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ORIGINAL ARTICLE

Heart rate variability in children with inflammatory bowel diseases

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Abstract

OBJECTIVE: Heart rate variability (HRV) oscillations are used in the detection of autonomic instabilities in various clinical disorders.
METHODS: We compared the HRV as a possible marker of chronic distress in children with inflammatory bowel disease (IBD) with HRV frequencies in the healthy controls. Participants were 29 children with IBD (19 Crohn's disease and 10 ulcerative colitis), 25 children were in remission and 4 presented mild disease activity. They were compared with the control group of 35 healthy children of the same age (13–16 years-old).
RESULTS: In HRV assessment, adolescents with IBD had significantly lower levels of the spectral activity in an LF band in all three positions; lower levels of VLF in both supine positions; and the ratio of the spectral activity at LF/HF was significantly lower in the second post (standing).
CONCLUSION: These results indicate children with IBD have less adaptability to stress.

INTRODUCTION

Most children illnesses are only minor and transient and cause only temporary disruption of everyday life. However, it is estimated that 2–3% children have medical illnesses that are severe enough to interfere with growth, development, school performance, or social relationships (Drell & White 2005). Inflammatory bowel diseases (IBD) include Crohn's disease and ulcerative colitis; those are chronic illnesses with an impact on quality of life.

Many authors propose that there is an autonomic dysfunction and reduced heart rate variability (HRV) in adult patients with chronic medical or mental conditions, like hypertension (Lucini *et al.* 2002), chronic heart disease (Huikukri *et al.* 1996), epilepsy (Lotufo *et al.* 2012), chronic gastrointestinal illnesses (Maunder *et al.* 2006; Coruzzi *et al.* 2007; Ganguli *et al.* 2007; Sharma *et al.* 2009, Maunder *et al.* 2012), and psychiatric disorders (Virtanen *et al.* 2003; Latalova *et al.* 2010; Prasko *et al.* 2011). The autonomic imbalance could be an important pathophysiological mechanism con-

nected with the chronic distress also in children and adolescents with chronic medical conditions (e.g. obese children (Taşçılar *et al.* 2011), young prehypertensives (Pal *et al.* 2013), pubertal girls with type 1 diabetes (Cho *et al.* 2014), and psychiatric conditions, e.g. adolescent depression (Tonhajzerova *et al.* 2009).

Respiration has a strong influence on changes in heart rate and is frequently involved as a covariate in statistical analysis of the association between stress and HRV changes (Bernston *et al.* 1997). Respiratory sinus arrhythmia is one of the primary mechanisms participating in the origin of HRV. Respiratory sinus arrhythmia is known as an index of cardiac parasympathetic activity and usually decreases under acute psychological stress (Houtveen *et al.* 2002).

HRV AND AUTONOMIC NERVOUS SYSTEM

HRV has been found to be the product of quickly reacting cardiovascular control structures, specifically, the sympathetic and parasympathetic divisions of the autonomic nervous system (Pagani *et al.* 1997). Continuous changes in sympathetic and parasympathetic impulses on the sinoatrial node exhibit shifts in heart rate and cause oscillations of the R–R interval around its mean value. Progressively refined calculations have been developed to measure HRV.

The obvious method, to quantify HRV oscillations, is linear – spectral analysis. This conventional method is known to be a valuable tool in the detection of autonomic instabilities in many clinical syndromes (Bernston 1997). The spectral analysis can offer data about physical mechanisms influencing three frequency bands: high-frequency (HF), low-frequency (LF) and very-low-frequency (VLF). The main difficulty is how to understand these frequency bands according to the function of branches of the autonomic nervous system (ANS) – sympathethic and parasympathethic. There is agreement that the HF represents parasympathethic activity, but we must be careful in the interpreting the sources of the LF and VLF frequencies. Some authors suggested that the LF characterizes sympathicus. Nevertheless, actual findings show that this is more complicated (Pagani *et al.* 2009; Malliani 2005). Others propose that the LF band describes both sympathicus and parasympathicus activity, the baroreflex activity, central oscillator. The interpretation of the VLF is also indefinite. It could be under the influences of thermoregulation, peripheral vasomotor, and the renin-angiotensin-aldosterone system (Goldstein *et al.* 2011; Moak *et al.* 2009).

This study compares the HRV in children with IBD and in the control group of healthy children suggesting the HRV being a possible marker of chronic stress. Our hypothesis is that compared to healthy controls, children with chronic disease would display lower resting HRV and that individual differences in autonomic function would be associated with differences in the illness course.

METHOD

Population

Participants were 29 adolescents with IBD and 35 healthy controls of the same age (13–16 years). Written informed consent was signed by all probands and their parents. Healthy controls were recruited from high school students. Patients were recruited from the Department of Pediatrics, University Hospital Olomouc. All patients had been dispensarized for IBD; 19 patients were diagnosed with Crohn's disease and 10 with ulcerative colitis. The diagnosis was confirmed by detailed examination, blood labs and colonoscopy by a specialist. There were 15 boys and 14 girls. Patients had to be diagnosed with IBD at least six months before testing in order to be included in the group of chronic disease patients. According to PUCAI (Pediatric Ulcerative Colitis Activity Index) and PCDAI (Pediatric Crohn's Disease Activity Index) at the time of assessment, 25 children were in remission, and 4 presented mild disease activity.

Data recording and analysis

The differences in the autonomic nervous system activity, indexed by HRV, have been measured by the analytic systems that are using the power spectral analysis of the beat-to-beat time series, which quantifies the HRV. HRV was assessed during 3 positions (1st – 5 min supine; 2nd – 5 min standing; 3rd – 5 min supine), recording beat-to-beat during paced breathing by ECG sensor with UniGel electrodes snapped on and placed on chest. Power spectra are computed using a fast Fourier transformation for very low frequency (VLF: 0.0033–0.04 Hz), low-frequency (LF: 0.04–0.15 Hz) and high frequency (HF: 0.15–0.40 Hz) powers (Weise *et al.* 1987; Lipsitz *et al.* 1990; Ponikowski *et al.* 1997; Javorka 2008). To examine heart rate we used the microcomputer system ProComp Infiniti, which allows the ECG signal radio transmission to the receiver connected by a USB cable to the PC. Data were processed by a software program ProComp Infiniti.

Assessment

The main assessment tools were used for measuring the level of depression (CDI in children, BDI in parents), anxiety (SAD in children, BAI in parents), quality of life (KidScreen-10 in children, PedsQL in parents). All questionnaires are self-report scales; they were filled at home; the control group of children filled them at school.

The CDI (Children's Depression Inventory) is a psychological tool widely used to assess depressive symptomatology in children and adolescents aged 7–17 years (Kovacs 1992). The scale is self-rated and symptom-oriented, composed of 27 items that are grouped into five-factor areas, including Negative Mood, Interpersonal Problems, Ineffectiveness, Anhedonia, and Negative Self Esteem. The high scores reflect more serious

depressive symptomatology. A score greater than nineteen is considered suggestive of depressive symptoms.

The SAD (scale of anxiety in children) assesses anxiety through self-report scale in children 10 to 15 years old (Müllner *et al.* 1983). This scale measures state anxiety and trait anxiety in two 20-item questionnaires; each item is rated on 3-point range.

The BDI (Beck Depression Inventory) is designed for evaluating subjective depression symptoms in adults (Beck *et al.* 1961). This self-rating scale with 21 depression indicators includes somatic and cognitive-affective symptoms; each item is rated on a 4-point scale. Scores of 19 or above indicate depression.

The BAI (Beck Anxiety Inventory) is a self-rating scale with 21 anxiety indicators focusing primarily on physiological manifestations of anxiety in adults. Items are rated on a 4-point scale; a score of 16 or above indicates anxiety (Beck *et al.* 1988).

PedsQL Family Impact Module is a parent-reported instrument that measures the impact of pediatric chronic health conditions on patient health-related quality of life (HRQOL) and their family functioning (Varni *et al.* 2004). This 36-item questionnaire involves eight dimensions: physical functioning, emotional functioning, social functioning, cognitive functioning, communication, worry, daily activities, and family relationships. It measures both parent self-reported functioning and parent-reported family functioning. Items are rated on a 5-point Likert-type scale, and then linearly transformed to a 0–100 scale, higher scores indicate better HRQOL.

KidScreen-10 – The KidScreen instruments assess children's and adolescents' subjective health and well-being (Ravens-Sieberer *et al.* 2005). It was developed as a self-report questionnaire appropriate for the healthy and chronically ill children and teenagers aged from 8 to 18 years. The KidScreen-10 is a short version of the KidScreen-52 and KidScreen-27 instruments, it contains 10 items from 10 HRQoL dimensions: Physical; Psychological Wellbeing; Moods and Emotions; Self-Perception; Autonomy; Parent Relations and Home Life; Social Support and Peers; School Environment; Social Acceptance (Bullying); and Financial Resources. Each question is rated in a 5-point response scale; a higher score is indicative of a better HRQOL.

Twenty-nine children with IBD were included in this study: nineteen (65.5%) patients with Crohn's disease and ten (34.5%) with ulcerative colitis. The diagnosis was established in accordance with recommended diagnostic approach (Levine *et al.* 2014, IBD WGESPGHN 2005). The treatment was based upon the current guidelines (Ruemmele *et al.* 2014, Turner *et al.* 2012). Median of treatment lasted 13 months (interquartile range 8–44 months). Clinical activity of the illness was evaluated according to the Pediatric Crohn's Disease Activity Index (PCDAI) (range from 0 to 100 points) and Pediatric Ulcerative Colitis Activity Index (PUCAI) (range from 0 to 85 points)(Hyams *et al.* 1991, Turner *et al.* 2009). The remission was defined as PCDAI or PUCAI of less than 10 points. Sixteen (86.4%) patients with CD and nine (90%) with UC achieved remission of the disease at the time of observation. Laboratory tests included CRP, thrombocytes, and hemoglobin. CRP (C-reactive protein) is a non-specific test detecting an inflammation, reference values are 0–5 mg/l. Elevated thrombocytes are well recognized as a marker of inflammatory bowel disease activity. Both Crohn's disease and ulcerative colitis are associated with abnormalities of platelet number; the thrombocyte count is typically increased; reference values are $150–400 \times 10^9$/l. Hemoglobin is often low in IBD causing anemia; the reference values are 120–160 g/l.

Statistical analysis and ethics

Demographic and clinical data were analyzed using column statistics. The Shapiro-Wilk W test determined normal distribution of the demographic and clinical variables. Group differences between patients and controls were analyzed using unpaired t-tests. The chi^2 test or Fisher´s exact test were used for the analyzes of categorical data. The relations between variables with a normal distribution were calculated using Pearson´s correlation analysis. Spearman´s rank correlation was used for variables with non-normal distribution. GraphPad PRISM version 5.0 was used for statistics, and the level of significance was set at 5%.

Study was carried out in agreement with the latest version of the Declaration of Helsinki, and the written informed consent was achieved from all subjects after the nature of the procedures had been fully explained. The local ethical Committee of University Hospital Olomouc approved this project.

RESULTS

Demographic and clinical characteristics

Participants were 29 adolescents with IBD and 35 healthy controls of the same age (13–16 years). Patients were engaged from the outpatient Department of Pediatrics of the University Hospital Olomouc. Out of 29 patients, 19 patients were diagnosed with Crohn's disease and 10 with ulcerative colitis. There were 15 boys (51.7%) and 14 girls. The mean age of the patients was 15.04±1.26 years, the control group one was 14.90±0.43 years. There are no statistical differences in the age between groups. The mean age at the disorder onset was 12.06±3.12 years; the duration of the disorder was 2.98±2.85 years. All patients used medication. This included infliximab (n=3); and some patients also used mesalazine (n=21), azathioprine (n=13), sulfasalazine (n=4), omeprazole (n=3).

As a control group, 72 children from three different high school classes were asked to participate in this study. A written consent was obtained from parents from 43 children. A possible chronic disease was assessed through an item in KidScreen-10 question-

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Tab. 1. Characteristics of the patients and controls.

	PATIENTS (n=29)	CONTROLS (n=35)	STATISTICS
Age	15.03 ± 1.27	14.86 ± 0.43	unpaired t-test: t=0.7766 df=62; n.s.
Age of disorder onset	12.06 ± 3.12		
Duration of the disorder	2.98 ±2.85		
Male: female	15: 14	27:8	Fisher exact test; ***p*<0.05**
VLF-supine 1	93.9 ± 68.61	179.6 ± 135.6	unpaired t-test: t=3.088 df=62; ***p*<0.005**
VLF-standing	74.98 ± 59.88	106.1 ± 66.13	unpaired t-test: t=1.954 df=62; n.s. (p= 0.0553)
VLF-supine 2	149.7 ± 223.4	268.7 ± 221.0	Mann Whitney test: U=242; ***p*<0.0005**
LF-supine 1	200.1 ± 124.5	589.8 ± 1049.0	Mann Whitney test: U=276; ***p*<0.005**
LF-standing	157.8 ± 163.6	321.6 ± 209.3	unpaired t-test: t=3.434 df=62; ***p*<0.005**
LF-supine 2	377.9 ± 628.5	875.4 ± 1222.0	Mann Whitney test: U=302; ***p*<0.01**
HF-supine 1	534.4 ± 611.4	688.8 ± 784.9	unpaired t-test: t=0.8643 df=62; n.s.
HF-standing	128.4 ± 197.3	139.5 ± 197.3	Mann Whitney test: U=414; n.s.
HF-supine 2	775.0 ± 1192.0	913.1 ± 985.3	Mann Whitney test: U=403; n.s.
LF/HF – supine 1	0.8052 ± 0.6949	1.304 ± 1.369	Mann Whitney test: U=379.5; n.s. (p= 0.0856)
LF/HF – standing	2.702 ± 2.413	4.638 ± 3.471	unpaired t-test: t=2.537 df=62; ***p*<0.05**
LF/HF –supine 2	0.9852 ± 1.084	1.342 ± 1.293	Mann Whitney test: U=402.5; n.s.
CRP	1.97 ± 2.50		
Thrombocytes	283.8 ± 87.86		
Hemoglobin	142.00 ± 45.34		
CDI	9.39 ± 8.91	7.11 ± 4.46	unpaired t-test; t=1.306 df=59; n.s.
SAD	29.42 ± 6.70	29.12 ± 4.66	unpaired t-test; t=0.2007 df=56; n.s.
KidS10	39.08 ± 8.32	38.21 ± 4.65	unpaired t-test; t=0.5804 df=65; n.s.
M-PQL-G	66.75 ± 15.37	76.64 ± 15.55	unpaired t-test; t=2.244 df=48; ***p*<0.05**
F-PQL-G	70.26 ± 17.67	82.05 ± 13.31	unpaired t-test; t=2.493 df=41; ***p*<0.05**
M-BDI	9.14 ± 9.18	6.83 ± 6.63	unpaired t-test; t=1.043 df=49; n.s.
F-BDI	6.20 ± 6.50	3.65 ± 3.47	unpaired t-test; t=1.632 df=41; n.s.
M-BAI	8.91 ± 10.08	5.17 ± 5.03	unpaired t-test; t=1.736 df=49; n.s. (sign.= 0.088)
F-BAI	5.30 ± 5.41	4.48 ± 4.99	unpaired t-test; t=0.08463 df=47; n.s.

VLF – very low-frequency band, LF – low-frequency band, HF – high-frequency band, CRP – C-reactive protein, CDI – Children's Depression Inventory, SAD – Scale of anxiety in children (state anxiety), KidS10 – KidScreen-10, M-PQL-G – PedsQL, mothers' global scores, F-PQL-G – PedsQL, fathers' global scores, M-BDI – Beck Depression Inventory, mothers' scores, F-BDI – Beck Depression Inventory, fathers' scores, M-BAI – Beck Anxiety Inventory, mothers' score, F-BAI – Beck Anxiety Inventory, fathers' scores

naire. Out of these children, HRV was measured in 35 randomly selected children.

There were no differences between patients and control groups in the mean age, and psychosocial properties, as the level of depression (CDI), anxiety state (SAD actual), anxiety trait (SAD usual) and quality of life (KidS10) (Table 1). However, there was statistical difference between groups in male: female ratio; there were more women in patient´s group.

Scores of quality of life of patients´ mothers were statistically significantly lower than in mothers of controls (Table 1). The same picture was shown in fathers. However, there was no difference between levels of mothers´ or fathers´ depression measured by BDI. There is also no difference in anxiety level measured with BAI between mothers or fathers of both groups.

Comparison of the groups in HRV

The comparison of the experimental group and controls showed that parameters of heart rate variability statistically differ in VLF in both supine positions and LF in all three positions but not in HF (Figure 1). There is a high statistical difference between ill children and controls in LF/HF ratio in a standing position (Figure 2).

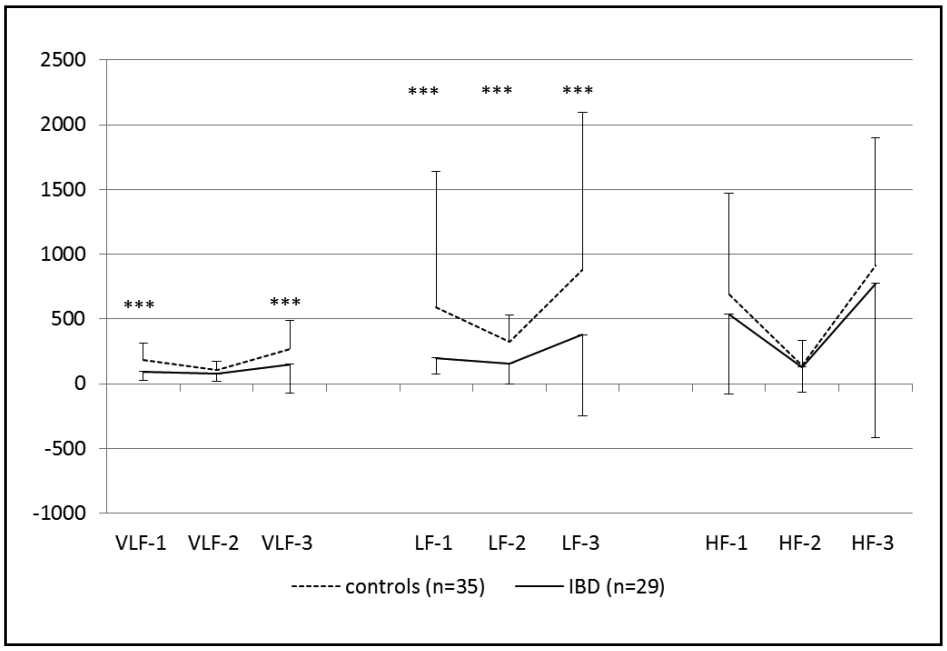

Fig. 1. Comparison between IBD patients and healthy controls in all frequencies in three positions. VLF – very low-frequency band, LF – low-frequency band, HF – high-frequency band. ***$p \leq 0.001$

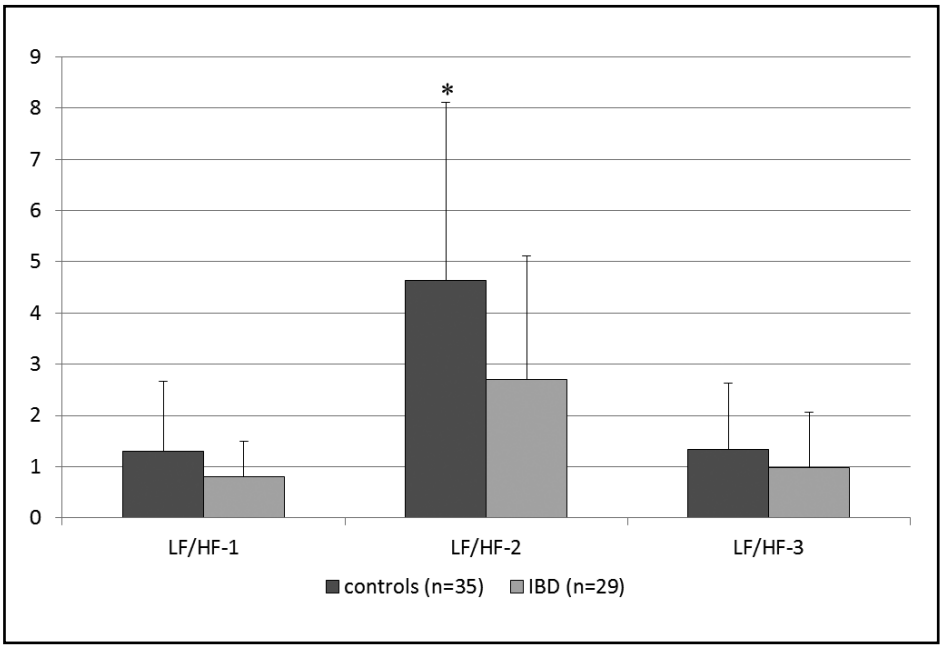

Fig. 2. Ratio LF/HF in all three positions – comparison of IBD and controls. LF – low-frequency band, HF – high-frequency band. *$p \leq 0.05$

The correlation of primary lab parameters, HRV parameters, and psychosocial measurements in patients´ group

Levels of CRP and thrombocytes did not correlate with any of HRV parameters or psychosocial measurements but levels of hemoglobin statistically significantly correlated with the VLF-1 (Spearman r=0.4408; $p<0.05$) and mother´s quality of life (M-PQL-Global score: Spearman r=0.4358; $p<0.05$), father´s quality of life at family – Family Functioning Summary Score (F-PQL-Family: Spearman r=0.5121; $p<0.05$) and father´s level of depression (F-BDI: Spearman r=0.5; $p<0.05$).

LF/HF-1 ratio in first position (supine) did not correlate with any above mentioned laboratory or psychosocial data, but LF/HF-2 ratio (standing) significantly correlated with mothers' Health Related Quality of Life Summary Score (M-PQL-HR: Pearson r=0.4475; $p<0.05$). LF/HF-3 ratio in third position (supine) did not correlate with any laboratory or psychosocial measurement (Table 2).

Gender differences in patients and controls

There were no significant differences between males and females patients in clinical results, HRV, and psychological measurements, with the exception of higher level of female anxiety measured by SAD (Table 3). There were no significant differences between males and females in the control group.

DISCUSSION

In HRV assessment, comparing to the healthy controls, adolescents with IBD had significantly lower levels of the spectral activity in an LF band in all three positions; lower levels of VLF in both supine positions; and the ratio of the spectral activity at LF/HF was significantly lower in the second post (standing). These results indicate less adaptability to stress in children with IBD.

We should be careful in understanding the numbers from the HRV measures. We have some facts that the HF band characterizes parasympathethic activity (Task Force ESC NASPE 1996), but the significance of the LF and VLF frequency bands is still uncertain. Some studies refer that the LF band represents sympathetic activity (Pagani *et al.* 2009, Malliani 2005). In our study, we have found all three frequency bands tend to decrease during orthostasis (there was no statistical significance, but we can see a downward trend). The correlation

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Tab. 2. Correlation between primary lab parameters, HRV parameters, and psychosocial measurements in patients´ group (Pearson or Spearman r and theirs significance).

measurements	CRP	Thrombocytes	hemoglobin	LF/HF-1	LF/HF-2	LF/HF-3
LF/HF-1	–0.0558$^{S\ n.s.}$	0.1134$^{P\ n.s.}$	0.1388$^{S\ n.s.}$		–0.09949$^{P\ n.s.}$	**0.8298^{S} p<0.0001**
LF/HF-2	0.0494$^{S\ n.s.}$	0.0044$^{P\ n.s.}$	0.0923$^{S\ n.s.}$	–0.09949$^{P\ n.s.}$		0.0643$^{S\ n.s.}$
LF/HF-3	–0.553$^{S\ n.s.}$	0.0729$^{S\ n.s.}$	0.2139$^{S\ n.s.}$	**0.8298^{S} p<0.0001**	0.06425$^{S\ n.s.}$	
CDI	–0.1827$^{S:n.s.}$	–0.0745$^{P\ n.s.}$	–0.1374$^{S\ n.s.}$	0.0118$^{P\ n.s.}$	–0.1929$^{P\ n.s.}$	0.0193$^{S\ n.s.}$
SAD	0.3404$^{S\ n.s.}$	0.0067$^{P\ n.s.}$	–0.1409$^{S\ n.s.}$	–0.0343$^{S\ n.s.}$	–0.0057$^{P\ n.s.}$	–0.2281$^{S\ n.s.}$
KidS10	–0.07641$^{S\ n.s.}$	0.0364$^{P\ n.s.}$	0.1526$^{S\ n.s.}$	0.0675$^{P\ n.s.}$	–0.0257$^{P\ n.s.}$	0.0827$^{S\ n.s.}$
M-PQL-G	0.1874$^{S\ n.s.}$	0.2108$^{P\ n.s.}$	**0.4358^{S} p<0.05**	–0.1378$^{P\ n.s.}$	0.3837$^{P\ n.s.(0.078)}$	0.0054$^{S\ n.s.}$
M-PQL-health	0.1463$^{S\ n.s.}$	0.1900$^{P\ n.s.}$	**0.4185^{S} p<0.05**	–0.08657$^{P\ n.s.}$	**0.4475^{P} p<0.05**	0.1596$^{S\ n.s.}$
F-PQL-G	–0.3134$^{S\ n.s.}$	0.0735$^{P\ n.s.}$	0.4274$^{S\ n.s.(0.06)}$	–0.01033$^{P\ n.s.}$	0.3558$^{P\ n.s.}$	–0.2306$^{S\ n.s.}$
F-PQL-Family	–0.1809$^{S\ n.s.}$	0.1852$^{P\ n.s.}$	**0.5121^{S} p<0.05**	0.2296$^{P\ n.s.}$	0.2437$^{P\ n.s.}$	–0.0989$^{S\ n.s.}$
M-BDI	–0.3151$^{S\ n.s.}$	–0.1882$^{P\ n.s.}$	–0.3380$^{S\ n.s.}$	0.1768$^{P\ n.s.}$	–0.1990$^{P\ n.s.}$	–0.0910$^{S\ n.s.}$
F-BDI	0.1559$^{S\ n.s.}$	–0.1684$^{P\ n.s.}$	–0.5000^{S} p<0.05	–0.1766$^{P\ n.s.}$	–0.0496$^{P\ n.s.}$	–0.0137$^{S\ n.s.}$
M-BAI	–0.0455$^{S\ n.s.}$	–0.3411$^{P\ n.s.}$	–0.2736$^{S\ n.s.}$	0.1086$^{P\ n.s.}$	–0.0502$^{P\ n.s.}$	–0.0731$^{S\ n.s.}$
F-BAI	–0.0670$^{S\ n.s.}$	–0.0570$^{P\ n.s.}$	–0.3511$^{S\ n.s.}$	–0.2969$^{P\ n.s.}$	–0.2590$^{S\ n.s.}$	–0.1627$^{S\ n.s.}$

P=Pearson; S=Spearman; LF – low-frequency band, HF – high-frequency band, CRP – C-reactive protein, CDI – Children's Depression Inventory, SAD – Scale of anxiety in children (state anxiety), KidS10 – KidScreen-10, M-PQL-G – PedsQL, mothers' global scores, M-PQL-health – PedsQL mothers' scores in health-related quality of life subscale F-PQL-G – PedsQL, fathers' global scores, F-PQL-Family – PedsQL fathers' Family Functioning Summary Score, M-BDI – Beck Depression Inventory, mothers' scores, F-BDI – Beck Depression Inventory, fathers' scores, M-BAI – Beck Anxiety Inventory, mothers' score, F-BAI – Beck Anxiety Inventory, fathers' scores

Tab. 3. Gender differences – patients and controls.

PATIENTS	MALES (n=15)	FEMALES (n=14)	STATISTICS
Length of the disorder	38.17 ± 35.41	33.24 ± 34.08	unpaired t-test: t=0.3810 df=27; n.s.
CRP	1.513 ± 1.921	2.450 ± 2.992	Mann Whitney test: MW U=90; n.s.
Thrombocytes	295.90 ± 50.98	270.90 ± 116.10	unpaired t-test: t=0.7579 df=27; n.s.
Hemoglobin	138.90 ± 8.49	145.40 ± 65.77	Mann Whitney test: MW U=67.5; n.s.
LF/HF-1 – supine 1	0.862 ± 0.777	0.750 ± 0.601	unpaired t-test: t=0.4318 df=27; n.s.
LF/HF-2 – standing	3.309 ± 3.075	2.064 ± 1.224	unpaired t-test: t=1.413 df=27; n.s.
LF/HF 3 – supine 2	0.901 ± 0.880	1.079 ± 1.280	unpaired t-test: t=0.4389 df=27; n.s.
CDI	7.39 ± 5.80	11.38 ± 11.09	unpaired t-test: t=1.152 df=24; n.s.
SAD	26.45 ± 3.86	31.92 ± 7.66	**unpaired t-test: t=2.143 df=22; p<0.05**
KidS10	40.62 ± 7.32	37.54 ± 9.24	unpaired t-test: t=0.9409 df=24; n.s.
CONTROLS	**MALES (n=27)**	**FEMALES (n=8)**	**STATISTICS**
LF/HF-1 – supine 1	1.426 ± 1.500	0.9125 ± 0.7396	Mann Whitney test: MW U=86.5; n.s.
LF/HF-2 – standing	4.959 ± 3.533	3.563 ± 3.220	unpaired t-test: t=1.000 df=33; n.s.
LF/HF-3 – supine 2	1.463 ± 1.393	0.975 ± 0.860	Mann Whitney test: MW U=86.5; n.s.
CDI	6.667 ± 4.674	8.625 ± 3.503	unpaired t-test: t=1.093 df=33; n.s.
SAD	28.96 ± 4.99	29.63 ± 3.62	unpaired t-test: t=0.3472 df=32; n.s.
KidS10	39.00 ± 3.50	38.00 ± 4.90	unpaired t-test: t=0.6473 df=33; n.s.

CRP – C-reactive protein, LF – low-frequency band, HF – high-frequency band, CDI – Children's Depression Inventory, SAD – Scale of anxiety in children (state anxiety), KidS10 – KidScreen-10

between VLF-1 and levels of hemoglobin is hard to interpret. There are no remarks about such coincidence in literature and also theoretically the explanation is missing. Hard is to interpret the correlation between the level of hemoglobin and parents´ quality of life and fathers´ depression. It could be the mistake of statistics of II.type.

There are several limitations of our study that need to be mentioned. The important limitation of the study is the small number of patients. Our sample may not be representative of the population of adolescent IBD patients. Generalization of findings is doubtful especially in a situation where the variability of autonomic nervous system responses is relatively high. Another important limitation is a significant difference between group of patients and controls in male/female ratio. Nevertheless, we did not find differences between males and females in HRV parameters both in the patients´ group and control group.

CONCLUSIONS

There is a lower HRV variability in children with IBD than in healthy controls. The meaning of this finding is unknown but could reflect chronic distress of the children suffering from IBD.

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