Heart rate variability and left ventricular mass in slim children and young adults with hypertension

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Abstract

Introduction: Uncontrolled arterial hypertension brings direct and long-term sequelae in adult age, such as stroke, ischaemic heart disease with myocardial infarction, left ventricular hypertrophy or cardiac arrhythmia.

Aim: To assess heart rate variability (HRV) spectral parameters and left ventricular mass in slim children with arterial hypertension, and to search for correlations between these two parameters.

Methods: 35 children aged 14.4±3.1 with idiopathic untreated arterial hypertension were enrolled. The control group included 30 age- and gender-matched healthy children (aged 14.1±2.9 years). In all analysed subjects an analysis of HRV parameters (high frequency (HF) and low frequency (LF) components) during 10-minute waking state and sleeping time was performed and left ventricular mass (LVM) as well as the left ventricular mass index (LVMI, $g/m^{2.7}$) were assessed based on echocardiographic measurements.

Results: There was no difference in LF during the waking state and sleep HF between the two groups, whereas HF values during the waking state were significantly lower ($p<0.05$) in children with hypertension. The LF/HF index from both registration intervals was significantly higher in the group of children with hypertension. In children with hypertension, LVM and LVMI correlated significantly with LF ($r=0.32$, $p<0.05$ and $r=0.39$, $p<0.01$). LVM and LVMI correlated positively with the LF/HF index during night hours ($r=0.45$, $p<0.004$ and $r=0.49$, $p<0.002$). No significant correlations were found between the analysed parameters in children from the control group.

Conclusions: The increase of sympathetic activity during sleep correlates significantly with left ventricular mass and corrected left ventricular mass index in children with arterial hypertension.

Key words: heart rate variability, left ventricular mass, hypertension, children

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Introduction

Arterial hypertension is a well known cardiac risk factor contributing to the development of coronary atherosclerotic lesions and heart failure [1, 2]. It has been reported that elevated blood pressure results in increased left ventricular (LV) mass, which is an additional cardiovascular risk factor of higher morbidity and mortality [3, 4]. Arterial hypertension may occur in children and adolescents and cause damage affecting many organs and systems in future years of life. Thus, early diagnosis and treatment can prevent an unfavourable natural history of the disease [5].

There is increasing interest in the role of the sympathetic nervous system in the pathogenesis of hypertension. It may be driven by the use of more effective methods of adrenergic activity assessment or by the appreciation of its key role in cardiovascular system regulation. β_1-adrenergic activation results in heart rate acceleration and α_1-adrenergic activation to contraction of the vessels, which in turn directly affects peripheral resistance and cardiac output – mechanisms responsible for blood pressure control [6, 7]. In normal conditions, an increase of blood pressure caused by sympathetic activation leads to activation of the arterial baroreceptor reflex and parasympathetic activation (via the vagus nerve). Additionally, depression of tonic activity of the sympathetic neurons in the upper segments of the antero-lateral medulla

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Table I. HRV parameters in frequency-domain during 10 min ECG recordings in the day and at night

	Hypertension n=35	Control group n=30	P
Awoken			
LF [ln ms²]	6.9±0.6	6.9±0.5	ns
HF [ln ms²]	5.7±0.7	6.1±0.9	0.05
LF/HF	1.2±0.1	1.1±0.11	0.002
Sleeping			
LF [ln ms²]	7.2±0.7	6.8±0.6	ns (0.08)
HF [ln ms²]	6.7±0.9	6.9±1.1	ns
LF/HF N	1.0±0.09	0.9±0.08	0.001

Abbreviations: *LF – low frequency, HF – high frequency*

oblongata occurs, leading to the return of blood pressure to the initial level [6, 7].

Sympathetic activity may be responsible for cardiac hypertrophy. Close interactions between the sympathetic nervous system and the tissue renin-angiotensin system in the heart play an important role in its development – increased angiotensin II level is responsible for cardiac hypertrophy and fibrosis [8].

Spectral analysis of heart rate variability (HRV) is a non-invasive method of neuroautonomic cardiovascular control assessment. Spectral analysis includes three main components: high frequency (HF), which reflects vagal tone, low frequency (LF), mainly but not exclusively linked with sympathetic activity, and very low frequency, probably associated with thermoregulation [7, 9].

The aim of this study was to assess HRV spectral parameters and left ventricular mass in slim children with arterial hypertension, and to search for correlations between these two parameters.

Methods

The study group consisted of 35 children (19 girls), aged 14.4±3.1 (11-19 years) with hypertension. All had blood pressure above the 95th percentile for the relevant gender and age [10]. All study subjects were in or after the pubescence period (Tanner stages III-V). Additional inclusion criteria were as follows: body mass index (BMI) between 10th and 50th percentile, secondary causes of hypertension excluded, no antihypertensive drugs used.

The control group consisted of 30 healthy children (13 girls) aged 14.1±2.9 (12-18 years). Inclusion criteria: normal blood pressure, no LV hypertrophy or cardiac abnormality on echocardiography.

Echocardiographic evaluation

Left ventricular mass was calculated based on measurements taken from the left lateral position M-mode views. Measurements of the LV, interventricular septum and LV posterior wall thickness were taken according to the recommendations of the American Society of Echocardiography. Left ventricular mass (LVM) was calculated using Deveraux's formula. The LVM index (LVMI) was calculated by dividing LVM by height to the power of 2.7 in order to minimize age, gender, and body mass biasing [11].

HRV analysis

In all studied subjects 24-hour Holter monitoring was performed (FD-3, Oxford Instruments Ltd., Abington, U. K.). All patients were instructed to note the time of going to bed and waking up. Heart rate variability analysis was performed using the Oxford Medilog Excel-2 software system. Spectral analysis parameters were subjected to fast Fourier transform conversion, and then the following spectral analysis components were calculated: HF (0.15-0.4 Hz in ms^2), LF (0.04-0.15 Hz in ms^2), and LF/HF index. Spectral analysis parameters were given as a natural logarithm because of the diagonal character of data dispersion in frequency tables [9]. To avoid the influence of different lifestyles on heart rhythm, first 10 min of ECG tracing after 30 min in the horizontal position and 10 min after 2 hours from falling asleep were used in the analysis.

Written consent was obtained from all children's parents or guardians. The study protocol was approved by the Local Ethics Committee.

Statistical analysis

The results are given as mean values and standard deviations (SD). Student's t and Mann-Whitney U tests were used for unpaired variables. Pearson's correlation coefficient was used to calculate the strength of correlation between the parameters; Spearman's correlation coefficient was calculated in case of inability to use the former test (qualitative data, small groups). A p value of <0.05 was considered statistically significant.

Results

There was no difference in body mass (53±5 vs 54±7 kg) or height (1.63±0.2 vs 1.67±0.1 m) between the study group and the control group. Significantly higher LVM (167±60 vs 140±40 g; $p<0.01$) and LVMI (43±10 vs 35±7 g/m$^{2.7}$; $p<0.001$) were observed in children with hypertension. The mean RR interval time did not differ between the analysed groups (awoken: 680±110 ms vs. 645±90 ms; during sleep: 890±150 ms vs. 880±120 ms, NS).

There was no difference between the two groups in LF during the waking state or HF during sleep. Awoken HF values were significantly lower ($p<0.05$), and LF during

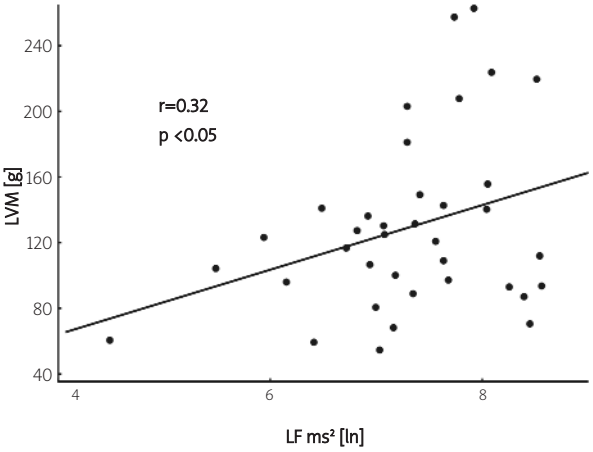

Figure 1. Correlations between LVM and LF values obtained during sleep in children with hypertension

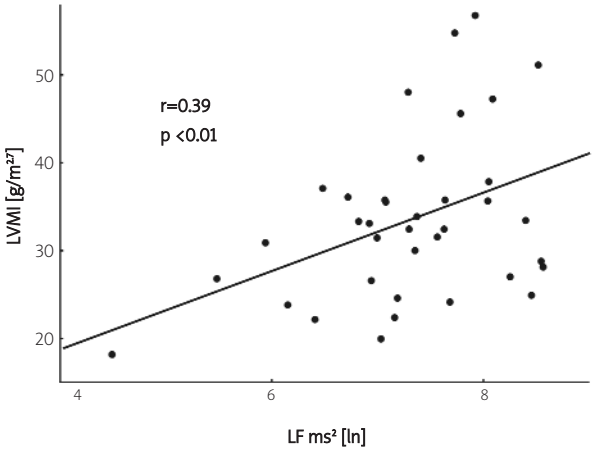

Figure 2. Correlations between LVMI and LF values obtained during sleep in children with hypertension

sleep were higher in children with hypertension, although the differences noted for LF did not reach statistical significance (Table I). The LF/HF index from both recording sessions was significantly higher in the group of children with hypertension (Table I).

In children with hypertension, LVM and LVMI correlated significantly with LF values ($r=0.32$, $p<0.05$ and $r=0.39$, $p<0.01$, Figures 1 and 2). Similarly, LVM and LVMI correlated with the LF/HF index during night hours ($r=0.45$, $p<0.004$ and $r=0.49$, $p<0.002$, Figures 3 and 4). No similar correlations were observed for LF ($r=0.28$, $p=0.08$ and $r=0.3$, $p=0.06$) or LF/HF recorded in the awoken subjects. No correlations between the awoken and night HF, and LVM as well as LVMI, were observed. No significant correlations were found between the analysed parameters in children from the control group.

Discussion

HRV analysis is more and more frequently used for noninvasive assessment of autonomic nervous activity. It is used to stratify the risk of sudden cardiac death after acute myocardial infarction, as well as in studies on congestive heart failure or arterial hypertension [12-15]. There are few studies reporting HRV parameter changes in children with hypertension; most investigations have been focused on adults [16, 17]. Our study revealed that in children with arterial hypertension not receiving treatment there is

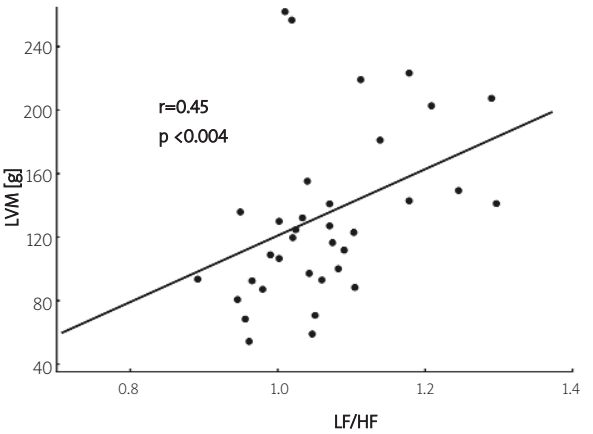

Figure 3. Correlations between LVM and LF/HF values obtained during sleep in children with hypertension

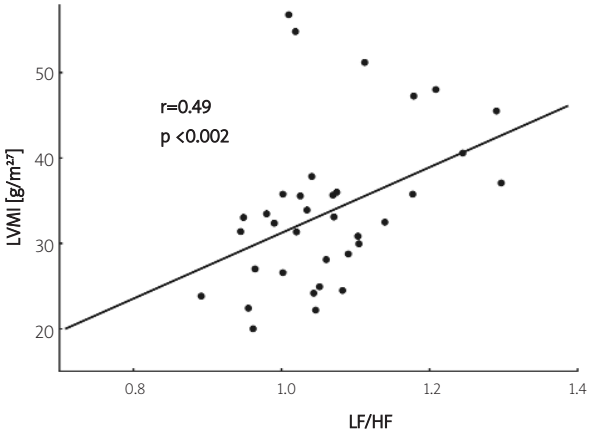

Figure 4. Correlations between LVMI and LF/HF values obtained during sleep in children with hypertension

domination of the sympathetic nervous system as expressed by the LF/HF index. These results are consistent with the data reported by Urbin et al., who found a trend towards sympathetic nervous system dominance in children with higher blood pressure [17]. Also in the adults, the higher values of parameters reflecting sympathetic nervous system effects are observed at an early stage of hypertension [18].

Hypertension is often associated with LV hypertrophy (LVH), which is known to be an independent risk factor for mortality and cardiovascular diseases [4]. It was reported that in patients with hypertension and LVH there were more ventricular arrhythmias present than in healthy subjects or people with hypertension but without LVH [19]. Higher LVMI in hypertensives compared to healthy controls was found in the present study. These data are consistent with results published by other authors [5, 11].

In patients with primary arterial hypertension, increased sympathetic activity was observed. This may be a result of an increase in primary activity at the level of the central nervous system and/or disturbance of peripheral receptor (baroreceptors, chemoreceptors, cardiopulmonary mechanoreceptors) activity [6, 7]. Genetic and environmental factors contribute to such a phenomenon. It has been demonstrated that hyperkinetic circulation is more common in the children of hypertensive parents [20]. These changes are the result of progress in inhibiting β-receptors, leading to decreased cardiac output and peripheral resistance increase [21].

Correlations between LMV, its index and sympathetic activity can be explained by its multi-factor and multi-organ function. One of these functions is the effect of sympathetic activity on rennin secretion, mediated through β-receptors in the juxtaglomerular apparatus, and rennin-angiotensin system activity, which results in sodium retention leading to an increase of intravascular volume, cardiac output and blood pressure [22]. Another one is hypertrophy of the media and collagen accumulation; collagen synthesis is controlled by angiotensin and aldosterone-dependent mechanisms [23]. As shown in experimental studies, collagen synthesis is also stimulated by the sympathetic nervous system via α_1 receptors [24]. Some authors suggest that a primary increase of sympathetic activity causes insulin resistance, in a mechanism of functional vessel lumen contraction [25, 26]. Also, high catecholamine plasma levels lead to excessive collagen production and increased myocardial mass [27]. Indirect confirmation of this hypothesis is the absence of significant correlations between the LF/HF index and parameters of left ventricular mass in healthy children.

There are also some limitations of the present study: one is the relatively small number of subjects included, another the fact that the phases of sleeping (REM, NREM) were not identified, which perhaps could influence HRV parameters.

Conclusions

The increase of sympathetic activity during sleep correlates significantly with left ventricular mass and corrected left ventricular mass index in children with arterial hypertension.

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Zmienność rytmu serca i masa lewej komory serca u szczupłych dzieci i młodzieży z nadciśnieniem tętniczym

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Streszczenie

Wstęp: Niekontrolowane nadciśnienie tętnicze (NT) niesie za sobą w wieku dorosłym bezpośrednie i odległe konsekwencje, jak udar mózgu, choroba niedokrwienna z zawałem serca, przerost lewej komory serca czy zaburzenia rytmu.

Cel: Ocena parametrów spektralnych zmienności rytmu serca oraz masy lewej komory serca u szczupłych dzieci z nadciśnieniem tętniczym oraz analiza wzajemnego związku pomiędzy tymi parametrami.

Metodyka: Badaniem objęto 35 dzieci w wieku 14,4±3,1 lat, dotychczas nieleczonych, ze stwierdzonym samoistnym nadciśnieniem tętniczym. Grupę kontrolną stanowiło 30 zdrowych, dobranych względem wieku i płci, dzieci (wiek 14,1±2,9 lat). U wszystkich badanych wykonano 10-minutową analizę zmienności rytmu serca (wysokie – HF, niskie częstotliwości – LF oraz wskaźnik LF/HF) w trakcie czuwania oraz w czasie snu oraz echokardiograficznie oceniono masę (LVM) oraz indeks masy lewej komory serca (LVMI, g/m$^{2.7}$).

Wyniki: Wartości LF z okresu czuwania oraz HF z okresu snu nie różniły się istotnie pomiędzy badanymi grupami, natomiast w trakcie czuwania wartości HF były istotnie niższe u dzieci z NT ($p<0,05$). Współczynnik LF/HF z obu okresów rejestracji był istotnie wyższy w grupie dzieci z NT. U dzieci z nadciśnieniem LVM oraz LVMI istotnie dodatnio korelowały z wartościami LF ($r=0,32$, $p<0,05$ i $r=0,39$, $p<0,01$). LVM i LVMI korelowały dodatnio ze współczynnikiem LF/HF z godzin nocnych ($r=0,45$, $p<0,004$ i $r=0,49$, $p<0,002$). U dzieci z grupy kontrolnej nie wykazano żadnych istotnych korelacji pomiędzy badanymi parametrami.

Wnioski: Uzyskane wyniki sugerują, że wzrost aktywności współczulnej jest silnie związany z wielkością masy oraz skorygowanego indeksu masy lewej komory serca u dzieci z nadciśnieniem tętniczym.

Słowa kluczowe: nadciśnienie tętnicze, dzieci, aktywność współczulna, masa lewej komory

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