

Relationship Between Overweight and Obesity and Cardiac Dimensions and Function in a Paediatric Population.

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Abstract

Obesity in adults is associated with left ventricular hypertrophy, dilatation and myocardial fibrosis, as well as heart failure and coronary heart disease. These associations have been studied to a lesser extent in the paediatric population. This study aims to investigate the relationship between obesity and cardiac structure and function in the paediatric population. In a southern Spanish town, we selected all inhabitants aged 6–17 years stratifying by age, gender, and educational centres. We performed a complete transthoracic echocardiogram evaluating all the cardiac morphological and functional parameters commonly measured in an echocardiographic study. There were 212 children and adolescents included. Of them, 48,1 % were males. The mean age was 10.9 ± 3.0 years. 106 (50%) were normal weight, 57 (26.9%) overweight and 49 (23.1%) obese. Sex and age were similar in all three groups. Overweight and obesity were associated with larger left ventricular end-diastolic and end-systolic volumes ($p < 0.0005$), greater left ventricular mass ($p < 0.0005$) and smaller ejection fraction ($p < 0.0005$). They were also associated with larger atrial, aortic and right ventricular size. Lateral and mean E/e' ratios were higher ($p = 0.007$ and $p = 0.01$ respectively). Body mass index was independently associated with all cavity size variables as well as left ventricular ejection fraction.

Conclusion: Childhood obesity is independently associated with larger heart chambers, greater left ventricle mass, and smaller left ventricle ejection fraction.

Introduction

Childhood obesity is one of the most significant public health issues of the 21st century. In Spain, the prevalence of overweight and obesity in the paediatric population is 34.1% and 10.3% respectively [1]. This prevalence is increasing at an alarming rate: childhood overweight and obesity is estimated to have increased globally by 47.1% over the past three decades [2].

Overweight and obesity are associated with the development of cardiovascular risk factors in the paediatric age group, such as hypertension, dyslipidaemia, hyperinsulinemia and chronic inflammation [3]. Childhood obesity has also been linked to the development of cardiovascular risk factors in adulthood and thus to increased morbidity and mortality [4, 5].

Obesity in adulthood has been identified as a causative agent of cardiovascular disease independently of other classical risk factors. Obesity-related clinical entities include the development of coronary heart disease, heart failure, atrial fibrillation and sudden death [6].

At the cardiac level, in adult obesity there is an increase in cardiac output because of the body's increased metabolic demands. This haemodynamic alteration secondary to obesity has been linked to left ventricular (LV) dilatation and hypertrophy, as well as to the development of obesity-related cardiomyopathy. This pathological entity involves an increase in ventricular mass and dilatation of the cardiac chambers, as well as myocyte hypertrophy and the development of myocardial fibrosis. The

presence of diastolic dysfunction related to this cardiomyopathy accounts for 50% of cases of heart failure in this group [7, 8, 9, 10].

In childhood, the relationship between overweight and obesity with cardiac morphological and functional alterations it's not completely defined. There are few studies relating overweight and obesity to cardiac geometry and function, although LV enlargement and alterations in diastolic function have been reported in childhood obesity [11, 12, 13].

The aim of our study is to research the relationship between the overweight and obesity with changes in cardiac structure and function in a paediatric population in our environment.

Methods

We carried out a cross-sectional study, selecting a consecutive sample of 265 primary and secondary school children and adolescents from a town of around 3000 inhabitants in Andalusia. The sample was stratified by age, gender, and educational centres. Healthy children and adolescents aged 6–17 years who accepted and signed consent by their parents or legal guardians were included. Those who were outside the age range, had previously known acquired or congenital cardiac pathology, or did not give consent were excluded. Likewise, those who presented cardiac pathology in the echocardiography study.

The anthropometric data of the children and adolescents were collected using standardised measurements of weight and height. As for the definition of childhood obesity, there is no agreed criterion for establishing overweight and obesity based on body mass index (BMI). In this study, the definition proposed by the World Health Organisation was used: overweight was defined for sex- and age-specific BMI values greater than one standard deviation and less than two standard deviations; and obesity was defined for sex- and age-specific BMI values greater than two standard deviations [14]. Blood pressure was measured, and blood biochemistry was performed to determine fasting basal glycaemia and lipid profile.

Each subject underwent a standard transthoracic echocardiographic study with a Philips iE33 and an S5-1 probe (Philips Medical Systems, Amsterdam, The Netherlands). All images were recorded and saved for posterior digital analysis. Parasternal long-axis M-mode images were obtained to measure left ventricular (LV) diastolic and systolic diameter, interventricular septal thickness, LV posterior wall thickness and aortic size. Calculation of LV mass was performed by the Devereux formula [15]: $0.8 \times \{1.04 [(LVDD + PW + IVS)^3 - (LVDD)^3]\} + 0.6$; with LVDD corresponding to LV diastolic diameter, PW to posterior wall thickness and IVS to interventricular septal thickness.

Two-, three- and four-chamber images were obtained through the apical window. The end-diastolic and end-systolic volumes were obtained using Simpson's method, and the left ventricular ejection fraction (LVEF) value was calculated from them. The basal diameter of the right ventricle was measured in the apical four-chamber plane focused on the right ventricle. Left atrial volume was calculated by the Simpson biplane method. Right atrial area was obtained by apical four-chamber planimetry.

By pulsed Doppler, LV diastolic function was analysed through mitral filling flow, placing the sample volume at the level of the free edges of the mitral leaflets in the apical four-chamber plane. E-wave and A-wave were measured, and the E/A ratio was calculated. By tissular Doppler, lateral and medial e' waves were measured; and average e' wave and lateral, medial and average E/e' ratios were calculated according to previous measurements. With continuous Doppler through the tricuspid valve in apical four chambers, the pressure gradient from the right ventricle to the right atrium was calculated by means of the maximum tricuspid regurgitation velocity.

All measurements were performed in accordance with current recommendations for echocardiography in the paediatric population [16].

For the descriptive analysis, quantitative variables are represented by their mean and standard deviation and qualitative variables by frequency and percentage. The Kolmogoroff-Smirnoff test was used to check which variables followed a normal distribution. For the comparison of subgroups, we used the ANOVA test for quantitative variables and the chi-square test for qualitative variables. Univariate regression analysis was performed to assess the relationship of BMI with the different echocardiographic parameters. Multiple regression analysis was performed to assess the independent influence of BMI on echocardiographic parameters, after adjusting for other baseline covariates. SPSS v 21.0 (SPSS Inc., Chicago, USA) was used for the analysis. A $p < 0.05$ value was considered significant.

Results

A total of 265 children and adolescents were initially selected, the final resulting sample was 212, after 53 subjects were excluded: 26 cases did not give consent, 4 cases did not meet age criteria, 8 cases presented cardiac pathologies in the echocardiographic study, 14 cases showed unacceptable quality or other technical problems in the echocardiographic study and in one case the anthropometric variables were missing.

Of the 212 children and adolescents, 106 (50.0%) were normal weight, 57 (26.9%) were overweight and 49 (23.1%) were obese. The mean age was 10.9 ± 3.0 years and 48.1% were boys. The main clinical characteristics of the different groups are shown in Table 1. Gender and age were similar in the three groups. Statistically significant differences were found in anthropometric parameters (weight, height, and body mass index), blood pressure, blood glucose, HDL, LDL and triglyceridaemia, with higher values in the overweight and obese groups for all parameters except HDL.

Table 1
Clinical characteristics.

	Total	Normal weight	Overweight	Obesity	p
Age (years)	10,9 ± 3,0	10,9 ± 3,2	10,7 ± 2,7	11,0 ± 2,8	0,8
Sex (% male)	102 (48,1%)	52 (49,1%)	29 (50,9%)	21 (42,9%)	0,7
Weight (kg)	43,4 ± 17,2	35,7 ± 12,8	44,3 ± 13,3	59,2 ± 18,4	< 0,0005
Height (cm)	143,2 ± 16,2	141,0 ± 17,2	143,3 ± 15,2	148,0 ± 14,9	0,046
BMI (kg/m ²)	20,3 ± 4,4	17,3 ± 2,2	20,9 ± 2,4	26,2 ± 3,6	< 0,0005
CSA (Dubois formula) (m ²)	1,3 ± 0,3	1,2 ± 0,3	1,3 ± 0,3	1,5 ± 0,3	< 0,0005
SBP (mmHg)	110,0 ± 11,0	106,9 ± 10,5	111,6 ± 10,2	114,6 ± 10,7	< 0,0005
DBP (mmHg)	68,2 ± 6,5	67,1 ± 5,9	68,7 ± 6,5	69,9 ± 7,2	0,03
Blood glucose level (mg/dL)	75,9, ± 6,8	74,7 ± 6,6	75,7 ± 5,7	78,5 ± 8,0	0,005
HbA1c (%)	5,3 ± 0,3	5,3 ± 0,3	5,3 ± 0,3	5,4 ± 0,3	0,2
Total Cholesterol (mg/dL)	167,1 ± 29,8	162,7 ± 26,7	170,6 ± 37,0	172,7 ± 25,4	0,09
HDL (mg/dL)	57,0 ± 12,8	59,4 ± 12,6	57,7 ± 11,3	51,1 ± 13,2	0,001
LDL (mg/dL)	94,9 ± 24,0	89,2 ± 21,5	100,8 ± 25,7	100,7 ± 24,3	0,002
Triglycerides (mg/dL)	73,1 ± 41,0	66,5 ± 31,1	71,2 ± 28,1	89,8 ± 63,2	0,004
BMS: body mass index; CSA: corporal surface area; DBP: diastolic blood pressure; HbA1c: glycosilated hemoglobin; HDL: high density lipoprotein; LDL: low density lipoprotein; SBP: systolic blood pressure;					

Table 2 shows the comparison of echocardiographic structural variables and LVEF in the three groups. For both the LV size and LV thickness variables, the overweight group had higher values than the normal weight group, and the obese group had higher values than the overweight group. Comparisons of diastolic diameter (p = 0.003), end-diastolic volume (p < 0.0005), end-systolic volume (p < 0.0005), interventricular septum size (p = 0.01), posterior wall (p < 0.0005) and LV mass (p < 0.0005) were statistically significant. Left atrial volume (p = 0.004), right atrial area (p = 0.001), basal diameter and right ventricular outflow tract (p = 0.001 and p < 0.0005 respectively) and aortic size (p < 0.0005) behaved in the same way. LVEF was significantly lower in the obese group than in the overweight group, and

significantly lower in the overweight group than in the normal weight group ($p < 0.0005$), with no significant post hoc comparison of the overweight and obese groups.

Table 2
Echocardiographic structural characteristics and LVEF.

	Total	Normal Weight	Overweight	Obesity	p	p ^a	p ^b	p ^c
LVDD (mm)	42,2 ± 5,6	41,1 ± 5,5	42,8 ± 5,4	44,2 ± 5,5	0,003	0,1	0,003	0,4
LVSD (mm)	26,0 ± 4,8	25,3 ± 4,7	26,1 ± 4,9	27,2 ± 4,8	0,07	0,6	0,06	0,4
IVS (mm)	6,6 ± 1,5	6,3 ± 1,4	6,9 ± 1,3	7,0 ± 1,7	0,01	0,2	0,03	0,5
PW (mm)	6,0 ± 1,5	5,6 ± 1,4	6,1 ± 1,3	6,8 ± 1,6	< 0,0005	0,03	< 0,0005	0,05
LV mass (g)	78,3 ± 33,2	69,3 ± 30,1	80,9 ± 30,2	94,8 ± 36,5	< 0,0005	0,05	< 0,0005	0,09
LVEDV (mL)	64,1 ± 20,9	57,9 ± 18,6	64,3 ± 18,3	78,1 ± 22,4	< 0,0005	0,1	< 0,0005	0,004
LVESV (mL)	23,1 ± 8,8	19,8 ± 6,7	23,5 ± 8,1	30,0 ± 10,1	< 0,0005	0,1	< 0,0005	0,002
LA volume (mL)	22,3 ± 7,5	19,7 ± 6,8	22,6 ± 6,5	27,9 ± 7,4	0,004	0,04	< 0,0005	0,002
RA area (cm ²)	9,1 ± 2,3	8,5 ± 2,1	9,3 ± 2,2	10,0 ± 2,6	0,001	0,06	0,002	0,3
RV basal diameter (mm)	28,3 ± 4,4	27,6 ± 4,5	28,0 ± 3,9	30,2 ± 4,2	0,001	0,8	0,001	0,01
RVOT (mm)	24,2 ± 4,7	22,6 ± 4,2	24,6 ± 4,2	27,1 ± 4,8	< 0,0005	0,02	< 0,0005	0,01
Aorta (mm)	21,6 ± 3,4	20,8 ± 3,4	21,5 ± 3,2	23,4 ± 3,0	< 0,0005	0,4	< 0,0005	0,008
LVEF (%)	64,2 ± 4,5	65,7 ± 3,6	63,6 ± 4,7	61,5 ± 4,6	< 0,0005	0,01	< 0,0005	0,08
<p>IVS: interventricular septum; LA: left atrium; LV: left ventricular; LVDD: left ventricular diastolic diameter; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; LVEF: left ventricular ejection fraction; LVSD: left ventricular systolic diameter; PW: posterior wall; RA: right atrium; RV: right ventricle; RVOT: right ventricle outflow tract.</p>								
<p>p^a: compared normal weight and overweight groups.</p>								
<p>p^b: compared normal weight and obesity groups.</p>								
<p>p^c: compared overweight and obesity groups.</p>								

Table 3 shows the diastolic function variables. E-wave and A-wave velocities were higher in the overweight group than in the normal weight group, and higher in obese than in overweight subjects, but the comparison did not reach statistical significance. Lateral and medial e' wave velocities were lower. Both lateral E/e' ratio and mean E/e' ratio showed significant differences ($p = 0.007$ and $p = 0.01$ respectively), with no significant post hoc comparison of normal weight and overweight groups in both cases. The pressure gradient between the right ventricle and right atrium was higher in the obese group ($p = 0.05$).

Table 3
Diastolic function parameters.

	Total	Normal Weight	Overweight	Obesity	p	p ^a	p ^b	p ^c
Peak E velocity (cm/s)	106,7 ± 13,2	105,5 ± 13,6	106,9 ± 11,2	109,1 ± 14,4	0,3	0,8	0,3	0,7
Peak A velocity (cm/s)	60,0 ± 13,5	58,3 ± 13,3	59,4 ± 12,8	64,8 ± 13,8	0,2	0,9	0,02	0,1
Mitral E/A ratio	1,9 ± 0,4	1,9 ± 0,5	1,9 ± 0,4	1,7 ± 0,4	0,1	0,9	0,1	0,2
Peak e' lateral velocity (cm/s)	20,9 ± 4,5	21,1 ± 4,5	21,6 ± 4,8	19,6 ± 3,6	0,06	0,8	0,09	0,06
E/e' lateral ratio	5,3 ± 1,2	5,2 ± 1,2	5,1 ± 2,0	5,7 ± 1,2	0,007	0,9	0,02	0,01
Peak e' medial velocity (cm/s)	14,1 ± 2,4	14,0 ± 2,1	14,3 ± 2,5	13,8 ± 2,8	0,5	0,7	0,9	0,6
E/e' medial ratio	7,7 ± 1,4	7,7 ± 1,4	7,6 ± 1,4	8,1 ± 1,4	0,2	0,9	0,2	0,3
E/e' average ratio	6,5 ± 1,1	6,4 ± 1,1	6,3 ± 1,0	6,9 ± 1,1	0,01	0,9	0,02	0,02
Gradient RV-RA (mmHg)	16,0 ± 4,7	15,8 ± 4,9	15,0 ± 3,5	18,0 ± 4,7	0,05	0,7	0,16	0,04
Gradient RV-RA: pressure gradient between right ventricle and right atrium.								
p ^a : compared normal weight and overweight groups.								
p ^b : compared normal weight and obesity groups.								
p ^c : compared overweight and obesity groups.								

The association of BMI with the different echocardiographic variables was assessed by univariate regression analysis. The results are shown in table 4. All chamber size variables assessed in the study were significant. The association was strongest for LV ventricular volumes (LV end-diastolic volume $r^2 = 0.48$, $p < 0.0005$, and LV end-systolic volume $r^2 = 0.51$, $p < 0.0005$), although for all other variables the association was weaker. For diastolic function parameters the association was weak, only the right cavity pressure gradient was significant.

Tabla 4. Univariate linear regression analysis.

	r	r ²	beta	CI 95%	p
LVDD (mm)	0,54	0,29	0,68	0,54 – 0,83	<0,0005
LVSD (mm)	0,41	0,17	0,40	0,28 – 0,51	<0,0005
IVS (mm)	0,44	0,19	0,14	0,10 – 0,19	<0,0005
PW (mm)	0,42	0,18	0,14	0,10 – 0,19	<0,0005
LV mass (g)	0,56	0,32	4,21	3,37 – 5,05	<0,0005
LVEDV (mL)	0,69	0,48	3,37	2,87 – 3,87	<0,0005
LVESV (mL)	0,71	0,51	1,48	1,27 – 1,68	<0,0005
LA volume (mL)	0,61	0,37	1,06	0,86 – 1,26	<0,0005
RA area (cm ²)	0,51	0,26	0,26	0,20 – 0,32	<0,0005
RV basal diameter (mm)	0,40	0,16	0,39	0,27 – 0,52	<0,0005
RVOT (mm)	0,58	0,34	0,62	0,50 – 0,74	<0,0005
Aorta (mm)	0,60	0,36	0,43	0,35 – 0,51	<0,0005
LVEF (%)	0,35	0,12	-0,36	-0,50 – -0,22	<0,0005
E/e' lateral ratio	0,14	0,02	0,04	0,00 – 0,07	0,05
E/e' average ratio	0,11	0,03	0,03	-0,01 – 0,06	0,1
Gradient RV-RA (mmHg)	0,21	0,04	0,26	0,03 – 0,49	0,03
Gradient RV-RA: pressure gradient between right ventricle and right atrium, IVS: interventricular septum, LA: left atrium, LV: left ventricular, LVDD: left ventricular diastolic diameter, LVEDV: left ventricular end-diastolic volume, LVESV: left ventricular end-systolic volume, LVEF: left ventricular ejection fraction, LVSD: left ventricular systolic diameter, PW: posterior wall, RA: right atrium, RV: right ventricle, RVOT: right ventricle outflow tract.					

Multivariate analysis was performed on those variables that were significant in the univariate analysis. The results are shown in Table 5. BMI was independently associated with all chamber size variables, as well as with LVEF, after adjusting for other baseline covariates. The best explained variables were LV mass and volumes (LV mass: $r^2 = 0.52$ $p < 0.0005$, LV end-diastolic volume: $r^2 = 0.66$ $p < 0.0005$, LV end-systolic volume: $r^2 = 0.63$ $p < 0.0005$), aortic size ($r^2 = 0.56$, $p < 0.0005$) and LVEF ($r^2 = 0.56$, $p < 0.0005$).

Table 5
Multiple regression analysis.

Dependent variables	r ²	beta	CI 95%	p	Explanatory variables
LVDD (mm)	0,53	0,32	0,17–0,46	< 0,0005	IMC, edad, PAS
LVSD (mm)	0,32	0,20	0,07–0,32	0,002	IMC, edad
IVS (mm)	0,31	0,10	0,05–0,14	< 0,0005	IMC, edad, PAS, LDL
PW (mm)	0,24	0,12	0,07–0,17	< 0,0005	IMC, PAS, LDL, glucosa
LV mass (g)	0,52	2,31	1,43–3,19	< 0,0005	IMC, edad, PAS, PAD, LDL
LVEDV (mL)	0,66	2,08	1,61–2,55	< 0,0005	IMC, edad, PAS
LVESV (mL)	0,63	0,98	0,76–1,20	< 0,0005	IMC, edad, PAS, TAG
LA volume (mL)	0,43	0,89	0,65–1,14	< 0,0005	IMC, edad, PAS, PAD, LDL
RA area (cm ²)	0,34	0,18	0,11–0,24	< 0,0005	IMC, edad
RV basal diameter (mm)	0,24	0,28	0,14–0,42	< 0,0005	IMC, edad, TAG
RVOT (mm)	0,39	0,47	0,35–0,60	< 0,0005	IMC, edad
Aorta (mm)	0,56	0,26	0,19–0,33	< 0,0005	IMC, edad
LVEF (%)	0,56	-0,36	-0,50 – -0,22	< 0,0005	IMC
IVS: interventricular septum; LA: left atrium; LV: left ventricular; LVDD: left ventricular diastolic diameter; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; LVEF: left ventricular ejection fraction; LVSD: left ventricular systolic diameter; PW: posterior wall; RA: right atrium; RV: right ventricle; RVOT: right ventricle outflow tract.					

Discussion

The main findings of this study are that the percentage of overweight and obesity in children and adolescents in our population is high compared to previous studies, and that overweight and obesity in children and adolescents is independently and negatively associated with cardiac morphology and function parameters measured by echocardiography.

In the study by Sánchez-Cruz et al. [17] the prevalence of childhood overweight is 26% and that of childhood obesity is 12.6%. Data from the recently published ENPE study show a prevalence of childhood obesity of 10.3% [1]. The percentage of overweight in our sample was 26.9% and the percentage of obesity was 23.1%, higher than that reported in previous population-based studies in Spain. These findings could be correlated with a heterogeneous distribution of obesity in the different areas of our country. The enKid study [18], designed to assess the dietary and nutritional habits of children and young people, reported that the Canary Islands and Andalusia had the highest rates of childhood obesity. These data are consistent with the high rates of overweight and obesity in our study.

Furthermore, the results of our study show that higher BMI in childhood is independently associated with increased ventricular wall thickness and LV mass, as well as with increased LV size in both diastolic and systolic volumes. Similarly, higher BMI is associated with increased size of both atria, right ventricle and ascending thoracic aorta. Regarding LV systolic function, the overweight and obese groups of children and adolescents had a lower ejection fraction compared to the normal weight group, and increased BMI was independently associated with decreased LVEF with acceptable goodness-of-fit.

Previous studies have described a relationship between childhood obesity and increased left ventricular mass and altered diastolic parameters. The group of Saltijeral et al [11], describes an increase in LV size and LV wall thickness in the childhood obesity group compared to the control group. Mangner et al [12] describe LV and left atrial enlargement and worse diastolic function in obese children and adolescents. Dias et al [13], agree with previous studies in that adolescents with obesity showed an increase in left ventricular thickness and size. In this respect, our results are in line with those of previous studies published on this topic.

However, these previous studies were case-control studies with small samples, and only the study by Saltijeral et al. was conducted in our setting. In this respect, our study provides relevant information from a large, randomly selected sample of a rural Spanish child population. Furthermore, none of these studies reported a significant worsening of LVEF in the obese group, nor an independent relationship of BMI with worsening LVEF.

Based on our results, in childhood obesity we observed an adaptation of the LV by dilation and hypertrophy, in a similar way that is reported in adult obesity, and it may be related to the increase in cardiac output needed to meet the metabolic demands. Our group is concerned about the high prevalence of childhood overweight and obesity, as well as the structural and functional changes observed in the cardiac cavities of overweight and obese children and adolescents, leading to an increased cardiac chamber size and an impaired LV systolic and diastolic function. Although these structural and functional changes are far from clinical significance, it is likely that these changes, present an early age, may persist over time, and should be considered as incipient changes for the development of obesity cardiomyopathy in adulthood.

It has been described that therapeutic intervention on obesity in adulthood and the reduction of BMI is accompanied by significant structural improvements, even reaching complete normalisation of the cardiac structure [19]. Extrapolating this information to children, this research group considers that therapeutic intervention on childhood obesity would set a great precedent in the primary prevention of cardiovascular events in this population risk group.

As a main limitation of the study, our group considers that, being designed as a cross-sectional study, it does not really allow us to assess whether these structural changes can be maintained over time into adulthood. Similarly, it does not allow us to assess whether an intervention on obesity in childhood could reverse the structural and functional changes observed. Further sample follow-up or obesity intervention studies would be needed to answer these questions. On the other hand, it is a study carried out in a

specific population in southern Spain and may be the results, at least in terms of prevalence of childhood obesity, may not be extrapolated to other regions.

Conclusion

The result of this study shows that obesity in childhood is independently associated with significant changes in the structure and function of the different cardiac chambers. These changes are associated with unfavourable alterations early in life.

Abbreviations

BMI: body mass index

LV: left ventricular

LVEF: left ventricular ejection fraction

Declarations

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