Is a short re-feeding program effective in reducing adverse cardiac events in eating disorder patients?

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Abstract

Eating Disorder (ED) patients who were admitted to an eating disorders program for a 6-week treatment and were assessed for changes in heart rate variability (HRV). Linear heart rate variability measures (HRV) were determined using Kubios software from 20 minute, Lead 3 ECG recordings following a 5-minute rest period. Eighteen patients and 31 controls were included in the analysis. Results were deemed significant if $p<0.05$. No significant differences in HRV parameters were noted for the control group between Pre- and Post-treatment. For the ED group, mean RR interval length decreased significantly compared to the control group ($p=0.006$). HF peak frequency increased significantly in the ED group ($p=0.001$). High frequency (HF) peak indicated that the respiratory frequency increased from Pre to Post measurement. RMSSD tended to decrease ($p=0.047$) in the ED group. Hence at admission to hospital the ED group was more parasympathetic during rest compared to controls, but they became more sympathetic after the intervention and thus approached the HRV measures of the controls suggesting improvement in ANS modulation of the heart.

1. Introduction

Eating disorders (EDs) are characterized by abnormal eating patterns and perceptual distortions related to food and weight, which in turn result in a significant impairment of physical health and psychosocial functioning [1-3]. Classification of ED includes any weight-loss behaviour independent of body mass index (BMI), whereas Anorexia nervosa (AN) is defined as BMI <18.5 kg.m^2. Possible cardiac complications related to QT-interval prolongation and T-wave changes, and electrolyte disturbances are of major concern in ED progression and associated with malnutrition [4-6].

Heart rate is controlled by the autonomic nervous system (ANS), which in turn is modulated by central nervous system connections, the peripheral baroreflex and metabolic factors. Impaired ANS modulation may also be a consequence of an adaptation to oxidative stress and inflammation [7, 8] and can be explored using heart rate variability (HRV) analysis. Linear and nonlinear HRV measures describe different characteristics of ANS influence on the heart [9, 10]. The study of HRV in patients with AN has provided clinically important information on the integrity and function of the complex physiologic mechanisms controlling heart rate [11, 12]. The current study explores the effect of a 6-weeks rehabilitation program on HRV in patients with ED.

2. Methods

Eighteen female patients underwent treatment at the Eating Disorders Unit of Sydney's Northside Clinic and fulfilled the DSM-V (Diagnostic and Statistical Manual of Mental Disorders, 5th edition) criteria for eating disorders. Thirty-one healthy female age-matched subjects were recruited from the University of Sydney. The study was approved by the University of Sydney Human Ethics Committee and the Ramsay Sydney Psychiatric Hospital Ethics Committee. All participants provided written consent following an information session at admittance to the program. Clinical and anthropometric data was obtained at the commencement of the study from all participants.

2.1. ECG recording and HRV analysis

A PowerLab data acquisition system and Chart™ (ADInstruments, Australia) set at a sampling rate of 400 Hz was used to obtain and record the ECGs. Resting ECGs were recorded for 20 minutes after a 5-minute resting period in a relaxed sitting position. (Version 5.0.1, ADInstruments, Australia). HRV parameters were calculated with Kubios HRV software (http://kubios.uef.fi/ Kuopio, Finland) [13]. All RR time

series were first preprocessed to remove very low frequency trends (< 0.04 Hz) and ectopic beats [14] and interpolated with 4 Hz cubic spline to have equidistantly sampled data for spectral analysis. Power spectral density estimates were computed using Welch's averaged periodogram method (150 s window and 50% overlap).

2.2. HRV measures

Time-domain measures of HRV included mean value of beat-to-beat RR intervals (Mean RR), standard deviation of all normal-to-normal RR intervals (SDNN), root mean square of successive RR interval differences (RMSSD) and percentage of successive RR intervals differing more than 50 ms (pNN50). In addition, the HRV triangular index (HRVtri) and triangular interpolation of RR interval histogram (TINN) were computed from the RR interval distribution function. Frequency-domain parameters evaluated from the power spectrum of RR time series included peak frequencies at low frequency (LF, 0.04-0.15 Hz) and high frequency (HF, 0.15-0.4 Hz) bands, powers of LF and HF bands both in absolute (ms^2) and normalized units (n.u.), power ratio between LF and HF bands (LF/HF ratio) and total spectral power. Poincaré plot analysis (quantified by standard deviations SD1 and SD2, and their ratio SD1/SD2) was also included.

2.3. Statistics

Statistical calculations were performed using Matlab (Version R2012a). Basic clinical data are expressed as mean ± standard deviation. The normality of all variables was checked by the Kolmogorov-Smirnov goodness-of-fit test. Non-normally distributed HRV data are expressed as median ± interquartile range (IQR) and analyzed using the non-parametric Wilcoxon rank-sum test at $p < 0.05$.

3. Results

Comparison of HRV measures evaluated from 5-minute sitting ECG recordings in control subjects and patients diagnosed with eating disorders following a 6-week program indicated significant differences for RMSSD, TINN, HFpeak (median change value for control = 0.003 / median change for ED 0.038), TP, and SD1.

Table 1. Changes in HRV features in control and ED group following 6-week intervention.

HRV Features	Control	ED	p
Mean RR (ms)	+7.2±130.6	-64.3±75.8	0.002
RMSSD (ms)	+1.97±16.1	-8.69±18.4	0.047
TINN (ms)	+22±67.8	-16.5±138	0.03
HFpeak (ms)	+0.003±0.06	+0.03±0.07	0.016
TP (ms^2)	+233.6±879.9	-124.9±2232.9	0.05
SD1 (ms)	+1.4±11.4	-6.15±12.9	0.047

For instance the change for control in RMSSD was 1.97 whereas for ED it was -8.69. The difference between the two is significant with the ED group RMSSD change indicating a substantial decrease in RMSSD. Similar observations for other HRV features can be observed in Table 1.

4. Conclusion

Approximately one third of deaths of AN patients are due to cardiac complications [17-19]. A lowered body mass index (BMI) is often cited as the main factor for the increased risk of cardiac morbidity and mortality due to arrhythmia and related to vagal overdrive as a response to low BMI [4, 15, 16] and Heart rate and heart rate variability as an independent predictor for cardiac morbidity and mortality was established by [20-22]. MeanRR, RMSSD, TINN, SD1 show differences (all decrease for ED post intervention) but HFpeak increased significantly. For ED pre-post intervention we see an increase in HFpeak in the ED group post treatment, which suggests a positive effect of the treatment. The HFpeak is the frequency corresponding to the maximum power of the HF component and based on physiology correlates with respiratory rate.

The present study clearly demonstrates that eating disorders are associated with cardiac autonomic dysfunction and that a 6-week intervention may have a positive outcome. Further follow-up studies are needed to clarify and substantiate the usefullness of HRV in monitoring disease

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