VIA MEDICA

ORIGINAL ARTICLE

Cardiology Journal
2012, Vol. 19, No. 5, pp. 501–506
10.5603/CJ.2012.0091

ISSN 1897–5593

The use of short-term analysis of heart rate variability to assess autonomic function in obese children and its relationship with metabolic syndrome

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Abstract

Background: *The cardiovascular autonomic nervous system in obese children is one of the main initiators of coronary heart disease and hypertension and may have a close relationship with insulin resistance. Heart rate variability is one non-invasive method to assess the cardiovascular autonomic system. In this method, low frequency parameters reflect sympathovagal activity, high frequency parameters reflect vagal activity and the ratio of these parameters reflects sympathovagal balance.*

Methods: *In this study, a short-term analysis of heart rate variability was conducted in 66 obese children and 40 healthy controls.*

Results: *While high frequency parameter values are lower in the obese group compared to the controls (16.02 ± 12.9 nu vs. 21.45 ± 13.6 nu, $p = 0.046$), the low frequency/high frequency ratio is found significantly higher (3.79 ± 2.34 vs. 2.25 ± 0.93, $p < 0.001$). A significant difference was not detected for the low frequency values ($p = 0.787$). Insulin resistance was found in 33 (50%) patients, dyslipidemia was found in 39 (59%) and hypertension was found in 18 (27%). Metabolic syndrome was detected in 39% patients in the obese group.*

Conclusions: *We found that vagal activity was decreased in the obese group and the autonomic nervous system balance was impaired in favor of sympathetic activity in the short-term heart rate analysis.* (Cardiol J 2012; 19, 5: 501–506)

Key words: heart rate variability, short-term, childhood, obesity

Introduction

Obesity is the most prevalent seen nutritional disorder in childhood, and it increases cardiovascular (CV) morbidity and mortality risk through various mechanisms [1–3]. The most common mechanisms include insulin resistance, dyslipidemia, hypertension, metabolic syndrome (MS), diabetes, and cardiac hypertrophy. Previous studies analyzing heart rate variability (HRV) parameters have shown that CV autonomic dysfunction occurs in various disorders. This condition leads to obesity-related hypertension, which affects the heart, kidneys and vasculature and coronary heart diseases [1].

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Received: 13.06.2012 Accepted: 17.07.2012

The key factor in the development of obesity, MS, and diabetes is insulin resistance. The topics related to insulin resistance are chronic low-grade inflammation, CV autonomic dysfunction and sympathetic hyperactivity. HRV is an indicator of cardiac control. Previously, a lower HRV has been linked to detrimental health changes and outcomes, such as the development of hypertension, diabetes, and coronary artery diseases (CAD) in individuals with diabetes [4–6].

In this study, we investigated MS parameters and the CV autonomic nervous system using HRV analysis. We investigated the effects of alterations in the autonomic nervous system and the effectiveness of short-term HRV analysis to reveal CAD risk in the early period in obese children.

Methods

A total of 66 children, 8–16 years of age were enrolled in the study. These children were admitted to our outpatient clinic with and obesity related complaint or were found to be obese when they were admitted for other complaints. During the first assessment, a detailed medical history was obtained, and a physical examination was performed. The children who had known systemic or metabolic diseases, used medications that may affect body weight or had syndrome findings were excluded. During the anamnesis, all subjects were questioned about the duration of obesity and family history of obesity, early-onset CAD, hyperlipidemia and diabetes. Forty healthy children, 8–16 years of age were included in the study as a control group. Local ethics committee approval was obtained for this study. Families were informed about the procedures, and written informed consent was obtained.

All anthropometric measurements were performed by the same person with child only wearing underclothing without socks and shoes. Height was measured with the child standing using a standard height measure scale fixed onto the wall with a margin of error of 0.5 cm. Weight was measured using a single bascule with a constant zero adjustment with a margin of error of 0.1 kg. Blood pressure was measured after resting using a standard mercury manometer. The mean value of two sequential measurements were obtained in the sitting position with a 10 min interval after a resting period of 10 min using a proper sized cuff for age that covered 2/3 of the left arm. Individuals with systolic and diastolic blood pressures above the 95th percentile for age and gender considered to be hypertensive. Body mass index (BMI) was calculated by dividing body weight [kg] by height [m^2]. Patients with a BMI above the 95th percentile for age and gender using national definitions were classified as obese [7].

Venous blood samples for glucose, insulin, cholesterol and triglyceride levels were obtained from all obese children after fasting for 12 h at night. Standard enzymatic methods were used to measure cholesterol and triglycerides levels. The serum high-density lipoprotein (HDL) cholesterol concentration was measured from the supernatant after precipitation of very low- and low-density lipoprotein (LDL) cholesterol. LDL cholesterol concentration was calculated with the Friedewald formula. The glucose concentration was analyzed enzymatically, and serum insulin was measured with a microparticle enzyme immunoassay kit. The oral glucose tolerance test (1.75 g/kg glucose, max 75 g) was performed for all of the obese children. Fasting plasma glucose ≥ 110 mg/dL was defined as impaired fasting glucose, and ≥ 126 mg/dL was defined as diabetes. Plasma glucose and insulin were measured at 0, 30, 60, and 120 min. A 2 h blood glucose < 140 mg/dL was classified as normal, 140–200 mg/dL as impaired glucose tolerance, and ≥ 200 mg/dL as diabetes. Insulin resistance was calculated using the homeostasis model assessment of insulin resistance (HOMA-IR; fasting insulin mU/L × × fasting glucose mmol/L/22.5), and a HOMA-IR > 3.16 was considered to represent insulin resistance [2]. The diagnosis of MS was made according to the modified criteria of the International Diabetes Federation (IDF) consensus report for children [1, 3]. The criteria were the presence of obesity with a BMI > 90th percentile for age and sex and the presence of at least two of the following conditions: 1) fasting blood glucose >100 mg/dL, diabetes mellitus, insulin resistance (the cut-off point for our study was > 3.16) or impaired glucose tolerance testing, 2) hypertension, 3) hypertriglyceridemia (≥ 150 mg/dL), and 4) HDL cholesterol levels < 40 mg/dL.

Heart rate analysis

While at rest in a sitting position and not speaking or moving unless necessary in a small room, a Holter electrocardiogram was recorded for each subject for 20 min (Rozinn Electronics, NY, USA). All measurements were then manually revised by one operator (O.B.). The ectopic beats were deleted and removed from the R-R sequences for HRV analysis. We calculated the mean heart rate and frequency domain indices during the short-term periods. The advantages of short-term HRV data anal-

Table 1. Anthropometric measurements in the study groups.

	Obese groups (n = 66)	Nonobese controls (n = 40)	P
Sex (male/female)	31/35	20/20	
Age [year]	11.6 ± 2.05	11.6 ± 2.15	0.932
Height [cm]	150.5 ± 12.39	142.2 ± 12.23	0.001*
Weight [kg]	67.8 ± 16.89	34.7 ± 8.93	0.001*
Body mass index [kg/m^2]	29.3 ± 3.65	16.6 ± 1.49	0.001*
Systolic blood pressure [mm Hg]	113 ± 12	104 ± 10	0.001*
Diastolic blood pressure [mm Hg]	73 ± 10	67 ± 7	0.001*

*Statistically significant

ysis include its simplicity. In addition, because the data are collected in a controlled environment, they may be more suitable for analysis. For the frequency domain analysis, 5-min long R-R time series were interpolated at 250 ms to obtain equidistant values. Subsequently, a fast Fourier transformation was applied. The spectral components of total power (TP), very low frequency (VLF, 0.003–0.04 Hz), low frequency (LF, 0.04–0.15 Hz) and high frequency (HF, 0.15–0.40 Hz) in normalized units (LF nu and HF nu, respectively) and in milliseconds squared were used [8–13]. We used the LF to HF ratio (LF/HF) as an index of cardiac sympathovagal balance.

Statistical assessment

All data are shown as the means ± SD. Statistical Package for the Social Sciences 11.0 (SPSS, Inc., Chicago, IL, USA) was used for data assessment using Student's t test. P values below 0.05 were considered to be statistically significant.

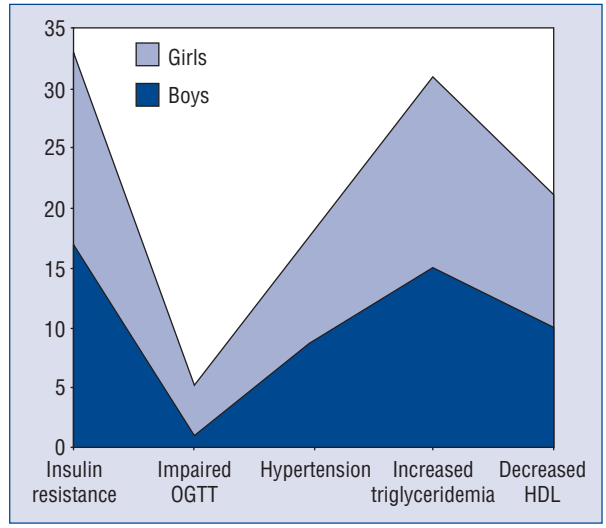

Figure 1. Distribution of risk factors in obese girls and boys; OGTT — oral glucose tolerance testing; HDL — high-density lipoprotein cholesterol.

Results

A total of 106 children (51.9% girls, 48.1% boys, mean age 11.6 ± 2 years) were evaluated in this study. The obese group had 66 children (31 boys and 35 girls). The nonobese group had 40 children (20 boys, 20 girls). Anthropometric measurements for the study group are shown in Table 1.

All of the obese children's BMI were higher than the 95th percentile for age and sex. Hypertension was detected in 18 (27.2%) subjects in the obese group. Arterial hypertension (systolic or diastolic) was present in 29% of the boys and 25.7% of the girls. The mean triglyceride level in the obese group was 161 ± 72 mg/dL, the mean HDL cholesterol was 46 ± 11 mg/dL and dyslipidemia was detected in 39 (59%) cases. The mean triglyceride level in the obese boys was 156 ± 73 mg/dL, and the mean HDL cholesterol was 47 ± 13 mg/dL. The mean triglyceride level in the obese girls was 166 ± 72 mg/dL, and the mean HDL cholesterol was found as 45 ± 9 mg/dL. Dyslipidemia was present in 64.5 and 54.3% of boys and girls, respectively.

None of the parameters in the obese group differed significantly between boys and girls. Insulin resistance, measured by HOMA-IR, was not significantly different between the sexes, (girls: 3.03 ± ± 2.09, boys: 3.57 ± 2.89, p = 0.381). In total, there were 33 cases of insulin resistance (17 obese boys [55%] and 16 obese girls [45%]). The distribution of risk factors between the obese girls and boys are shown in Figure 1.

In terms of MS diagnosis, in addition to obesity, the coexistence of insulin resistance and hypertension was found in 4 patients; insulin resistance and dyslipidemia was found in 8 patients; and finally a combination of insulin resistance, hypertension

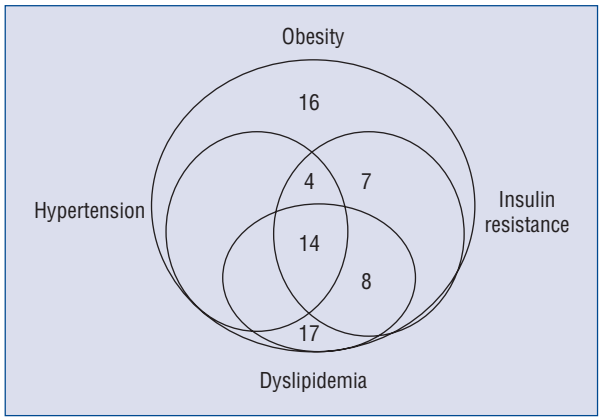

Figure 2. Coexistence of risk factors in the obese group.

and dyslipidemia was found in 14 patients. In total, MS was found in 26 (39.4%) cases. The diagnosis of MS according to modified IDF criteria is given in Figure 2.

The mean heart rate was 95.33 ± 8.37 bmp in the obese group compared to 77.53 ± 4.3 bpm in the control group ($p < 0.001$). The mean VLF was 1040 ± 314 ms^2 in the obese group compared to 1107 ± 454 ms^2 in the control group ($p = 0.419$). The mean LF was 40.68 ± 13.4 nu in the obese group compared to 39.97 ± 12.6 nu in the control group ($p = 0.787$). The mean HF was 16.02 ± 12.90 nu in the obese group compared to 21.45 ± 13.66 nu in the control group ($p = 0.046$). The mean LF/HF ratio was 3.79 ± 2.34 in the obese group compared to 2.25 ± 0.93 in the control group ($p < 0.001$). The HRV parameters in the study group are given in Table 2.

At the subgroup analysis, the mean VLF, the mean LF, the mean HF and the mean LF/HF ratio were not different in the obese with and without MS groups ($p > 0.5$). And also these parameters were not different in the obese with and without insulin resistance patients ($p > 0.5$).

Of the HRV parameters, TP, VLF, LF and HF were higher in the obese boys compared to the girls. LF elevation was statistically significant ($p = 0.042$); however the others were not significant ($p = 0.160$, $p = 0.660$, $p = 0.404$, respectively). The LF/HF ratio was higher in the obese girls; however, this difference was not significant ($p = 0.558$).

Discussion

Children who are obese in childhood are at risk for obesity and CAD in adulthood. The frequencies of type 2 diabetes and insulin resistance, which are particularly severe risk factors for CAD, have begun to increase dramatically among children in recent years in parallel with the incidence of obesity [3]. Insulin resistance coexists with increased sympathetic nervous system activation. The association between fasting insulin levels in hypertensive obese individuals and sympathetic system activation in the first and the second decades of life have been detected [14].

Rabbia et al. [15] studied 50 obese children; 11––15 years of age to detect CV autonomic functional changes in obese children. The mean heart rate, TP, LF, HF and LF/HF were estimated using the HRV method with a 24 h recording period. The high HRV and mean heart rate, which indicate sympathetic nervous system activity, and LF ratios indicate the sympathovagal interaction, were increased. The HF band, which indicates parasympathetic activity, was decreased, and the LF/HF ratio, which indicates autonomic nervous system balance, was increased in favor of sympathetic activity in the obese group. Based on these results, researchers have advocated that increased cardiac activity is one of the main factors for the emergence of insulin resistance and obesity-related hypertension [15].

Martini et al. [16] investigated 32 obese children and adolescents, 11–16 years of age to detect early CV autonomic dysfunction, and to identify the accompanying risk factors. In the obese group, they found that their HF values, which indicate parasympathetic activity, were significantly lower in the 24 h recording period. The LF values were higher

Table 2. Heart rate variability parameters in the study groups.

	Obese groups (n = 66)	Nonobese groups (n = 40)	P
Mean heart rate [bpm]	95 ± 8.3	77 ± 4.3	0.001*
Total power [ms^2]	1847 ± 893	2077 ± 1012	0.240
Very low frequency [ms^2]	1040 ± 314	1107 ± 454	0.419
Low frequency [nu]	40.68 ± 13.4	39.97 ± 12.6	0.787
High frequency [nu]	16.02 ± 12.9	21.45 ± 13.6	0.046*
Low frequency/high frequency	3.79 ± 2.34	2.25 ± 0.93	0.001*

*Statistically significant

in the control group, although the difference was insignificant. The LF/HF ratio was high indicating a reduction in vagal activity. The fasting blood glucose, fasting insulin, mean blood pressure, HOMA-IR and triglyceride values were elevated and the HDL cholesterol was low in the obese children. Researchers have suggested that insulin resistance facilitates the emergence of CV diseases through increased sympathetic autonomic activity [16].

Guizar et al. [17] compared HRV in 34 obese male children and adolescents, 12–17 years of age to a control group. In the obese children, they found a low HF which indicates decreased parasympathetic activity, and increased LF/HF which indicates impaired autonomic balance. They found high insulin, blood pressure, triglyceride, HOMA-IR values and low HDL cholesterol in the obese group [17].

Additionally, Riva et al. [18] investigated HRV in 24 obese children and found high LF/HF, and low HF which indicates that autonomic balance is impaired in childhood obesity. Riva et al. [18] claimed that increased sympathetic activity and impaired autonomic balance are important factors that facilitate the long-term development of hypertension.

One of the significant and striking factors that make our study unique and differentiates it from other studies is that the recordings were meticulously performed during a 20 min period. LF parameter values, which indicate sympathovagal activity, were higher, but the difference was insignificant. This result represents a significant reduction in parasympathetic activity. In conclusion, in our study, the LF/HF was increased significantly, and the CV autonomic system balance was impaired in favor of sympathetic activity, which is consistent with the literature [15–18]. Based on this result, we may claim that cardioautonomic function may be checked by measuring HRV through 20 min recordings without the need for 24 h recordings.

In our study, CV autonomic balance was impaired in favor of the sympathetic system in obese children and 50% of the patients had insulin resistance. In the literature, it has been stated that there is a close relationship between obesity and insulin resistance and the development of MS is higher among those individuals [1, 3]. There are some difficulties concerning making comparisons because different definitions are used in studies investigating the incidence of MS. In the Bugalosa Heart Study, the MS incidence was 4% in white children and 3% in black children based on fasting insulin and insulin resistance [19, 20]. Cook et al. [21] found that the incidence of MS was 28.7% when only the obese group was taken into consideration. Additionally, in our study, insulin resistance was detected in 50% of patients, and MS was detected in 39.4% patients. Insignificant HRV parameters in obese children with and without MS and insulin resistance suggest that there might be unknown issues about relations obesity and autonomic nervous systems.

Conclusions

Various impairments occur in the autonomic nervous system during the development of obesity. The balance was changed in favor of sympathetic activity, and vagal activity was decreased and had a significant role in obesity-related hypertension. In addition, insulin resistance is perhaps the most important factor that impairs sympathovagal activity, which is supported with studies.

In childhood obesity and in children with insulin resistance, HRV measurement that is a noninvasive and relatively cheap technique that may be used for the early diagnosis of CV diseases, and valuable data may be obtained with short recording times. A population-based study with a larger sample and a longer follow up period would better identify the relationship between obesity and metabolic disorders and CV autonomic balance, and would enable the use of new treatments in the early period.

Conflict of interest: none declared

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