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The relevance of left ventricular functions to clinical and metabolic characteristics of prepubertal children with obesity

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Abstract

Background: Paediatric obesity is a worldwide health burden, with growing evidence linking obesity to myocardial function impairments. The study aims to evaluate left ventricular functions among prepubertal obese children to obesity-related clinical and metabolic parameters. *Methods:* Between June 2019 and March 2020, 40 prepubertal children with obesity were recruited and compared to 40 healthy controls. Patients were assessed for body mass index z scores, waist circumference, body adiposity by bioimpedance analysis, and obesity-related laboratory tests, for example, serum chemerin. Left ventricular functions were assessed using variable echocardiographic modalities, such as M-mode, tissue Doppler, and two-dimensional speckle tracking. *Results:* Mean patients' age was 9.25 ± 1.05 years. Left ventricular mass index, E/E', and myocardial performance index were significantly increased in obese children than controls. Although M-mode-derived ejection fraction was comparable in both groups, two-dimensional speckle tracking-derived ejection fraction, global longitudinal strain, and global circumferential strain were significantly lower in cases than controls. Left ventricular mass index displayed a positive correlation with body mass index z score ($p = 0.003$), fat mass index ($p = 0.037$), and trunk fat mass ($p = 0.021$). Global longitudinal strain was negatively correlated with body mass index z score ($p = 0.015$) and fat mass index ($p = 0.016$). Serum chemerin was positively correlated with myocardial performance index ($p = 0.01$). *Conclusion:* Alterations of left ventricular myocardial functions in prepubertal obese children could be detected using different echocardiographic modalities. Chemerin, body mass index z score, fat mass index, and trunk fat mass were correlated with subclinical left ventricular myocardial dysfunction parameters before puberty. Our results reinforce early and strict management of childhood obesity upon detection of changes in anthropometric and body adiposity indices.

Paediatric obesity is one of the most deleterious global public health challenges of the 21st century.[1] Worldwide, over the past four decades, the number of children and adolescents with obesity has risen more than 10-fold.[2] Moreover, childhood obesity is considered the most prevalent early risk factor for developing chronic diseases, particularly type 2 diabetes, hypertension, and heart disease.[3] The clustering of cardiovascular risk factors in early childhood is concerning, given the high risk of continuing into adulthood.[4] Insulin resistance has been proposed as the critical element linking obesity and clustering of cardiovascular risk factors among youth with obesity.[5] Moreover, chemerin, an adipocytokine, has been shown to play a role in the pathogenesis of obesity-related cardiometabolic comorbidities.[6]

Childhood obesity was suggested as an aetiologic factor for subclinical myocardial dysfunction that represents a first step towards developing overt heart failure in adulthood. Thus, early delineation is warranted to ensure early proper management of obesity. The influence of obesity on the left ventricular functions was investigated in several studies using conventional parameters or tissue Doppler in the paediatric age group.[7–10] Another unique echocardiographic modality is two-dimensional speckle tracking echocardiography that allows for the assessment of subclinical cardiac dysfunction by tracking the speckles on the myocardium throughout the cardiac cycle. Reduction of myocardial functions using two-dimensional speckle tracking in obesity has been described in children and adolescents without other comorbidities in few studies.[11–13] Nevertheless, the relationship between cardiac alterations in children and the obesity-related physical and body composition parameters has not been sufficiently investigated, especially in prepubertal children. Although body mass index is the most frequently used adiposity measure in all ages, it does not provide sufficient information on body fat distribution and its relation to heart status. Therefore, the primary purpose of this study was to assess the subclinical alterations of left ventricular myocardial functions using different echocardiographic modalities in prepubertal children in relation to anthropometric measurements, body adiposity indicators, metabolic profile, and serum chemerin.

Materials and methods

The study was a prospective observational study that was conducted between June 2019 and March 2020. It included 40 prepubertal obese children with a mean age of 9.25 ± 1.05 years and 40 healthy controls. The Institutional Research Board of the Faculty of Medicine, Mansoura University, approved the study with informed written consent obtained from all patients ' parents.

Children with obesity were recruited during their routine visits at Pediatric Endocrinology Outpatients Clinic at Mansoura University Children's Hospital, Mansoura, Egypt. Normal weight-control children were recruited from a primary school in the same locality. According to the World Health Organization 2007 body mass index standard deviations criteria for age and gender in children 5–19 years, obesity was defined as body mass index z score exceeds +2 SD, while normal weight defined as body mass index z score between −2 SD and +1 SD.[14]

Exclusion criteria included the following: children who had syndromic or secondary obesity, those with congenital or acquired heart diseases such as cardiac valvular diseases or clinically evident cardiomyopathy, or arrhythmias. Patients suffering from significant chronic comorbidities or receiving medication known to affect the study variables were excluded as well. The average of two blood pressure measurements by the standard technique was calculated, and patients with blood pressure average ≥90th percentile, according to the guidelines of the American Academy of Pediatrics,[15] were excluded from the study.

Data regarding age, sex, and duration of obesity were collected from study patients and were subjected to thorough physical examination, including the following.

Anthropometric measurements

Anthropometric measurements were obtained using standardised techniques. Weight was measured to the nearest 0.1 kg. Height was measured to the nearest 0.5 cm using a wall-mounted stadiometer. Body mass index was calculated by dividing a child's weight in kilograms by the square of height in metres (kg/m^2). Height and body mass index standard deviation scores were calculated using reference data for Egyptian children and adolescents.[16] Waist circumference (cm) was measured using an inextensible measuring tape at a point midway between the costal margin and lateral iliac crest at the end of normal expiration.

Body adiposity parameters

Total body fat percentage, total fat mass (kg), legs fat mass (kg), and trunk-fat mass (kg) as a marker of central (abdominal) adiposity were measured by bioelectrical impedance technique using Tanita BC-418MA body composition analyser (Tanita Corp., Tokyo, Japan) according to the manufacturer's instructions. The fat mass index was calculated as fat mass (kg) divided by square height in metre (m^2).[17] The fat mass-related ratios were calculated to assess body fat distribution (central versus peripheral), including trunk/legs fat mass ratio and trunk/appendicular fat mass ratio, while appendicular fat mass reflects the sum of fat mass of the four limbs.

Biochemical evaluation

Lipid profile was evaluated, including total cholesterol, triglycerides, and high-density lipoprotein cholesterol. Homoeostasis model assessment of insulin resistance was calculated as fasting blood glucose (mg/dl) × fasting insulin (mIU/L)/405. Serum chemerin level (ng/mL) was measured using a human enzyme-linked immunosorbent assay (Sandwich technique).

Left ventricle functions assessment by different echocardiographic modalities

Conventional echocardiography

Transthoracic echocardiographic examinations were performed for all children using a standard Echocardiography machine, Philips Epiq C7 (Philips Medical Systems, Bothell, WA, United States of America 2014), equipped with an S5-1 MHz transducer. Images were taken from the apical four-chamber, three-chamber, two-chamber, and parasternal short-axis or long-axis views based on the American Society of Echocardiography recommendations.[18] The M-mode images of the left ventricle were obtained from two-dimensional images with parasternal long-axis views. Interventricular septal thickness, left ventricular posterior wall thickness, and internal left ventricular diameter in both systole and diastole were measured. In addition to left ventricular mass index estimation, left ventricular systolic functions were expressed as fractional shortening and ejection fraction as recommended by the American Society of Echocardiography.[19] A pulsed Doppler study for the mitral valve was performed, including peak velocities determination for early diastolic flow (E-wave) and late diastolic flow (A-wave) with calculation of E/A ratio.

Pulsed-wave tissue Doppler imaging

Early diastolic (E' wave), late diastolic (A' wave) velocities were measured at the lateral parts of the mitral annulus on the apical four-chamber views by pulsed-wave tissue Doppler imaging. Tissue Doppler imaging-derived myocardial performance index (Tei index) for the lateral edge of mitral annulus was calculated using the following formula IVCT'+IVRT'/ET', where isovolumic relaxation time (IVRT') was calculated as the time from the S' wave end to E' wave beginning while isovolumic contraction time (IVCT') from the A' wave end to S' wave beginning. ET' is the ejection time from the S' wave beginning to its end. E/E′ ratio was calculated as E-wave velocity by pulsed Doppler divided by E' velocity derived by tissue Doppler. The signal quality was enhanced by lowering the Nyquist limit to 10–20 cm/s and optimising the sweep speed to at least 100 mm/s.

Two-dimensional speckle tracking

Echocardiographic views were recorded and then analysed using Automated Cardiac Motion Quantification software on QLAB version 10.4. The software tracked the speckle patterns semi-automatically for left ventricular global circumferential strain and global longitudinal strain assessments were performed as described in the literature.[20] For assessing global circumferential strain, three left ventricular short-axis planes were used at the basal, middle, and apical levels. The region of interest generation process was automatically performed as the software place a circle on the image area, which could be manually adjusted to the desired parts. For assessing global longitudinal strain, three left ventricular apical views (apical four-chamber, two-chamber, and long-axis views) were acquired, and strain of the selected tissue can be evaluated by identifying three points: one point on each side of the mitral

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Table 1. Demographic, anthropometric, body adiposity, and biochemical characteristics of the study groups

	Cases group (n = 40)*	Control group (n = 40)*	p-value**
Age (years)	9.25 ± 1.05	9.07 ± 2.39	0.659
Gender			
Male	18 (45%)	24 (60%)	0.469
Female	22 (55%)	16 (40%)	
Height Z score	1.71 (−0.64 to −2.52)	0.02 (−1.2 to −1.94)	**0.006**
BMI (kg/m^2)	29.92 ± 4.14	16.41 ± 2.26	**<0.0001**
BMI Z score	3.72 (2.25–6.03)	−0.27 (−1.03 to −0.87)	**<0.0001**
WC (cm)	94.1 ± 12.26	66.65 ± 8.98	**<0.0001**
Waist-to-height ratio	0.65 (0.62–0.68)	0.51 (0.43–0.53)	**<0.0001**
%BF	38.65 (26.7–47.3)	16.6 (8.2–24.7)	**<0.0001**
Total FM (kg)	24.45 (10.0–47.0)	6.7 (3.5–25.0)	**<0.0001**
FMI (kg/m^2)	12.18 (10.25–14.4)	2.77 (2.14–4.22)	**<0.0001**
Trunk-FM (kg)	10.3 (4.6–16.4)	2.15 (0.30–13.9)	**<0.0001**
Trunk/legs FM ratio	1.77 (1.54–2.06)	0.96 (0.72–1.2)	**<0.0001**
Trunk/appendicular FM ratio	1.36 (1.2–1.58)	0.76 (0.54–0.9)	**<0.0001**
Total cholesterol (mg/dl)	165.30 ± 30.68	106.5 ± 9.02	**<0.0001**
Triglycerides (mg/dl)	121.95 ± 28.25	81.83 ± 8.48	**<0.0001**
HDL-C (mg/dl)	44.70 ± 11.37	54.12 ± 13.26	**0.001**
FBG (mg/dl)	88.85 ± 9.35	86.5 ± 5.11	0.167
Fasting insulin (μU/ml)	18.84 (11.54–35.0)	5.21 (2.9–9.1)	**<0.0001**
HOMA-IR	4.8 (3.1–9.3)	0.68 (0.4–1.9)	**<0.0001**
Chemerin (ng/ml)	168.5 (90–830)	80.65 (20–195)	**<0.0001**

BMI = body mass index; FBG = fasting plasma glucose; FM = fat mass; FMI = fat mass index; HOMA-IR = homoeostasis model assessment of insulin resistance; HDL-C = high-density lipoprotein cholesterol; WC = waist circumference. Significant values are in bold.
*Data are presented as mean ± SD or median, IQR (inter-quartile range), or number (%).
**Statistically significant difference if ($p < 0.05$).

annulus and one point at the apex. Then, the software automatically tracked the speckle pattern, which could be manually adjusted whenever needed. The software automatically generates the left ventricular strain profiles with global and segmental strains demonstrated automatically in Bull's eye model. Two-dimensional speckle tracking-derived end-diastolic volume, end-systolic volume, and ejection fraction were automatically calculated upon obtaining the global longitudinal strain by the software.

Reproducibility

Inter-observer and intra-observer variability were evaluated in a randomly selected sample of 10 patients by offline assessment of global longitudinal strain and global circumferential strain by two-dimensional speckle tracking, using the QLAB version 10.4 software. Inter- and intra-observer reproducibility was quantified using the intraclass correlation coefficient.

Statistical analysis

All the statistical analyses were carried out using SPSS software (version 25, IBM Corp., Armonk, NY, United States of America). The numeric variables are presented as mean± SD or median (inter-quartile range), while categorical variables are expressed as frequencies and percentages. Comparisons between groups were performed using independent samples Student's t-test for parametric normally distributed data, Mann Whitney test for non-normally distributed variables, and Chi-square for gender variable. Spearman correlation was used for linear correlation analysis. Multivariate linear regression analysis was performed for each echocardiographic parameter as the dependent variable with adiposity, anthropometric, and biochemical parameters as independent variables. A p-value <0.05 was considered statistically significant.

Results

Two groups were included in the study obesity group (n = 40) and the control group (n = 40). The mean duration of obesity was 3.5 ± 0.76 years. Demographic, clinical, and biochemical characteristics of the study groups are presented in Table 1. The two groups had no statistically significant differences in age, gender, and blood pressure. However, height z score, body mass index, body mass index z score, waist circumference, and waist-to-height ratio were significantly higher in the obesity group than the control group.

Additionally, children with obesity showed significantly higher total body fat percentage, total fat mass, fat mass index, trunk fat mass, trunk/legs fat mass ratio, and trunk/appendicular fat mass ratio than healthy children. Regarding the biochemical parameters, total cholesterol, triglycerides, fasting insulin, homoeostasis model assessment of insulin resistance, and chemerin values were

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Table 2. Left ventricular functions measured using different echocardiographic modalities in obesity and control groups

Echocardiographic modality	Variable	Obesity group (n = 40)*	Control group n = 40*	p-value**
M-mode	FS (%)	39.09 ± 7.87	41.96 ± 4.29	0.160
	EF (%)	62.32 ± 9.41	66.14 ± 4.88	0.113
	IVSD	0.92 ± 0.18	0.69 ± 0.07	**0.028**
	IVSD-Z score	2.38 (1.45–3.17)	0.76 (0.255–1.17)	**0.005**
	LVDD (cm)	4.13 ± 0.54	3.30 ± 0.43	**0.037**
	LVDD-Z score	1.06 (0.7–2)	−1.09(-1.77 to −0.51)	**0.006**
	LVDS(cm)	2.7 ± 0.39	2.3 ± 0.28	0.090
	LVDS-Z score	0.4(0.2–1.59)	−1.01 (−1.8 to 0.4)	0.064
	LVPWD(cm)	0.83 ± 0.18	0.58 ± 0.16	**0.035**
	LVPWD-Z score	0.62 (0.28-1.05)	−0.9(−1.2 to 0.57)	0.09
	LVMI (gm/m2)	71.59 ± 12.7	55.54 ± 9	<**0.0001**
TDI	lateral E' (cm/s)	13.63 ± 1.72	18.16 ± 3.79	<**0.0001**
	lateral A' (cm/s)	6.99 ± 1.69	8.04 ± 2.36	0.112
	Lateral E/E'	7.31 ± 0.95	5.0 ± 0.94	<**0.0001**
	lateral E'/A'	2.3 ± 0.43	2.07 ± 0.13	0.042
	Lateral MPI (Tie index)	0.48 ± 0.07	0.41.08	**0.007**
2D-STE	ESV (ml)	34.52 ± 4.69	33.17 ± 2.57	0.290
	EDV (ml)	77.68 ± 16.89	63.35 ± 4.17	**0.001**
	2D-STE derived EF(%)	59.02 ± 2.35	62.06 ± 2.92	**0.001**
	GLS (%)	−17.52 ± 1.93	−19.89 ± 1.08	<**0.0001**
	GCS (%)	−17.47 ± 1.91	−24.5 ± 2.89	<**0.0001**

2D-STE = 2D-speckle tracking echocardiography; EF = ejection fraction; EDV = end-diastolic volume; ESV = end-systolic volume; FS = fractional shortening; GCS = global circumferential systolic strain; GLS = global longitudinal systolic strain; LV = left ventricle; LVDD = left ventricular internal diameter in diastole; LVDS = left ventricular internal diameter in systole; LVMI = left ventricular mass index; LVPWD = left ventricular posterior wall diameter; MPI = myocardial performance index (Tie index); TDI = Tissue Doppler imaging. Significant values are in bold.
*All parameters described as mean ±SD or median (interquartile range).
**Statistically significant if (p < 0.05).

significantly higher. In contrast, high-density lipoprotein cholesterol value was significantly lower in the obesity group than in the control group, and fasting blood glucose levels were comparable between the study groups.

Table 2 illustrates the results of the echocardiographic assessment of left ventricular functions between the study groups using different modalities. Using M-mode, it is notable that there was a significantly higher left ventricular mass index in the children with obesity than in the healthy children (71.59 ± 12.7 gm/m^2 versus 55.54 ± 9 gm/m^2; $p < 0.001$). Moreover, interventricular septal thicknesses, left ventricular internal diameter in diastole, and left ventricular posterior wall thicknesses were significantly increased in children with obesity. Nevertheless, left ventricular systolic functions expressed as ejection fraction and fractional shortening were not significantly different between both groups.

Of tissue Doppler-derived parameters, mitral annular E' was significantly lower in the obesity group than the control group ($p < 0.001$). Consequently, the mitral E/E' ratio was found to be significantly higher in the obesity cohort than in the control group 0.95 ±7.31) versus 5.0 ± 0.94; $p = 0.001$). Similarly, the left ventricular tissue Doppler-derived myocardial performance index was significantly increased in the obese prepubertal group than the healthy control group ($p = 0.007$).

The two-dimensional speckle tracking-derived ejection fraction of left ventricle in children with obesity was significantly lower than normal children despite the non-significant difference in ejection fraction calculated using the conventional method. The mean global longitudinal strain was significantly reduced in patients with obesity when compared with normal children (−17.52 ± 1.93% versus −19.89 ± 1.08%; $p < 0.001$). Similarly, the mean global circumferential strain was lower in the children with the disease than in the unaffected control group (−17.47 ± 1.91% versus −24.5 ± 2.89%; $p < 0.001$). Figure 1 shows basal circumferential speckle tracking and global circumferential strain in a child of the study patients who was an 8-year-old boy with obesity.

The intraclass correlation coefficient for intra-observer variability of left ventricular global longitudinal strain and global circumferential strain was 0.87 and 0.82, respectively; however, the intraclass correlation coefficient for inter-observer variability of the corresponding values was 0.81 and 0.79, respectively.

No significant differences were detected between males and females in the current work on comparing laboratory tests, adiposity, or echocardiographic parameters.

The linear correlations between echocardiographic parameters and anthropometric and biochemical parameters in children with obesity are presented in Table 3. Body mass index z score was positively correlated with left ventricular mass index (rho = 0.63, $p = 0.003$) and was negatively correlated with global longitudinal strain (rho = −0.54, $p = 0.015$). Chemerin level was found to have a linear positive relation with myocardial performance index

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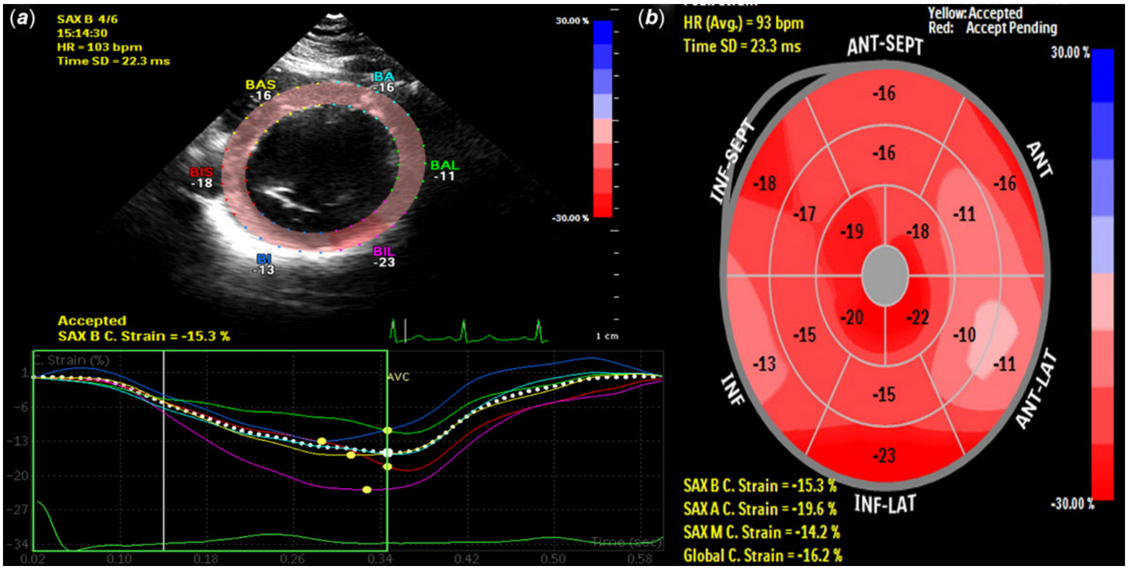

Figure 1. (***a***) Basal circumferential speckle tracking in a child of the study patients who was an 8-year-old boy diagnosed with obesity showing basal circumferential strain −15%, (***b***) Bull's eye 16 segments' model with global circumferential strain (GCS) demonstrated for the same patient as −16.2%.

(rho = 0.55, p = 0.01). However, there were no statistically significant correlations between echocardiographic parameters and each of the following variables: waist circumference, waist-to-height ratio, height z score, or homoeostasis model assessment of insulin resistance. Furthermore, none of the lipid profile parameters displayed significant correlations with echocardiography-related variables (results not expressed in Table 3). No significant correlations were observed between echocardiography measurements and the duration of obesity.

Table 4 demonstrates the correlation between echocardiography and body adiposity parameters in children with obesity. A significant positive correlation was found between the left ventricular mass index and each fat mass index (rho = −0.47; p = 0.037) and trunk fat mass (rho = −0.52; p = 0.021). Besides, the fat mass index was negatively correlated with left ventricular global longitudinal strain (rho = −0.53; p = 0.016).

Other body adiposity indicators, including total body fat percentage, total fat mass, trunk/leg fat mass ratio, and trunk/appendicular fat mass ratio, did not significantly correlate with echocardiography-related variables on univariate analysis.

On multivariate linear regression analysis model for each echocardiographic parameter separately with adiposity, anthropometric, and biochemical parameters as independent variables, none of the echocardiographic parameters had a statistically significant p-value in multivariate models.

Discussion

Obesity is an anabolic state with a resultant increase in lean body mass, accelerated linear growth, and advanced skeletal maturation.[21] As a result, plasma volume is increased with a more expanded circulatory system. Consequently, the myocardium hypertrophies and cardiac chambers enlarge with more significant stroke volumes and cardiac outputs.[22] Therefore, we documented the changes of left ventricular myocardial functions in prepubertal children with obesity and how these changes relate to metabolic and clinical anthropometric or body composition parameters.

Using conventional echocardiography, left ventricular mass index, left ventricular diameter, septal, and left posterior wall thickness in the current work were significantly increased in the obesity group. This finding copes with various previous studies on obesity in children.[11,13,23,24] It was suggested that these changes might be a way to compensate haemodynamic load, while another suggestion is that excess adipose tissue is responsible for insulin resistance leading to excess insulin, which may aggravate hypervolemia due to the retention of salt and water; additionally, insulin may act as a myocardial growth factor.[25,26] Moreover, insulin may activate the sympathetic nervous system with an aggravated response to angiotensin, a well-known vasoconstrictor, hypertrophic, and fibrosing agent.[27] The higher insulin level in our cohort further supports the incrimination of insulin in myocardial hypertrophy.

Tissue Doppler imaging has been widely used for the assessment of left ventricular diastolic function. E/E' ratio may be used to predict left ventricle filling pressures and has been shown to correlate with pulmonary capillary wedge pressure.[28] In our study, E/E' was higher in the cases group suggesting ongoing diastolic function deterioration due to impaired left ventricular filling pressure. Similar results were documented in multiple studies on both paediatric and adult populations.[23,29,30] Tissue Doppler-derived myocardial performance index is another parameter for global cardiac function assessment that was significantly affected in our patients compared to controls, a finding that was proved by Van Putte-Katier et al as well in paediatric obesity.[7]

Speckle tracking is a modality for quantifying myocardial deformation and strains, which in contrast to tissue Doppler, is angle-independent and less affected by dropout artefacts.[31,32] In our study, despite the apparent maintenance of average ejection fraction and fractional shortening using conventional echocardiography, two-dimensional speckle tracking-derived ejection fraction along with global longitudinal and circumferential strains was significantly decreased in prepubertal children with obesity. Mangner et al and Vitarelli et al demonstrated comparable longitudinal and circumferential strains in children with obesity.[23,30] A lower left ventricular global longitudinal strain was found in another research on obese adolescent patients.[33] However, in a study on

Table 3. Linear correlations between echocardiographic parameters and anthropometric and biochemical parameters in children with obesity

Variable		BMI	BMI Z	WC	Waist/ height	Chemerin
FS (%)	Rho	−0.32	−0.37	−0.33	−0.26	−0.39
	p	0.18	0.11	0.16	0.27	0.08
LVMI (gm/m^2)	Rho	**0.59**	**0.63**	0.28	0.12	0.21
	p	**0.007***	**0.003****	0.24	0.62	0.37
E/E'	Rho	−0.33	0.132	−0.05	0.06	0.15
	p	0.16	0.58	0.84	0.81	0.53
MPI	Rho	0.33	0.05	0.33	−0.12	**0.55**
	p	0.16	0.83	0.16	0.61	**0.01***
2D-STE derived EF (%)	Rho	−0.14	−0.21	−0.01	−0.08	−0.1
	p	0.55	0.37	0.97	0.74	0.68
GLS (%)	Rho	−0.33	**−0.54**	−0.16	−0.08	−0.23
	p	0.16	**0.015***	0.51	0.71	0.34
GCS (%)	Rho	−0.3	−0.43	−0.15	−0.33	−0.22
	p	0.20	0.05	0.53	0.150	0.35

2D-STE = 2D-speckle tracking echocardiography; BMI = body mass index; EF = ejection fraction; FS = fractional shortening; GCS = global circumferential systolic strain; GLS = global longitudinal systolic strain; LV = left ventricle; LVMI = left ventricular mass index; MPI = myocardial performance index (Tie index); Rho = Spearman's rank correlation coefficient. Significant values are in bold.
*Correlation is significant if P value is < 0.05 level (2-tailed).
**Correlation is significant if P value is < 0.01 level (2-tailed).

Table 4. Linear correlations between echocardiography and body adiposity parameters in children with obesity

Variable	FM%	%BF	Total FM	FMI	Trunk-FM
FS	rho	−0.26	−0.31	−0.29	−0.29
	p	0.27	0.18	0.22	0.22
LVMI	rho	0.39	0.37	**0.47**	**0.52**
	p	0.09	0.11	**0.037***	**0.021***
E/E'	rho	−0.18	−0.22	−0.18	−0.35
	p	0.44	0.36	0.46	0.13
MPI	rho	0.25	0.32	0.24	0.29
	p	0.29	0.17	0.32	0.21
2D-STE derived EF	rho	−0.33	−0.19	−0.18	−0.135
	p	0.15	0.43	0.44	0.57
GLS	rho	−0.40	−0.35	**−0.53**	−0.27
	p	0.078	0.127	**0.016***	0.24
GCS	rho	−0.29	−0.24	−0.35	−0.17
	p	0.21	0.31	0.13	0.47

EF = ejection fraction; FFM = FM fat mass; FM = fat mass, FS = fractional shortening; GCS = global circumferential systolic strain; GLS = global longitudinal systolic strain; LV = left ventricle; MPI = myocardial performance index (Tie index); Rho = Spearman's rank correlation coefficient. Significant values are in bold.
*Correlation is significant if p value is <0.05 (2-tailed).

an adult cohort, the global circumferential strain was affected but not the longitudinal strain.[34] This subclinical evidence of myocardial dysfunction could result from the pro-inflammatory state that may be detected in children with obesity from the age of 3 years.[35] The deleterious effect of chronic inflammation on left ventricular cardiac function has been reported with inflammatory mediators inducing extracellular matrix alterations, hypertrophy, and even negative inotropic effect.[36,37]

There is growing evidence suggesting that different anthropometric parameters could be potentially valuable markers of cardiac changes. In our study, on univariate analysis, body mass index and body mass index z scores were positively correlated with left ventricular mass index. Similarly, Rodicio et al and Kamal et al demonstrated a significant positive correlation between body mass index and left ventricular mass index.[24,29] However, waist circumference and the waist-to-height ratio were correlated with the left ventricular mass index in Rodicio et al study. Meanwhile, Kamal et al found that waist circumference was positively correlated with left ventricular mass index, interventricular septal thicknesses, left ventricular internal diameter, and left ventricular posterior wall thicknesses.[24,29] Nevertheless, Mehta observed that an elevated body mass index, with an average waist circumference in children, did not have a higher left ventricular mass.[38] In our data, although waist circumference and waist-to-height ratio were significantly higher in our study group, it had a weak linear relation to cardiac data. This may be explained by the prepubertal age group in the current work, while, in other studies, they included more adolescent cases with more tendency towards developing the metabolic syndrome.

Moreover, the body mass index z score was negatively correlated with left ventricular global longitudinal strain and global circumferential strain in our current study. These findings are consistent with other studies found in children showing that left ventricular global longitudinal strain was negatively correlated with body mass index.[11,12] On multivariate analysis, Labombarda et al proved that body mass index z score was independently related to the longitudinal and circumferential strains.[39] However, Mangner et al found that global longitudinal strain was independently associated with body mass index z score and high-density lipoprotein cholesterol, whereas global circumferential strain was solely linked with body mass index z score.[23]

The bioelectrical impedance analysis is a non-invasive analysis of body composition that uses tissue resistance to a small electrical charge to estimate total body water and thereby estimates the free fat mass.[40] It is a helpful tool in the paediatric population with minimal intra- and inter-observer variability and is reproducible with <1% error.[41,42] It also allows regional body fat distribution assessment, which is considered a more appropriate indicator for the increased risk of obesity-related metabolic and cardiovascular disorders.[42,43] In the current study, fat mass index and trunk fat mass have shown a significant positive linear correlation with the left ventricular mass index with a lack of a correlation between body fat distribution ratios such as trunk to leg and trunk to appendicular fat mass ratios with the change in cardiac parameters. This finding may reflect homogenous body fat distribution centrally and peripherally in our prepubertal cohort, which could be attributed to the lack of the sex hormones influence on body fat distribution among the studied children. Rodicio et al showed that the left ventricular mass index was positively correlated with fat mass percentage and a negative correlation with the percentage of lean body mass.[24] On correlation analysis in the current work, a significant negative linear correlation was detected between the fat mass index and global longitudinal strain, as well as a moderate negative correlation with global circumferential strain. Moreover, total body fat percentage was negatively correlated with global longitudinal strain. As far as we know, no previous study has correlated

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bioelectrical impedance analysis-induced data to two-dimensional speckle tracking-derived measurements. However, the non-significant multivariate regression models suggested that the probability of predicting echocardiographic parameters is limited on using cofactors of adiposity, anthropometric, and biochemical parameters that could be related to sample size.

The significant limitation of this study is the sample size, as studies on larger samples are required to confirm the detected correlations. Furthermore, the case-control observational design does not demonstrate the long-term progression pattern of cardiac dysfunction in obesity from prepubertal childhood to adulthood.

Conclusion

Alterations of left ventricular myocardial functions could be detected using variable echocardiographic modalities in prepubertal children with simple obesity. Moreover, chemerin, body mass index z score, fat mass index, and trunk fat mass could be correlated with this subclinical cardiac dysfunction. Therefore, strict early management of paediatric prepubertal obesity could be investigated in the future to limit the ongoing myocardial dysfunction upon detection of these metabolic and clinical changes. The combination of adiposity, anthropometric, and biochemical parameters was non-significant in predicting cardiac variables, warranting further studies on a larger-sized sample of patients.

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Conflicts of interest. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and have been approved by the Institutional Research Board of the Faculty of Medicine, Mansoura University.

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