

Original Article

Left ventricular hypertrophy induced by weight excess in children and adolescentsKyriaki Papadopoulou-Legbelou¹, Maria Gogou¹, Maria Kavga¹, Aggeliki Kleisarchaki¹, Assimina Galli-Tsinopoulou¹*¹4th Department of Pediatrics, School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, "Papageorgiou" General Hospital, Thessaloniki, Greece.***Abstract**

Background: Obesity is associated with left ventricular hypertrophy, an independent risk factor of cardiovascular morbidity. The aim of the present study was to evaluate obesity-induced left ventricular hypertrophy in overweight/obese children and adolescents and demonstrate possible early echocardiographic abnormalities in overweight children compared to obese children. The study included 55 children and adolescents (24 overweight and 31 with obesity) and 55 normal weight children. Standard M-mode echocardiography was performed in all participants. Parameters associated with left ventricular structure and function were recorded and statistically analysed. Left ventricular hypertrophy (LVmass/height³>95th percentile) was diagnosed in 33% of overweight children and 66.5% of children with obesity (p=0.01). Mean left ventricular mass/height³ and left ventricular mass/height^{2.7} were significantly higher in children with obesity compared to overweight children, as well as compared to the normal weight children. On the contrary, mean values of the index left ventricular mass/body surface area did not differ significantly among study groups. Furthermore, mean left ventricular end-diastolic diameter, interventricular septal thickness and left atrial diameter, presented significant differences among the 3 studied groups, even between overweight and normal weight children. Both systolic and diastolic function of left ventricular function were normal in our study groups. In conclusion, overweight children demonstrate significant early changes in left ventricular wall dimensions compared to normal weight children, while children with obesity additionally present a significant increase in left ventricular mass. Future studies are needed to explore the effect of dietary programs and other interventions on cardiac function parameters in these children.

Keywords: cardiovascular abnormalities, echocardiography, left ventricular hypertrophy, overweight, pediatric obesity

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Abbreviations:

BMI: Body Mass Index

BSA: Body Surface Area

EF: Ejection Fraction

FS: Fractional Shortening

IVSD: Interventricular Septal Thickness at Diastole

LAD: Left Atrial Diameter

LV: Left Ventricle or Left Ventricular

LVH: Left Ventricular Hypertrophy

LVIDD: Left Ventricular Internal Diameter end-diastole

LVMI: Left Ventricular Mass Index

LVPWD: Left Ventricular Posterior Wall thickness at Diastole

Introduction

The number of overweight children and the prevalence of obesity have been dramatically increasing worldwide (Freedman et al, 2006). Children and adolescents with obesity are at greater risk for cardiovascular diseases, diabetes, as well as metabolic syndrome (Daniels et al, 2005). Moreover, childhood obesity is a predictor of adult adiposity and therefore risk factors for cardiovascular disease detectable in childhood may predict cardiovascular morbidity and mortality in adulthood (Lakshman et al, 2012; De Simone et al, 1994).

In adulthood there is also evidence that obesity is strongly associated with left ventricular hypertrophy (LVH), which is an important diagnostic and prognostic indicator of cardiovascular disease (Kinik et al, 2006). There are also few studies indicating that hypertrophy originates in childhood (Boyras et al, 2013; Jing et al, 2016; Kharod et al, 2014).

In general LVH can be determined by left ventricular (LV) mass during echocardiographic assessment. A widely used approach in adults is to index LV mass by body surface area (LV mass index) (Devereux et al, 1984). With regards to children and adolescents, other authors have suggested to index LV mass by height^{2.7} or by or by height³ in order to avoid a possible effect of body weight excess (De Simone et al, 1992; Daniels et al, 1995).

The aim of this study is to evaluate obesity-induced LV hypertrophy in overweight/obese children and adolescents and demonstrate possible early echocardiographic abnormalities in overweight children compared to obese children.

Patients and Methods

We conducted a cross-sectional study approved by the Ethical Committee of the local University. Parents of all children provided informed consent to our study and all procedures were in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments.

A total of 118 children and adolescents were initially recruited for the study from the Outpatient Clinic for General Pediatrics of a University Hospital. Exclusion criteria included a significant concomitant disease such as endocrinological disorder (hyperinsulinemia, hyperuricemia), systemic inflammatory disease, cardiac disease, as well as medication known to modify cardiac function. We also excluded children with arterial hypertension, in order to avoid left ventricular changes due to hypertension.

Finally, 110 children were eligible for our study. The study group consisted of 55 children and adolescents (24 overweight, 31 with obesity) and the control group included 55 normal weight children. Criteria for obesity or overweight was based on World Health Organization definitions (obesity is defined as BMI $\geq 95^{\text{th}}$ percentile and overweight as BMI between 85^{th} and 95^{th} percentile).

All children underwent full multisystem clinical evaluation, including measurement of height and body weight. Body mass index (BMI) and body surface area (BSA) were calculated: BMI was calculated using the formula: (body weight in kilograms)/(height in meters)² and BSA using the formula: square root of [(body weight in kilograms)x(height in centimetres)/3600]. Blood pressure was measured by the cuff method (Dinamap automated vital signs monitor).

Echocardiographic study was performed in all subjects in the left decubitus position by a single experienced sonographer, using a General Electric-Vivid 3 ultrasound machine with a 5 MHz transducer. Guided by two-dimensional echocardiography short axis view, standard M-mode parameters of LV were obtained in accordance with the recommendations of the American Society of Echocardiography (Lang et al, 2005). Measurements included LV internal diameter at end-diastole (LVIDD), interventricular septal thickness at diastole (IVSD), LV posterior wall thickness at end-diastole (LVPWD), LV ejection fraction and fractional shortening (EF, FS), as well as LV mass. LV mass index (LVMI) was obtained by the following formula: LV mass/body surface area (g/m^2) (Devereux et al, 1984). We also indexed LV mass by $\text{height}^{2.7}$ and by height^3 (De Simone et al, 1992; Daniels et al, 1995).

Measurement of left atrial diameter (LAD) was performed from M-Mode by parasternal short axis view at the level of the aortic valve. From parasternal 4-chamber view using pulsed-wave Doppler echocardiography we estimated diastolic function of LV by measuring peak early diastolic wave velocity of mitral valve (E wave), peak late diastolic atrial contraction wave velocity (A wave), and E/A ratio.

Statistical analysis

Statistical analysis was performed using SPSS 20 software. Kolmogorov-Smirnov test was used to assess normal distribution of values. All continuous variables are presented as mean \pm standard deviation and all categorical data as proportions. Student T-test was used to compare continuous variables between two independent samples. One way analysis of variance

(ANOVA) and multiple comparisons test (Tukey's range test) were used to compare means among three or more independent groups. Chi-square test was used to compare categorical data. Two-tailed $p < 0.05$ was considered statistically significant.

Results

Demographic and basic clinical traits of our sample are summarized in Table 1. LVmass/ height^3 was >95 th percentile in 8 out of 24 (33%) overweight and 20 out of 31 (66.5%) children with obesity ($p=0.01$). Furthermore, mean values of LV mass, LVmass/ $\text{height}^{2.7}$ and LVmass/ height^3 were significantly higher in the obesity-overweight group compared to controls, while LV mass index did not differ among study groups (Table 1).

When 3 groups were compared (overweight, obese, controls), mean LVmass/ $\text{height}^{2.7}$ and LVmass/ height^3 were significantly higher in the obesity group compared to overweight and controls, but not between overweight and controls (Table 2). LV mass was significantly higher only in the obesity group compared to control group and LV mass index did not differ among study groups (Table 2).

Mean values of LVIDD, IVSD and LAD were significantly higher in children with obesity compared to controls and in overweight compared to normal-weight children, but did not exhibit significant differences between overweight and obesity group (Table 2). Systolic function (EF,FS) and diastolic function (E wave, A wave, E/A ratio) did not present significant differences among groups of our study.

Discussion

According to our results, LV mass/ $\text{height}^{2.7}$ and LV mass/ height^3 have demonstrated a higher prevalence of LVH in children with obesity compared to controls and highlighted

Table 1: Basic demographic, clinical characteristics and echocardiographic parameters of the study population.

Parameter	Overweight/ children with obesity (N=55)	Controls (N=55)	p value
Age (years)	9.85±3.16	9.06±3.26	NS
Sex (Female to male ratio)	0.83 (25/30)	0.77 (24/31)	NS
BMI (kg/m ²)	28.06±4.52	17.03±2.69	<0.001
BSA (m ²)	1.49±0.37	1.1±0.3	<0.001
LVIDD (mm)	43.09±6.1	38.72±6.22	<0.001
LAD (cm)	2.94±0.42	2.56±0.32	<0.001
IVSd (mm)	7.76±1.49	6.63±1.29	<0.001
LVPWd (mm)	7.84±1.54	7.58±2.02	NS
LV mass (gr)	106.27±39.78	78.75±32.54	<0.001
LV mass index	69.65±13.57	69.34±13.58	NS
LV mass/height ^{2.7}	38.62±7.71	33.37±5.22	<0.001
LV mass/height ³	34.95±7.56	30.55±4.88	<0.001
EF (%)	66.16±3.25	65.29±3.56	NS
FS (%)	36.07±2.58	35.33±2.74	NS
E wave (m/sec)	0.97±0.12	0.96±0.15	NS
A wave (m/sec)	0.54±0.07	0.52±0.1	NS
E/A ratio	1.8±0.24	1.87±0.27	NS

(NS: not significant, BMI: Body Mass Index, BSA: Body Surface Area, LVIDD: Left Ventricular internal diameter end-diastole, LAD: Left Atrial Diameter, IVSD: Interventricular septal thickness at diastole, LVPWD: Left Ventricular Posterior Wall thickness at Diastole,

LV mass: Left Ventricular mass, LVMI: Left Ventricular Mass Index, EF: Ejection Fraction, FS: Fractional Shortening)

Table 2: Differences in echocardiographic parameters among 3 groups: overweight children, children with obesity, controls.

Parameter	Overweight (N=21)	Obese (N=34)	Controls (N=55)	p value (between groups VS within group variability)	p value (overweight VS controls)	p value (obese VS controls)	p value (overweight VS obese)
LVIDD (mm)	42.8±4.1	43.32±7.35	38.72±6.22	0.002*	0.025	0.004	NS
LAD (cm)	2.88±0.37	2.99±0.46	2.56±0.32	<0.0001*	0.002	<0.001	NS
IVSd (mm)	7.57±1.35	7.91±1.59	6.63±1.29	<0.0001*	0.02	<0.001	NS
LVPWd (mm)	7.4±1.25	8.17±1.70	7.58±2.02	NS	-	-	-
LV mass	97.92±30.96	112.74±44.79	78.75±32.54	<0.0001*	NS	<0.001	NS
LV mass index	67.02±10.74	71.69±15.27	69.34±13.58	NS	-	-	-
LV mass/height^{2.7}	38.62±7.71	40.75±8.19	33.37±5.22	<0.0001*	NS	<0.001	0.018
LV mass/height³	32.24±5.92	37.06±8.09	30.55±4.88	<0.0001*	NS	<0.001	0.015

(NS: not significant, LVIDD: Left Ventricular internal diameter end-diastole, LAD: Left Atrial Diameter, IVSD: Interventricularseptal thickness at diastole, LVPWD: Left Ventricular Posterior Wall thickness at Diastole, LV mass: Left Ventricular mass, LVMI: Left Ventricular Mass Index)

* For these parameters ANOVA revealed that for between groups variability was significantly higher than within group variability and they were included in the multiple comparisons test. The rest of parameters did not present significant variability between groups and were not further analyzed.

differences between them and overweight children. However, no significant differences were identified between overweight and normal weight children, implying that LVH is not an early echocardiographic abnormality.

Furthermore, LV mass was significantly different only between children with obesity and normal weight children, while LVMI did not differ among groups. With regards to LV dimensions, LVIDD, IVSd and LAD were significantly affected by weight excess both in overweight and obese children and adolescents.

Our findings are consistent with previous studies on this topic conducted in children of other nationalities. Ghanem et al (2010), report that young children with obesity have significant early changes in LV wall dimensions compared to normal weight, while various studies reveal that obesity has a direct effect on LV mass in childhood and plays an important role in the development of LVH (Ghanem et al, 2010; Malcolm et al, 1993; Urbina et al, 1995; Li et al, 2004; Chinali et al, 2006; Ozdemir et al, 2010). Moreover, the Bogalusa Heart Study showed a strong association between obesity beginning in childhood and the development of LVH in young adulthood (Li et al, 2004). More recently, Kharod et al (2014), have shown that BMI presents a stronger association with cardiac sequelae in overweight/ obese children in comparison to other clinical factors (Kharod et al, 2014).

An additional finding of our study was that overweight children present early signs of cardiac involvement (increased IVSD compared to normal weight children). Therefore, ventricular septal hypertrophy seems to represent an early event in the development of obesity-related LVH (Sivanandam et al, 2006).

In general, obesity is associated with increased metabolic demand, leading to increased blood volume, preload and afterload of the heart (Alpert, 2001). This is an obvious mechanism of LVH in these patients. As none of the patients included in the study had arterial hypertension, the increase in LV mass cannot be attributed to hemodynamic factors, but may be due to neurohormonal effects, which influence LV growth. According to Davis et al (2012), specific metabolic abnormalities (insulin resistance, hyperglycaemia, dyslipidemia) constitute a subclinical metabolic syndrome and can be involved in the modulation of LV structure (Davis et al, 2012). Moreover, a transient insulin-resistant state often occurs in children during normal pubertal development, thus enhancing cardiac remodeling (Moran et al, 1999).

LV systolic and diastolic function were normal in our patients. On the other hand, there are studies that have identified early diastolic abnormalities both in overweight and in children with obesity (Harada et al, 2001; Mehta et al, 2004; Van Putte-Katier et al, 2008). These discrepancies among studies could be attributed to different methodologies (e.g. Tissue Doppler Imaging) or to varying samples' size.

Although dietary interventions or physical activity in adult patients with obesity showed improvement or even prevention of obesity-related cardiac changes, these effects have not been systematically studied in childhood (Alpert et al, 1985; Himeno et al, 1996). However, various protocols of clinical trials aiming at improving nutrition behaviours of children and parents have been published in recent years and demonstrate encouraging outcomes (Morgan et al, 2014; Minossi et al, 2015; Peñalvo et al, 2015).

The main limitations of our study are the relatively small sample size, as

well as the fact that children were recruited from a single tertiary centre and they may not be representative of the general pediatric population. Moreover, associations between echocardiographic findings and anthropometric, as well as metabolic factors (e.g. values of plasma lipids) have not been studied.

Conclusion

In conclusion, the vast majority of children with obesity in our cohort present a significant increase in LV mass, as evidenced by the ratio LV mass/height³, thus confirming the results of previous studies. Furthermore, even overweight children demonstrate early significant changes in LV wall dimensions compared to normal weight children, with septal hypertrophy being a preceding indicator. Despite changes in LV structure, LV function remains normal in the early stages of obesity in childhood. As cardiovascular abnormalities associated with adult obesity are likely to originate in childhood and since most of them are preventable and reversible, early identification is necessary to start prevention interventions as soon as possible.

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