control subjects and 11.1± 6.2% in the patients with AN ($p<0.05$).

The correlations of LF, HF powers and the ratio of LF/HF with ABPM parameters in control subjects are shown in Table 4 and in the patients with AN in Table 5.

The correlation between orthostatic change of HRV and sleep BP decline was significant for HF (r=0.441, $p<0.05$) and LF (r=0.423, $p<0.05$) but not for LF/HF in control subjects. No significant correlation between orthostatic change of HRV and sleep BP decline was detected in patients with AN.

DISCUSSION

Both the physiological and pathological functions of cardiovascular organs are closely related to circadian rhythm. Heart rate and blood pressure show diurnal variation within a day (Takeda *et al.* 2011).

In our study we confirmed the results of the previous reports that blood pressure values in active period are significantly lower in the patients with AN in comparison with control subjects but no difference is present during sleeping period (Cong *et al.* 2004; Oswiecimska *et al.* 2007; Awazu *et al.* 2000). Circadian variation of blood pressure is associated with autonomic and baroreflex-mediated modulation of the sinoatrial node (Guasti *et al.* 2005). The previous study have shown that the patients with AN have reduced sympathetic nervous responsiveness, increased parasympathetic nervous responsiveness, and increased complexity of the interbeat interval time series compared with healthy controls (Guasti *et al.* 2005; Ishiyawa *et al.* 2008). It is also known that anorectic patients have the lower blood pressure values than healthy subjects and suffer from bradycardia and orthostatic symptoms (Galletta *et al.* 2003; Casiero & Frishman 2006; Misra *et al.* 2004).

In our study blood pressure values in the patients with AN were comparable with healthy controls in supine position but significantly lower in standing position.

HF power depends on respiration-related alterations in parasympathetic cardiovagal outflow, however, whether LF power provides an indirect measure of cardiac sympathetic activity has been contentious. Pagani reported that LF power increased during states associated with sympathetic noradrenergic activation (Pagani *et al.* 1986). However the recent study revealed that LF power reflects baroreflex function and not cardiac sympathetic innervation (Moak *et al.* 2007). The ratio LF/HF was therefore suggested as a parameter related more to sympathetic activity (Cerutti *et al.* 1995).

In our study the lower BP values during standing position in the patients with AN were accompanied with the higher HF powers during supine position and mainly with lack of LF powers increase on standing. This result suggests that deterioration of baroreflex activation is a cause of the lower BP after standing in patients with AN.

Tab. 1. Basic characteristic of the AN patients and control subjects.

	Control group (n=30)	AN patients (n=30)	*p*-value
Age (years)	25±5	25±4	NS
Height (cm)	168±4	168±5	NS
Weight (kg)	58±6	38±5	*p*<0.01
BMI (kg/m^2)	20.2±1.8	13.7±1.2	*p*<0.01

AN: anorexia nervosa
BMI: body mass index

Tab. 2. Orthostatic change of HRV components, BP, and heart rate in the patients with AN and control subjects.

Position	Anorexia nervosa		Control subjects		ANOVA
	Supine	Standing	Supine	Standing	
LF (ms^2)	430±286	436±313	414±129	751±220*	F=6.2; p=0.016
HF (ms^2)	1934±938*	240±180	464±208	278±236	F=6.6; p=0.013
LF/HF	0.62±0.51	2.56±0.87	0.89±0.41	2.87±0.71	F=1.8; p=0.18
BPs (mmHg)	124±6	110±6*	126±7	118±6	F=10.2; p<0.01
BPd (mmHg)	73±6	66±5*	74±6	71±5	F=7.2; p<0.01
BPm (mmHg)	97±6	87±5*	98±6	94±5	F=8.2; p<0.01

HRV: heart rate variability; BP: blood pressure; AN: anorexia nervosa; LF: low frequency power; HF: high frequency power; BPs: systolic blood pressure; BPd: diastolic blood pressure; BPm: mean blood pressure

Tab. 3. Results of ABPM in patients with AN and control subjects.

		24 hours	Active period	Sleeping period
BPs	Controls (n=30)	120.7±6.1	123.7±6.2	108.0±7.3
	AN (n=30)	114.6±9.6*	116.9±10.6*	106.7±8.3
BPd	Controls (n=30)	81.8±4.0	84.8±4.3	68.9±6.7
	AN (n=30)	75.0±7.7**	77.7±8.1**	65.8±6.5
BPm	Controls (n=30)	94.8±4.5	97.6±4.8	82.1±6.9
	AN (n=30)	90.2±8.8	90.6±8.9**	79.2±6.9
HR	Controls (n=30)	89.8±7.4	92.7±7.4	74.9±6.3
	AN (n=30)	70.2±8.3**	73.2±8.5**	58.6±9.2**

*p<0.05; **p<0.01; ABPM: ambulatory blood pressure monitoring; BPs: systolic blood pressure; BPd: diastolic blood pressure; BPm: mean arterial pressure; HR: heart rate

Using 24 hours heart rate variability examination Cong *et al.* (2004) has shown that in the patients with AN blood pressure values are reduced during active period but not sleeping period and HF power is increased while the ratio of LF/HF is decreased over

Tab. 4. Correlation of ABPM values with heart rate variability parameters in control subjects.

	LF1	LF2	HF1	HF2	LF1/HF1	LF2/HF2
24 hours						
BPs	–0.599*	0.389	–0.339	0.371	–0.017	–0.520*
BPd	–0.514*	0.245	–0.403	0.256	0.346	–0.319
BPm	–0.575*	0.326	–0.385	0.319	0.171	–0.476*
HR	–0.331	0.414	–0.146	0.552*	–0.315	–0.551*
Active period						
BPs	–0.659*	0.490*	–0.185	0.450*	–0.294	–0.584*
BPd	–0.580*	0.457*	–0.371	0.440*	0.147	–0.496*
BPm	–0.599*	0.482*	–0.326	0.483*	–0.033	–0.513*
HR	–0.480*	0.483*	–0.117	0.627*	–0.352	–0.651*
Sleeping period						
BPs	–0.292	–0.104	–0.574*	–0.057	0.486*	–0.030
BPd	–0.309	–0.121	–0.569*	–0.015	0.470*	–0.052
BPm	–0.311	–0.072	–0.561*	0.014	0.457*	–0.082
HR	–0.112	0.358	0.483*	0.479*	–0.397	–0.355

LF1: low frequency power in supine position; LF2: low frequency power in standing position; HF1: high frequency power in supine position; HF2: high frequency power in standing position; BPs: systolic blood pressure; BPd: diastolic blood pressure; BPm: mean arterial pressure; HR: heart rate

Tab. 5. Correlation of BP values with heart rate variability parameters in the patients with AN.

	LF1	LF2	HF1	HF2	LF1/HF1	LF2/HF2
24 hours						
BPs	0.203	0.312	0.180	0-072	0.286	–0.096
BPd	0.481*	0.466*	0.308	0.198	0.489*	0.058
BPm	0.437*	0.392	0.220	0.365	0.464*	0.112
HR	0.205	0.048	0.503*	0.316	0.035	–0.081
Active period						
BPs	0.250	0.333	0.015	0.016	0.472*	–0.121
BPd	0.538*	0.522*	0.328	0.276	0.493*	0.041
BPm	0.446*	0.467*	0.216	0.166	0.502*	–0.021
HR	0.171	0.024	0.489*	0.360	–0.007	–0.080
Sleeping period						
BPs	0.127	0.026	0.210	0.340	0.330	0.043
BPd	0.033	0.068	0.335	0.323	0.301	0.197
BPm	0.063	0.059	0.306	0.265	0.284	0.153
HR	0.384	0.254	0.557*	0.340	0.070	–0.031

AN: anorexia nervosa; LF1: low frequency power in supine position; LF2: low frequency power in standing position; HF1: high frequency power in supine position; HF2: high frequency power in standing position; BPs: systolic blood pressure; BPd: diastolic blood pressure; BPm: mean arterial pressure; HR: heart rate

period of 24 hours monitoring. The results of our study using only short-term recording are compatible with Cong *et al.* (2004) conclusion. The ratio LF/HF was lower in the patients with AN – in supine position due to higher HF power and in standing position due to lower LF power.

The analysis of ABPM values and HRV parameters in healthy control subjects has shown the positive correlation between LF power as well as HF power and negative correlation of ratio LF/HF in standing position with blood pressure values during active period. These findings suggest the higher drop of BP after standing is associated with sympathetic activation and the more preserved baroreflex activity with the higher BP values. Contrary during sleeping period the negative correlation of HF powers and positive correlation of LF/HF measured in recumbent position were detected with blood pressure values during sleeping period. It means that overnight parasympathetic activation decreases and sympathetic one increases blood pressure values.

In patients with AN the relation of ABPM and HRV demonstrate the serious abnormalities. There is no correlation between HF power and ratio LF/HF in standing position with blood pressure during active period and the correlation of LF powers with systolic BP is not significant. The absence of relation between HRV parameters and blood pressure values may explain the lower BP values in patients with AN during active period.

The desorganization of relations between HRV parameters and BP is supported also by lack of the correlation between orthostatic change of HRV and sleep BP decline in patients with AN.

The increased parasympathetic activity in the patients with AN correlated with heart rate both in active and sleeping period. Bradycardia is frequently associated with another ECG abnormalities such a prolongation of the QTc interval (Casiero & Frishman 2006; Portilla 2011). The increased parasympathetic activity is associated with bradycardia and may predispose to the serious arrhytmias.

We conclude the lower ABPM values in AN patients during active period in comparison with control subjects may be explained by complex of HRV abnormalities, mainly by its impaired relations with blood pressure values in standing position.

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