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Effect of Obesity on Left Ventricular Diastolic Function in Children

Çocuklarda Obezitenin Sol Ventrikül Diyastolik Fonksiyonları Üzerine Etkisi

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ABSTRACT

Introduction: *We aimed to asses two dimensional, M-Mode, conventional and tissue Doppler echocardiographic parameters of left ventricle and to evaluate the effects of antropometric and biochemical factors on these parameters in obese and normal weight children.*

Patients and Methods: *This observational cross-sectional study included 60 obese and 60 non-obese children aged 8-15 years. Echocardiographic parameters of left ventricle were measured in all subjects and investigated the relationship with anthropometric and biochemical factors.*

Results: *Waist circumference, body mass index-Z (BMI-Z) score, systolic and diastolic blood pressure, triglyceride, fasting glucose, insulin concentrations, and homeostatic model assessment (HOMA) index were significantly higher, whereas high density lipoprotein-cholesterol (HDL-C) concentration was significantly lower in the obese than in the non-obese group. Mitral annulus septal E' and E'/A', mitral annulus lateral E' and E'/A', anterior E' and E'/A', inferior E' and E'/A' values were significantly lower, whereas mitral E/septal E' and mitral E/lateral E' values were significantly higher in obese than in non-obese subjects. Most of the tissue Doppler parameters were correlated with waist circumference, BMI-Z score, fasting blood glucose, HOMA, systolic and diastolic blood pressure, serum insulin levels, triglyceride and HDL. Waist circumference and BMI-Z score were decisive for some tissue Doppler parameters.*

Conclusion: *Left ventricular diastolic functions are impaired in obese children compared to that of their peers. Although there were correlation between diastolic dysfunction parameters and risk factors, obesity itself is related with reduction of left ventricular diastolic functions.*

Key Words: *Child, pulsed Doppler echocardiography, left ventricle, obesity.*

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ÖZET

Amaç: *Bu çalışmada obez ve normal kilolu çocuklarda iki boyutlu, M-Mod, geleneksel ve doku Doppler ekokardiyografiyle sol ventrikül diyastolik fonksiyon parametrelerini ölçmeyi ve bu parametreler üzerine antropometrik ve biyokimyasal faktörlerin etkilerini değerlendirmeyi amaçladık.*

Hastalar ve Yöntem: *Bu olgu-kontrollü kesitsel çalışmaya, 8-15 yaş arası 60 obez ve 60 normal kilolu çocuk dahil edildi. Çocukların antropometrik ve biyokimyasal değerleriyle sol ventrikül ekokardiyografik parametreleri ölçüldü ve aralarındaki ilişki araştırıldı.*

Bulgular: *Obez grupta bel çevresi ve beden kitle indeksi (BKİ-Z) skoru, sistolik ve diyastolik kan basıncı, trigliserid, açlık kan şekeri, insülin ve homeostatik modeli değerlendirmesi (HOMD) indeksi anlamlı olarak yüksekken yüksek yoğunluklu lipoprotein kolesterol (YYL-K) konsantrasyonu anlamlı derecede düşük bulundu. Mitral annulus septal E' ve E'/A', mitral annulus lateral E' ve E'/A', anteriyor E' ve E'/A', inferiyor E' ve E'/A' değerleri anlamlı derecede düşük bulundu, mitral E'/septal E' ve mitral E/lateral E değerleri anlamlı olarak daha yüksekti. Çoğu doku Doppler parametreleri ile bel çevresi, BKİ-Z skoru, açlık kan şekeri, HOMD, serum insülin düzeyi sistolik ve diyastolik kan basıncı, trigliserid ve YYL-K arasında korelasyon vardı. Bel çevresi ve BKİ-Z skoru bazı doku Doppler parametreleri için belirleyiciydi.*

Sonuç: *Obez çocuklarda akranlarına göre sol ventrikül diyastolik fonksiyonları bozulmuştur. Risk faktörleriyle diyastolik fonksiyon parametreleri arasında korelasyon olsa da, obezitenin kendisi sol ventrikül diyastolik fonksiyonlarında azalmayla ilişkilidir.*

Anahtar Kelimeler: *Çocuk, atımlı Doppler ekokardiyografi, sol ventrikül, obezite.*

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INTRODUCTION

Obesity, epidemic, a significant public health problem, is one of the complex clinical syndromes affecting both children and adults over the world(1). Eleven percent of children in the US are obese. Childhood obesity is associated with hypertension, dyslipidemia and abnormal glucose metabolism(2,3). The prevalence of metabolic syndrome is higher in obese than in normal-weight children(4). In children, the numbers of cardiovascular risk factors are increase in parallel with increasing body mass index (BMI)(5).

Obesity has been shown to be an important risk factor for heart failure in adults(6). Subclinical diastolic dysfunction is reported to be correlated with BMI in isolated adult obesity(7). Left ventricular diastolic dysfunction (LVDD) is a predictor of future development of heart failure(8). In addition to risk of early atherosclerosis, childhood obesity is leading to cardiac structural and functional changes. As a result of changes in the heart associated with obesity in childhood, cardiac function may be impaired, and the risk of heart failure may increase in early adulthood(9). Tissue Doppler imaging is a suitable method for the detection of subclinical LVDD(10).

Various publications showed that LVDD related to childhood obesity by conventional and tissue Doppler echocardiography. These publications found a relationship between LVDD, BMI, waist circumference, insulin, blood pressure and diastolic function(11-14).

In the present study, we aimed to asses two dimensional, M-Mode, conventional and tissue Doppler echocardiographic parameters of left ventricle and to evaluate the effects of anthropometric and biochemical factors on these parameters in obese children.

PATIENTS and METHODS

Study Design

The study included children aged between 8 and 15 years who presented to the pediatric outpatient clinic at our institution without concomitant diseases. Informed consent was obtained from the children's parents. Children with congenital cardiac disease, hypertension, any systemic disease, thyroidal disorders, kidney or renal diseases, other endocrine disease such as diabetes, Cushing's disease, hypoparathyroidism or acromegaly, the children with macrosomic or low birth weight, rheumatic heart disease and arrhythmia on electrocardiogram (ECG) were excluded. This case-control study consisted of 60 obese children with a mean age of 11.5 ± 2.1 years, 34 (56.7%) girls and 26 (43.3%) boys; and 60 non-obese children with a mean age of 11.3 ± 2.2 years, 35 (58.3%) girls and 25 (41.7%) boys. After weighed and their heights were measured, BMI-Z score were calculated. Childhood obesity was defined as a BMI equal to or greater than the 95th percentile for children of the same age and gender (Z score ≥ 1.645) (15). The study groups were matched for age and gender. The protocol of the study was approved by the Institutional Ethics Committee.

Echocardiography

While the subjects were in the left lateral decubitus position, two-dimensional, pulsed-wave Doppler transmitral recordings and tissue Doppler imaging (TDI) recordings of the mitral annulus diastolic velocities were performed with conventional views (parasternal long and short axes, apical 4-chamber) by a cardiologist with a 3.5-MHz sector transducer (Esaote MyLab 50, Genoa, Italy) and with simultaneously ECG recordings according to the recommendations of the American Society of Echocardiography (ASE) proposals[16]. Ejection fraction and left ventricle mass index (LVMI) were determined as described previously[17,18]. We performed pulsed-wave Doppler to measure mitral inflow velocity in apical 4-chamber view during diastole. Peak early (E) and late (A) mitral inflow velocity, E/A ratio and deceleration time (DT) of E velocity were obtained, and left ventricular ejection time (LVET), left ventricular isovolumetric contraction time (IVCT) and left ventricular isovolumetric relaxation time (IVRT) were measured as described previously[19]. For tissue Doppler measurements, velocities were recorded from the two- and four-chamber views after a 3-5 mm pulsed wave Doppler volume was placed. Early (E') and late (A') diastolic velocities, peak systolic velocity (S') were obtained subsequently. All of these measurements were performed on the anterior, inferior, septal and lateral mitral annulus in accordance with the recommendations of the ASE[19].

Diastolic function parameters of 20 children (12 obese, 8 normal) were re-examined after 10 days to determine the coefficients of intraobserver variation between visits. The intraobserver variability was 2.9% for mitral E, 3.0% for mitral E/A, 3.2% for septal E', 3.1% for septal E'/A', 3.4% for lateral E', 3.4% for lateral E'/A', 2.8% for anterior E', 3.0% for anterior E'/A', 2.9% for inferior E', 2.7% for inferior E'/A', 2.9% for mitral E/septal E' and 3.2% for mitral E/lateral E' respectively.

Statistical Analysis

Data were analyzed using Predictive Analysis Software (PASW) Statistics 18 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as mean ± standard deviation or median (min-max). Normally distributed variables were compared by using independent sample t-tests, and non-normally distributed variables were compared using Mann-Whitney U tests. A p value < 0.05 was considered statistically significant. Correlations between tissue Doppler parameters and anthropometric, biochemical findings were calculated by using Spearman's rank correlation. The variables detected as a significant difference between obese and non-obese group were entered stepwise multiple linear regression analysis.

RESULTS

Anthropometric and Biochemical Characteristics

The study group, obese group, consisted of 60 children with a mean BMI-Z score of 2.1 (1.74-2.74), 34 (56.7%) girls and 26 (43.3%) boys, mean age 11.5 ± 2.1 years and mean obesity duration of 8.75 ± 1.8 years; the control group, non-obese group, consisted of 60 children with a mean BMI-Z score of 0.5 (0.4-0.7), 35 (58.3%) girls and 25 (41.7%) boys, mean age 11.3 ± 2.2 years (Table 1). Waist circumference, BMI-Z score, BMI and systolic and diastolic blood pressures, fasting blood glucose, insulin concentrations and HOMA index, and triglyceride were significantly higher in the obese than in the non-obese group (all $p< 0.001$). HDL-C concentration was significantly lower ($p= 0.003$) in the obese than in the non-obese group, and total cholesterol and low density lipoprotein cholesterol (LDL-C) concentrations were similar in the two groups (all $p> 0.05$).

Left Ventricular M-Mode and Conventional Doppler Flow Parameters

Left ventricular systolic and diastolic diameter, interventricular septum and posterior wall thicknesses, LVMI, left atrial and aortic root diameters were significantly higher (all $p< 0.001$), and mitral peak E and E/A ratio (all $p< 0.05$) were significantly lower in the obese than in the non-obese group. Ejection fraction and other conventional diastolic parameters were similar in the two groups (all $p> 0.05$, Table 2).

Left Ventricle Tissue Doppler Parameters

Compared to controls, septal E', septal E'/A', lateral E', lateral E'/A', anterior E', anterior E'/A', inferior E'and inferior E'/A' were all significantly lower (all $p= 0.001$, Table 3) and mitral E/ septal E' and mitral E/ lateral E' values were significantly higher in the obese group (both $p< 0.001$, Table 3).

Association Between Diastolic Function Parameters and Anthropometric and Biochemical Variables

Septal E' and septal E'/A'were found to be negatively correlated with waist circumference (r: -0.719; $p< 0.001$, r: -0.582; $p< 0.001$), BMI-Z score (r: -0.356; $p= 0.005$, r: -0.359; $p= 0.005$), fasting glucose (r: -0.320; $p= 0.013$, r: -0379; $p= 0.003$), insulin levels (r: -0.671; $p< 0.001$, r: -0583; $p< 0.001$), HOMA (r: -0.644; $p\leq 0.001$, r: -0.568; $p< 0.001$), triglyceride (r: -0.615; $p< 0.001$, r: -0.511; $p< 0.001$), but positively with HDL-C (r: 0.617; $p< 0.001$, r: 0.517; $p< 0.001$), (Table 4,5).

Lateral E' was inversely correlated with waist circumference, BMI-Z score, insulin, HOMA, triglyceride and pos-

Table 1. Anthropometric and biochemical characteristics of obese and non-obese children

Variable	Obese group (n= 60)	Non-obese group (n= 60)	p*,**
Age (years)	11.5 ± 2.1	11.3 ± 2.2	0.756
Gender, male	26 (43.3)	25 (41.7)	0.845
Weight (kg)	65.5 (41-95)	41 (22-54)	< 0.001
BMI (kg/m^2)*	33.3 (30-38.5)	23 (15-24.9)	< 0.001
BMI-Z score*	2.1 (1.74-2.74)	0.5 (0.4-0.7)	< 0.001
Waist circumference (cm)*	86 (72-101)	64 (51-87)	< 0.001
Obesity duration (years)	8.75 (5-13.75)	-	-
Systolic BP (mmHg)*	120 (92-150)	110 (90-120)	< 0.001
Diastolic BP (mmHg)*	82 (62-91)	70 (50-84)	< 0.001
Glucose (mg/dL)*	95 (75-107)	80 (65-105)	< 0.001
HOMA index*	3.2 (0.3-8.3)	0.7 (0-4.7)	< 0.001
Insulin (mIU/L)*	13.9 (1.9-42)	3.4 (1.9-21.7)	< 0.001
Total cholesterol (mg/dL)	160 (121-256)	158 (110-242)	0.329
Triglyceride (mg/dL)	93 (69-302)	70 (50-244)	0.001
LDL-cholesterol (mg/dL)	102 (34-302)	100 (32-344)	0.461
HDL-cholesterol (mg/dL)*	42 (26-84)	47 (29-75)	0.003

* Variables were entered in stepwise multiple linear regression. Data are presented as mean ± standard deviation, median (minimum-maximum) or n (%).
** By independent sample t-test or Mann-Whitney U-test, as appropriate.
BMI: Body mass index, BP: Blood pressure, HDL: High-density lipoprotein, HOMA (Homeostatic model assessment) index = (fasting glucose x fasting insulin concentration x0.0555)/22.5, IU, International unit, LDL: Low-density lipoprotein.

Table 2. Left ventricular M-mode and conventional Doppler flow parameters in obese and non-obese children

Variable	Obese group (n= 60)	Non-obese group (n= 60)	p*
LVDD (mm)	43 (32-47)	36 (26-42)	< 0.001
LVSD (mm)	26 (20-29)	22 (17-27)	< 0.001
IVS (mm)	9 (6-10)	8 (6 - 10)	< 0.001
PWT (mm)	9 (6-10)	8 (6-10)	< 0.001
LVMI (g/m^2)	62.3 (46.3-97.9)	46 (22.6-70.6)	< 0.001
EF (%)	66 (60-75)	68 (60-74)	0.149
LAD (mm)	28 (21-33)	24 (18-34)	< 0.001
AO (mm)	29 (20-32)	23 (18-29)	< 0.001
Mitral E (cm/s)	96.5 ± 12.5	104.8 ± 14.9	0.001
Mitral A (cm/s)	64 (40-99)	65 (33-98)	0.354
E/A ratio	1.49 (0.7-2.8)	1.56 (1.1-2.6)	0.043
DT (ms)	148.7 ± 25.9	145.5 ± 23.9	0.48
IVRT (ms)	76 (38-102)	70 (57-102)	0.264
IVCT (ms)	38 (32-74)	38 (32-51)	0.051
ET (ms)	268 (197-318)	268 (216-331)	0.752

* by independent sample t-test or Mann-Whitney U-test, as appropriate.
Data are presented as mean ± standard deviation or median (minimum-maximum). AO: Aortic root diameter, DT: Deceleration time, EF: Ejection fraction, ET: Ejection time, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, IVS: Interventricular septum, LAD: Left atrial diameter, LVDD: Left ventricular diastolic diameter, LVMI: Left ventricle mass index, LVSD: Left ventricular systolic diameter, PWT: Posterior wall thickness.

Table 3. Left ventricle tissue Doppler parameters of obese and non-obese children

Variable	Obese group (n= 60)	Non-obese group (n= 60)	p*
Septal E' (cm/s)	9 (8-17)	13 (10-18)	< 0.001
Septal A' (cm/s)	8.7 (8-15)	8.5 (8-15)	0.207
Septal S' (cm/s)	9 (7-18)	9.05 (8-18)	0.231
Septal E'/A'	1.02 (0.53-2)	1.4 (1-2.2)	0.001
Lateral E' (cm/s)	8.8 (7-14)	15 (8-20)	< 0.001
Lateral A' (cm/s)	9 (8-16)	9.05 (8-17)	0.358
Lateral S' (cm/s)	11.5 (8-19)	11.8 (7.9-18.5)	0.564
Lateral E'/A'	1.0 (0.54-1.75)	1.4 (1-2.35)	0.001
Anterior E' (cm/s)	9 (7-16)	15 (9-20)	< 0.001
Anterior A' (cm/s)	11 (8-15)	11.2 (8-18)	0.745
Anterior S' (cm/s)	9.6 (8-18)	9.7 (8.2-14.3)	0.604
Anterior E'/A'	0.93 (0.5-2.0)	1.35 (1.04-2.4)	0.001
Inferior E' (cm/s)	9.2 (7-16)	15.6 (8.6-20)	< 0.001
Inferior A' (cm/s)	10.5 (7.5-15)	11.05 (8-18.7)	0.237
Inferior S' (cm/s)	12.4 (8.1-14.3)	12.6 (8-18.2)	0.813
Inferior E'/A'	1.0 (0.6-1.9)	1.4 (1-2.3)	0.001
Mitral E/Septal E'	10 ± 2.1	7.96 ± 1.78	0.001
Mitral E/Lateral E'	9.4 (4.7-12.9)	7.05 (3.74-14.6)	0.001

* by independent sample t-test or Mann-Whitney U-test, as appropriate.
Data are presented as mean ± standard deviation or median (minimum-maximum).

Table 4. Spearman rank correlation analysis of tissue Doppler E' parameters with anthropometric and biochemical variables

	Septal E'		Lateral E'		Anterior E'		Inferior E'	
Variable	r	p	r	p	r	p	r	p
Age	-0.232	0.074	-0.193	0.140	-0.135	0.303	-0.102	0.439
Obesity duration	-0.034	0.795	-0.143	0.274	-0.016	0.901	-0.076	0.565
Waist circumference	-0.719	< 0.001	-0.579	< 0.001	-0.398	0.002	-0.279	0.031
BMI-Z score	-0.356	0.005	-0.341	0.008	-0.408	0.001	-0.212	0.104
Glucose	-0.320	0.013	-0.242	0.063	-0.194	0.138	-0.106	0.422
Insulin	-0.719	< 0.001	-0.581	< 0.001	-0.405	0.001	-0.285	0.027
HOMA index	-0.644	< 0.001	-0.516	< 0.001	-0.367	0.004	-0.266	0.040
Systolic BP	-0.062	0.637	-0.205	0.117	-0.285	0.027	-0.363	0.004
Diastolic BP	-0.099	0.450	-0.194	0.138	-0.078	0.568	-0166	0.205
Triglyceride	-0.615	< 0.001	-0.475	< 0.001	-0.317	0.014	-0.195	0.135
HDL	0.617	< 0.001	0.479	< 0.001	0.327	0.011	0.209	0.109

BMI: Body mass index, BP: Blood pressure, HDL: High-density lipoprotein, HOMA: Homeostatic model assessment.

itively with HDL (r: -0.579; p< 0.001, r: -0.341; p= 0.008, r: -0.541; p< 0.001, r: -0.516; p< 0.001, r: -0.475; p< 0.001, r: 0.479; p< 0.001, respectively, Table 4). Lateral E'/A' was negatively correlated with waist circumference, insulin, HOMA, and positively with HDL-C (r: -0430; p= 0.001, r: -0.444; p< 0.001, r: -0.433; p= 0.001, r: 0.276; p= 0.033; respectively, Table 5).

Anterior E' was negatively correlated with waist circumference, BMI-Z score, insulin levels, HOMA, systolic blood pressure, triglyceride and positively with HDL-C (r: -0.398; p= 0.002, r: -0.408; p= 0.001, r: -0.405; p= 0.001, r: -0.367; p= 0.004, r: -0.285; p= 0.027, r: -0.317; p= 0.014, r: 0.327; p= 0.011; respectively, Table 4), in addition anterior E'/A' were negatively correlated with waist circumference, BMI-Z score, and insulin levels (r: -0.258; p= 0.046, r: -0.322; p= 0.012, r: -0.266; p= 0.040, respectively, Table 5).

Inferior E' was negatively correlated with waist circumference, insulin levels, HOMA and systolic blood pressure (r: -0.279; p= 0.031, r: -0.285; p= 0.027, r: -0.266; p= 0.040, r: -0.363; p= 0.004, respectively, Table 4) and inferior E'/A' was negatively correlated with systolic and diastolic blood pressures (-0.299; p= 0.020, r: -0.394; p= 0.002 respectively, Table 5).

Mitral E/septal E' was positively correlated with waist circumference (Figure 1), BMI-Z score, fasting glucose, insulin levels, HOMA and triglyceride, and negatively with HDL-C (r: 0.674; p< 0.001, r: 0.421; p= 0.001, r: 0.383; p= 0.003, r: 0.574; p< 0.001, r: 0.561; p< 0.001, r: 0.332; p= 0.010, r: -0.354; p= 0.006, respectively, Table 6 and Figure 2).

There was a positive correlation between mitral E/lateral E' and BMI-Z score, (r: 0.537; p< 0.001, Table 6).

Age and obesity duration did not correlate with TDI parameters in obese group (all p values > 0.05; Tables 4-6).

According to multivariate linear regression analysis, waist circumference was associated with septal E' (β ± SE: -0.197 ± 0.043), septal E'/A' (β ± SE: -0.024 ± 0.006), lateral E' (β ± SE: -0.178 ± 0.043), lateral E'/A' (β ± SE: -0.016 ± 0.006) and mitral E/ septal E' (β ± SE: -0.173 ± 0.033), respectively (all p< 0.001, Table 7). BMI-Z score was related to anterior E' (β ± SE: -2.432 ± 1.143, p= 0.039) and mitral E/lateral E' (β ± SE: 4.880 ± 1.060, p< 0.001) (Table 7).

DISCUSSION

Obesity is often associated with cardiac changes such as increased left ventricular (LV) mass, LV hypertrophy, LV dilatation, left atrial dilation and LV diastolic, and systolic dysfunction[20]. We compared two dimensional, M-mode, conventional pulsed Doppler and tissue Doppler echocardiographic parameters as well as conventional anthropometric parameters in groups of obese and non-obese children. We found that BMI, BMI-Z score, waist circumference, systolic and diastolic blood pressures were significantly higher in the obese group than in the non-obese group. In addition, glucose, HOMA index, insulin and triglyceride serum levels were significantly higher and HDL-cholesterol concentrations were significantly lower in the obese group.

Studies showed that obese children had higher absolute chamber dimensions, volumes, wall thickness, and left ventricular mass than their age and gender-matched normal controls[12,21,22]. Similarly, we found that left ventricular wall dimensions, interventricular septum, posterior wall, LVMI, left atrial and aortic diameters were higher in the obese than in the non-obese group.

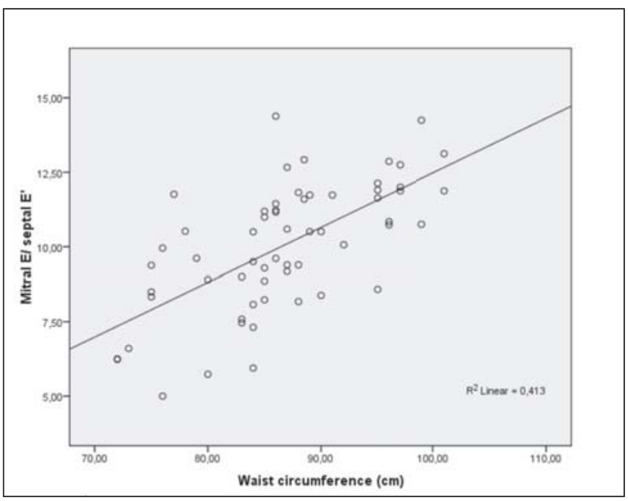

Figure 1. Correlation graphic between the ratio of mitral E to septal E' and waist circumference.

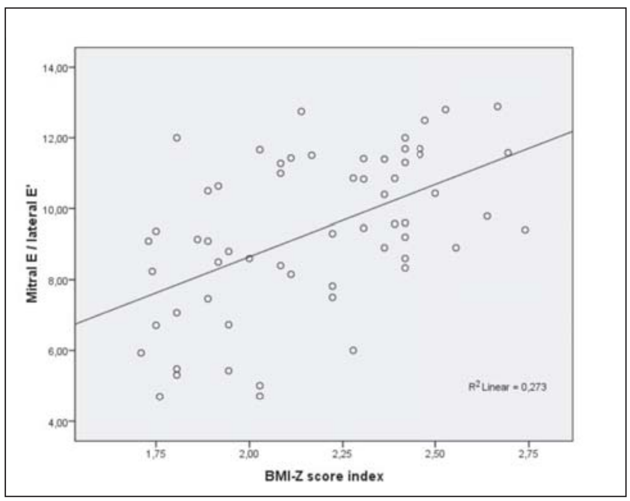

Figure 2. Correlation between the ratio of mitral E to lateral E' and BMI-Z score index.

Table 5. Spearman rank correlation analysis of tissue Doppler E'/A' parameters with anthropometric and biochemical variables

	Septal E'/A'		Lateral E'/A'		Anterior E'/A'		Inferior E'/A'	
Variable	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**
Age	-0.198	0.129	-0.227	0.081	-0.131	0.320	-0.231	0.076
Obesity duration	-0.023	0.859	-0.155	0.237	-0.085	0.520	-0.229	0.078
Waist circumference	-0.582	< 0.001	-0430	0.001	-0.258	0.046	-0.212	0.104
BMI-Z score	-0.359	0.005	-0.217	0.096	-0.322	0.012	-0.159	0.226
Glucose	-0379	0.003	-0.199	0.28	-0.026	0.846	0.140	0.287
Insulin	-0583	< 0.001	-0.444	< 0.001	-0.266	0.040	-0.217	0.096
HOMA index	-0.568	< 0.001	-0.433	0.001	-0.196	0.134	-0.222	0.089
Systolic BP	-0.044	0.740	-0.130	0.323	-0.207	0.113	-0.299	0.020
Diastolic BP	-0.142	0.279	-0.119	0.165	-0.110	0.402	-0.394	0.002
Triglyceride	-0.511	< 0.001	-0.228	0.079	-0.175	0.181	-0.151	0.248
HDL	0.517	< 0.001	0.276	0.033	0.187	0.152	0.158	0.229

BMI: Body mass index, BP: Blood pressure, HDL: High-density lipoprotein, HOMA: Homeostatic model assessment.

Table 6. Spearman rank correlation analysis of mitral E/Septal E' and mitral E/Lateral E' with anthropometric and biochemical variables

	Mitral E/Septal E'		Mitral E/Lateral E'	
Variable	**r**	**p**	**r**	**p**
Age	0.120	0.360	0.194	0.137
Obesity duration	0.013	0.922	0.029	0.827
Waist circumference	0.674	< 0.001	0.234	0.072
BMI-Z score	0.421	0.001	0.537	< 0.001
Glucose	0.383	0.003	0.137	0.296
Insulin	0.574	< 0.001	0.238	0.067
HOMA index	0.561	< 0.001	0.237	0.068
Systolic BP	0.132	0.316	0.076	0.562
Diastolic BP	0.075	0.570	0.030	0.820
Triglyceride	0.332	0.010	0.211	0.105
HDL	-0.354	0.006	-0.213	0.102

BMI: Body mass index, BP: Blood pressure, HDL: High-density lipoprotein, HOMA: Homeostatic model assessment.

Our findings potentially suggest that both increased adipose tissue and elevated serum insulin levels are associated with the increased heart's workload, LV dimension and LVMI in obese children. Previous studies found that there were significant differences in conventional and tissue Doppler diastolic parameters between obese and non-obese groups[11-14]. The importance of insulin resistance in obesity is well recognized and insulin increase heart rate, blood pressure and the workload of the heart by activating the sympathetic nervous system as well as in increased LV size and mass as a result of increased intravascular volume, changed myocardial structures and functions[23-25]. Furthermore, myocardial structural changes have been associated with insulin resistance and volume excess that predispose to heart failure in obese subjects[24]. Insulin resistance and hyperinsulinemia also relate to glucose intolerance, an increase in plasma triglyceride and a decrease in HDL cholesterol concentrations, high blood pressure, hyperuricemia, and smaller denser LDL particles[26]. Some hormones and cytokines such as leptin, nonesterified free fatty acids, tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), C-reactive protein (CRP), are released from adipose tissue, change the sympathetic activity and insulin sensitivity[27]. In addition, myocardial energy metabolism shifts to the use of free fatty acids in obesity, and then oc-

Table 7. Stepwise multiple regression analysis for determinants of tissue Doppler parameters

Dependent variable	Independent variable	B ± SE	p
Septal E’	Waist circumference	-0.197 ± 0.043	< 0.001
Lateral E’	Waist circumference	-0.178 ± 0.043	< 0.001
Anterior E’	BMI-Z score	-2.432 ± 1.143	0.039
Septal E’/A’	Waist circumference	-0.024 ± 0.006	< 0.001
Lateral E’/A’	Waist circumference	-0.016 ± 0.006	< 0.001
Mitral E/septal E’	Waist circumference	0.173 ± 0.033	< 0.001
Mitral E/lateral E’	BMI-Z score	4.880 ± 1.060	< 0.001

cur cardiac lipotoxicity leading to programmed cell death. In addition, fatty infiltration can induce structural and functional changes in the heart as well as diastolic dysfunction occurs[28].

We observed deterioration in conventional and tissue Doppler parameters in the obese than in the non-obese group. Although waist circumference, BMI-Z score, fasting blood glucose, HOMA, systolic and diastolic blood pressure, serum insulin levels, triglyceride and HDL were found to be correlated with the number of tissue Doppler parameters in the study. In some previous studies, both BMI[11,12] and waist circumference were found to be independent predictors for various diastolic function parameters[13]. In our study, while waist circumference was the most important variable affecting septal E, lateral E’, septal E’/A’, lateral E’/A’ and mitral E/septal E’, BMI-Z score was seemed to be affect anterior E’and mitral E/lateral E’. These findings suggested that waist circumference and BMI-Z score in obesity were the most important determinants for the deterioration of diastolic function.

The main limitation of this study was its small sample size. If heart rate, sympathetic activity level, cytokine levels and adipose tissue derived hormones were measured and morbid obese children could be included as different group in the study, our results would have been validated.

CONCLUSION

Left ventricular diastolic functions are impaired in obese children compared to that of their peers. Although there were correlation between diastolic dysfunction parameters and risk factors, waist circumference and BMI-Z score as markers of obesity were associated with changes in cardiac structures and diastolic functions in childhood. Consequently, obesity itself is related with reduction of left ventricular diastolic functions. Further observational prospective studies concerning adipose tissue related cytokines and hormones are needed to determine the effects of these changes in adulthood.

CONFLICT of INTEREST

None declared.

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