Effect of Obesity on Left Ventricular Longitudinal Myocardial Strain by Speckle Tracking Echocardiography in Children and Adolescents

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Background: Impaired subclinical ventricular function may contribute to the risk of cardiovascular disease in obesity.

Aims: The aim of this study was to determine the influence of obesity on left ventricular (LV) longitudinal myocardial function in normotensive obese children using two-dimensional (2D) speckle tracking echocardiography (STE).

Study Design: Case-control study.

Methods: Sixty normotensive obese children aged 10-16 years (mean age, 13.9±2.3 years) were compared with 50 normal-weight controls. Obese participants had a body mass index (BMI)≥95th percentile. Regional strain/strain rate (SR) values were compared with left ventricular (LV) parameters. The correlation was studied by linear regression analysis.

Results: Obese subjects exhibited a significantly higher LV end-diastolic diameter, left atrium/aortic diameter ratio, and LV mass/index when compared to controls (p<0.001). Left ventricular ejection fraction and regional systolic myocardial velocities were similar in the obese and control groups. By 2D STE, regional strain of both the septal wall (average strain: -16.0±3.9% vs -21.9±2.4%, p<0.001) and lateral wall (average strain: -15.6±2.3% vs -22.9±3.5%, p<0.001); regional SR of both the septal wall (average SRsys: -0.7±0.22 s⁻¹ vs -1.3±0.32 s⁻¹, p<0.001) and lateral wall (average SRsys: -0.67±0.19 s⁻¹ vs -1.33±0.31 s⁻¹, p<0.001); regional SRₑₐ of both the septal wall (average SRₑₐ: 1.8±0.83 vs. 2.2±0.91, p: 0.004) and lateral wall (average SRₑₐ: 1.4±0.43 vs. 2.4±1.21, p<0.001); and global strain (-14.6±7.34% vs -20.9±3.24%, p<0.001) were lower in the obese group compared with the controls. These strain imaging parameters appear to be related to the severity of obesity and can contribute to increased BMI. Left ventricular mass was found to be correlated with a decrease in global LV strain.

Conclusion: Our study showed that childhood obesity is associated with an alteration in the longitudinal LV function. Segmental analysis of the LV can provide subtle markers for the emergence of future obesity-related cardiac disease.

Keywords: Childhood obesity, left ventricular function, strain, two-dimensional speckle tracking echocardiography

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Childhood obesity is one of the most serious public health problems (1-3). Obesity and cardiac involvement has been reported frequently in the literature, but analysis of regional myocardial function in children by two-dimensional (2D) speckle tracking echocardiography (STE) is rarely documented (4-8).

Subclinical left ventricular dysfunction is an important finding in obese people and is an early sign of heart failure (2, 7). Moreover, it is also noted that developed subclinical cardiac effects in different studies reverse the process during weight loss (9-11, 12-13). In addition, 2D STE is a new and more sensitive echocardiographic modality, which allows the assess regional and myocardial function with strain and strain rate (SR) measurements (11, 13-15). These strain parameters are affected to a much lesser extent by cardiac rotation and passive cardiac motion (2, 11, 16). Previous studies have demonstrated decreased regional myocardial function related to body mass index (BMI) by strain imaging studies (7, 8, 11, 13, 17-20).

Apparent myocardial contractile dysfunction is rare, and also generally preserved reserve capacity with exercise in obese patients. Our reports have showed the effects of obesity on cardiac size, function, and subclinical myocardial damage in the pediatric age group. Study aims to evaluate, the effect on cardiac size, function, and subclinical myocardial damage obese patients. Our reports have showed the effects of obesity on cardiac size, function, and subclinical myocardial damage in the pediatric age group. Study aims to evaluate, the effect on cardiac size, function, and subclinical myocardial damage obese patients. Our reports have showed the effects of obesity on cardiac size, function, and subclinical myocardial damage in the pediatric age group. Study aims to evaluate, the effect on cardiac size, function, and subclinical myocardial damage obese patients. Our reports have showed the effects of obesity on cardiac size, function, and subclinical myocardial damage obese patients. Our reports have showed the effects of obesity on cardiac size, function, and subclinical myocardial damage obese patients. Our reports have showed the effects of obesity on cardiac size, function, and subclinical myocardial damage obese patients. Our reports have showed the effects of obesity on cardiac size, function, and subclinical myocardial damage obese patients. Our reports have showed the effects of obesity on cardiac size, function, and subclinical myocardial damage obese patients. Our reports have showed the effects of obesity on cardiac size, function, and subclinical myocardial damage obese patients. Our reports have showed the effects of obesity on cardiac size, function, and subclinical myocardial damage obese patients. Our reports have showed the effects of obesity on cardiac size, function, and subclinical myocardial damage obese patients.

MATERIALS AND METHODS

Study groups and patient population

This prospective and cross-sectional study in obese children was conducted in our hospital’s Department of Pediatric Cardiology during the period from June 2010 to November 2011. The study included 110 children aged 10-16 years, including 60 obese children and 50 healthy children as the control group.

Overall, we studied 110 subjects divided into two groups as: (i) obese children (Group 1: n=60; mean age, 13.9±2.3 years) and (ii) control subjects (normal weight), comparable for age and sex, recruited from the community without family history of hypertension or obesity (Group 2: n=50; mean age, 13.2±1.8 years).

Obesity in children was defined as a BMI greater than the 95th percentile for age and sex according to the reference values for the Turkish pediatric population (4). BMI of the patients was calculated using the equation: BMI = Body weight (kg)/Height (m)².

The research protocol was approved by the local ethical committee. All parents gave their written informed consent for participation in the study.

Exclusion criteria

This study excluded children with structural or functional cardiac abnormality, hypertension, the presence of sleep apnea, systemic diseases, history of medical treatment, or any secondary causes of obesity. Participants who refused echocardiography measurement, obese cases had poor image quality, and and blood sampling were also excluded.

Clinical assessment

Demographic details of age, gender, and blood pressure (BP) were derived standard measurements. Obese and healthy children exhibiting normal results were included in this study. The obese group underwent standard blood analyses (complete blood count, biochemistry, and thyroid function tests), BP measurement, chest X-ray, electrocardiography, and echocardiography. All measurements were performed by well-trained technicians. The anthropometric measurements were performed in the outpatient clinic. All of the measurements were repeated twice, and the average was used.

Arterial blood pressure (BP) was measured twice on the right arm after a 10-minute (min) rest in the supine position in a quiet room using a calibrated sphygmomanometer, and the measurements were averaged. The <90th percentile of Systolic and diastolic blood pressure values for each age and gender were compared with the Turkish pediatric population (21). Hypertensive patients were excluded by history and measurement of BP, and ambulatory blood pressure measurements (ABPM) were taken.

Ambulatory blood pressure measurements (ABPM) normative data by 24-hour (h) systolic and 24-h diastolic BP were included (<90th percentile for age and sex). A Rozinn Ambulatory Blood Pressure (ABP) Recorder, RZ250 monitor (Day & Night analysis, Glendale, New York, NY, USA) weighing 250 g (including batteries) was used for ABPM.

Determination of pubertal development was according to Marshall and Tanner and categorized into two groups (pre-pubertal: stage I, pubertal: stage ≥2) (22).

Biochemistry examination

All cases in the obese group underwent standard blood analyses including complete blood count, biochemistry, and thyroid function tests. In all of the obese children, insulin and glucose levels were measured (after an overnight fast >12h). Measurement of the concentration of glucose in the blood using the glucose-oxidase method by an autoanalyzer. Insulin levels were measured with an immunoradiometric assay.
HOMA-IR (homeostatic model assessment of insulin resistance) was calculated using the formula given below. HOMA-IR cut-off values for insulin resistance during childhood were calculated to be 2.5 (22).

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\text{HOMA-IR} = \frac{\text{fasting insulin (mIU/mL)} \times \text{fasting blood glucose}^*}{22.5}
\]

(*Blood glucose: mg/dL / 18 = mmol/L)

**Echocardiographic measurements**

Left ventricular functions were investigated in a silent setting in the pediatric cardiology outpatient clinic. All subjects were evaluated by the same observer in the left lateral position. After the subject had been resting for 10 min. Echocardiographic evaluation were made using General Electric Medical Systems Vivid 7 Dimension system and 4 MHz probes (GE Vingmed Ultrasound AS, Horten, Norway). All of the measurements were performed based on the American Echocardiography Society standards (23). Images are obtained relative to the axis of the parasternal long axis and apical four chamber (A4C) were used. Measurements were taken from the records stored in the digital media Standard Echocardiography:

Through standard echocardiography, we measured the left ventricular end-diastolic diameter (LVEDD) and the left atrium (LA) and aortic diameter at the parasternal long axis in the M-mode. The left ventricular mass (LVM, g) was calculated using the predefined Devereux and Reichek formula (24). LVM was divided by the body surface area to obtain the left ventricular mass index (LVMI, g/m²).

Measurement of left atrium (LA) and left ventricular (LV) volumes were computed from apical two chamber (A2C) views by Simpson’s method biplane method (25). LA and LV volume index was divided by the body surface area to obtain the LA and LV volume (mL/m²).

Velocity of tricuspid regurgitation (TR) flow was obtained, the maximal systolic pressure gradient between the right atrium and right ventricle V using the Bernoulli equation \(P=4V^2\). The systolic pulmonary artery pressure was calculated by adding the mean right atrium pressure (RAP) to this pressure (26).

**Analysis of regional and global myocardial deformation using 2D strain Speckle-Tracking Echocardiography (STE)**

Two-dimensional (2D) strain data were stored in digital format and analyzed offline with the workstation (Echopac, PC 2008, GE, Horten, Norway).

Quality ECG signal and the frame rate is between 40-100 frames/seconds (sn) were recorded in digital format using 2D harmonic image cineloop (A4C view). Effective evaluation of the echocardiographic measurements was used digital recordings (DVD-CD) to enable subsequent investigation.

The analyses were performed using a commercially available computer software program by Echopac software. Sampling volumes were placed using the 2D strain software under the mitral valves at lateral annulus and septum. The cardiac motion was determined from a user-defined tracing along the endocardial-myocardial border. After manual tracing of the endocardial border in the end-systolic frame of a 2D image and selecting the appropriate wall thickness, the software automatically (speckle tracking) determined six segments for longitudinal function: apical, mid and basal segments in the septum and LV lateral wall from apical views. Data were derived when the values for all six segments were considered acceptable by the software or when a value of any one segment with poor tracking (fewer than two segments) was rejected by the software but tracking of that segment was determined to be acceptable. Obtain the average value after repeated three measurements. Strain parameters of 2D STE-derived systolic and diastolic strain, SR, and the global strain was used in in the assessment of left ventricular function. By using the speckle tracking algorithm, we measured peak systolic (VELsys), early diastolic (VEL1) and late diastolic (VELA) myocardial velocities, longitudinal peak systolic strain (%), peak systolic SR (SRSys) (s⁻¹), peak early diastolic (SRE) and late diastolic (SRL) SR at the septal and lateral attachments of the mitral valve in patients with obesity.

**Statistical analysis**

The statistical evaluation was executed using the Statistical Package for the Social Sciences (SPSS) software version 12.5 (SPSS Inc.; Chicago, IL, USA). When presenting the results of such categorical data analysis, and percentages, and continuous data were expressed as means± standard deviation. The Kolmogorov-Smirnov test was applied to check the distribution of parameters.

The independent t test was used to compare continuous variables in the obese and control groups. As with correlation is used to analyze the relation between two groups. Pearson’s linear correlation coefficient analysis was used to assess the relationship between strain imaging-derived indexes of LV systolic-diastolic functions (global strain, strain, strain rate, etc.) and other parameters (LVM, BMI).

**RESULTS**

**Clinical and demographic characteristics**

The study sample included 60 obese subjects (Group 1) and 50 healthy subjects were used as controls (Group 2). Clinical and demographic characteristics of the two groups are described in Table 1. Groups were similar with respect to age, sex, pubertal stage, heart rate, and BP. As expected, weight,
BMI and body fat were elevated in obese subjects (p<0.001). The mean insulin value was 12.2±8.6 mIU/mL and HOMA-IR was 2.7±1.2 in the obese subgroups. Insulin resistance (HOMA-IR >2.5) was identified in 35 (55.3%) obese subjects. All patients were already in puberty (Tanner stage ≥2). Onset of the average age at obesity was 3.7±1.3 years (range, 2-8 years). No pulmonary hypertension was determined in any patient, as measured by CW Doppler echocardiography.

**Standard echocardiographic study**

Measurements comparing both groups are shown in Table 2. Global indices of systolic function (left ventricular ejection fraction (LVEF)) were not different between the two groups. As expected, all other M-mode measurements (LVEDD, LA/aortic diameter ratio), LVM, and LVMI were increased (p<0.001) in obese patients (Group 1) when compared with controls (Group 2). A significant positive correlation was detected between BMI, duration of obesity (r=0.527, p<0.001), and the LVM/LVMI (r=0.506, p<0.001).

**2D strain speckle tracking analysis**

Longitudinal analysis of the LV myocardium was calculated by STE in obese patients in the A4C view. All of the strain and SR tracings were acceptable for the analysis.

There were significant difference between in obese children and controls, with respect to 2D strain longitudinal myocardial deformation properties in the basal, mid and apical segments of the LV walls (p<0.001) (Tables 3, 4). Peak systolic strain and SR, global strain, and indices of systolic function were significantly reduced in all three segments in patients with obesity. The obese children had a significantly lower LV global strain (-14.6±7.34%) compared to the control subjects (-20.9±3.24, p<0.001). Our studies demonstrates a statistically significant difference in obese children; early and late diastolic SR and early/late SR ratio (SR E/A) values using strain imaging of diastolic function when comparing different segments of different LV walls (Tables 3, 4). Left ventricular ejection fraction (LVEF) and regional systolic myocardial velocities were similar between the obese and control groups.

However, by 2D STE, regional strain of both the septal wall (average strain: -16.0±3.9% vs -21.9±2.4%, p<0.001) and lateral wall (average strain: -15.6±2.3% vs -22.9±3.5%, p<0.001); regional SR of both the septal wall (average SRsys: -0.7±0.22 s¹ vs -1.3±0.32 s¹, p<0.001) and lateral wall (average SRsys: -0.67±0.19 s¹ vs -1.33±0.31 s¹, p<0.001); regional SR E/A of both the septal wall (average SR E/A: 1.8±0.83 vs. 2.2±0.91, p: 0.004) and lateral wall (average SR E/A: 1.4±0.43 vs. 2.4±1.21, p<0.001); and global strain (-14.6±7.34% vs -20.9±3.24%, p<0.001) had significantly lower in the obese group compared with the controls.
Relationship between obesity and the strain imaging parameters

Left ventricular longitudinal average peak systolic strain, SR were correlated significantly with LV mass and BMI. No correlation was found between duration of obesity and these strain parameters. The average longitudinal peak systolic strain (%) and SR correlated significantly with BMI ($r=0.698$, $p<0.001$) and between global strain and LVM ($r=0.363$, $p<0.01$). Moreover, average LV lateral wall $SR_{EA}$ ($r=-0.458$, $p<0.001$) and septum $SR_{EA}$ ($r=-0.219$, $p=0.022$) were negatively correlated with BMI.

DISCUSSION

Cardiovascular risk has been described not only in obese adults but also in obese children and adolescents (5-8, 27).
Recent studies indicate that this trend of subclinical depression in LV function among obese subjects is observed in the pediatric years (7, 13). Therefore, LV peak systolic longitudinal strain and SR values were significantly reduced in these patients combined strain imaging studies (2, 8, 11, 17, 18, 28). The effect of obesity on left ventricular myocardial function has shown an early finding during childhood (5, 7).

We analyzed the association between measures of obesity and LV subclinical dysfunction, measured by STE-derived parameters. The results obtained in our study: 1- Left ventricular longitudinal peak systolic strain and SR values was significantly lower in obese patients than in normal-weight controls; 2- These strain imaging parameters appear to be related to the severity of obesity and can contribute to increased BMI; 3- Early clinical stage longitudinal strain parameters (peak systolic strain and SR, global strain, diastolic SR) in obese patients may provide the opportunity to assess the regional myocardial function, and aid in monitoring the progression of the disease. Therefore, it is suggested that even young obese patients should be carefully cardiac monitoring in order to detect myocardial damage.

Impaired LV systolic and diastolic function is the first sign of obesity cardiomyopathy and is evident in obese children (12). In this study, the standard echocardiographic evaluation of obese patients (non-hypertensive children), had higher morphological and functional echocardiographic abnormalities, such as larger LA and LV diameters, increased LV end-diastolic volume/index, and LVM/LVMI, despite being in normal range (5, 10, 13, 28). LV dilatation and hypertrophy as a response to sustained, pressure overload and extended wall stress were decreased LV longitudinal function. Among obese children have increased left ventricular mass (5, 7). In fact, BMI was the main predictor of LVM, leading to the development of myocardial dysfunction.

Left ventricular hypertrophy secondary to increased mechanical stress can damage the subendocardial myocardial fibers, which is responsible for regional myocardial function (2, 24, 28). Therefore, increased afterload left ventricular end-systolic wall stress and tension are adversely affected. (28). Left ventricular mass was found to correlate with a decrease in global LV strain by STE, suggesting that the increased mass can lead to incipient ventricular systolic dysfunction in the early stages of obesity, even in the presence of a normal LVEF. Previous studies that systolic function in obese subjects have shown normal (13, 29). This may be attributed to the fact that these studies only used parameters to analyze LVEF which are relatively insensitive in detecting incipient preclinical changes in obese patients. In our study, obese patients with preserved LVEF and peak systolic myocardial velocities.

The STE-derived strain parameter is a relatively new parameter that is used to assess systolic and diastolic myocardial function (11, 13, 30). Obese subjects also had higher risk of a pseudonormalized diastolic pattern. The use of STE-derived parameters is less load-dependent than Doppler flow analysis (6). Up to this time, studies on 2D speckle tracking strain has a limited number of studies in obese children. It is clear that this method is useful in obesity (7, 13, 30). Previous studies of obesity LV function to show subclinical abnormalities was used color Doppler strain or 2D speckle tracking strain (7, 8, 11, 13, 18-20, 30). Barbosa et al. (7) reported 50 obese children without comorbidities in 2D speckle tracking analysis, a significant reduction in the longitudinal strain association with BMI. In the same study, they found that EF was not different between obese subjects and controls. Similar results has been reported in 21 obese children with lipid abnormalities by Koopman et al. (8). Our study demonstrated that by 2D STE, regional LV systolic and diastolic strain parameters of both the septal and lateral wall and global strain were lower in the obese group compared with the controls (Tables 3, 4). These strain imaging parameters appear to be related to the severity of obesity and can contribute to increased BMI. Furthermore, our results are similar to the previous study of results (6,7,30). Di Salvo et al. (11) Di Salvo et al reported that normotensive obese children have detected reduction in the LV longitudinal myocardial systolic function using color Doppler imaging.

Di Bello et al. (30) evaluate the regional myocardial function in obese adult patients (n=48; mean age, 32.8 years) and showed that systolic strain and SR values were lower in the obese group than the controls, both at the septum and lateral wall level. It was reported by Lorch et al. (2) that decreased diastolic dysfunction in obese children have recorded using the strain parameters (early diastolic SR and SR\textsubscript{E/A} ratios ) in the LV septal and lateral walls.

Our study showed that childhood obesity, in the absence of hypertension, is associated with an altered in the longitudinal LV function by STE. However, LV longitudinal strain parameters (peak systolic strain and SR, global strain, diastolic SR) using 2D STE were lower in the obese group compared with the controls. There strain parameters are showing LV systolic and diastolic dysfunction obese subjects in early preclinical stage. Furthermore, LV 2D strain parameters for the assessment of regional myocardial dysfunction obese children may be a new approach to non-invasive method.

There are several limitations in this study. As this is a small observational study has been studied in healthy obese children. We were not study about long-term changes in the myocardium. Usual limitations about strain, SR, and the angle dependence should be considered. Our study selected patients can be provided at a certain age range cooperation was held in obese children; therewith myocardial velocities associated relatively shows some changes. For patients to be included, measurements of strain had to be adequately visualized to al-
low for wall. Therefore, we assessed left ventricular longitudinal myocardial function in our study. However, the radial and circumferential strain, intima-media thickness (IMT), and endothelial function can provide additional information in obese children. These parameters would be added to useful data also to be obtained in obese patients.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Türkiye Yüksek İhtisas Training and Research Hospital.

**Informed Consent:** Written informed consent was obtained from the patients' parents who participated in this study.

**Peer-review:** Externally peer-reviewed.


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