Subclinical cardiac alterations detected by echocardiography in Mexican schoolchildren with overweight and obesity

Alteraciones cardíacas subclínicas detectadas por ecocardiografía en escolares Mexicanos con sobrepeso y obesidad

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Abstract

Objective: The purpose of this study was to evaluate early changes in myocardial function in overweight and obese children without hypertension. **Methods:** This was a cross-sectional study involving 150 participants of both sexes between 6 and 15 years old. Anthropometric and biochemical evaluations were performed. Ventricular function was assessed by conventional echocardiographic methods and myocardial deformation analysis by two-dimensional speckle tracking echocardiography. One-way analysis of variance was employed for the global comparison of study variables between groups (children with normal weight, overweight, and obesity), and post hoc analysis with Bonferroni correction was used for multiple comparisons, considering normal weight children as the reference category. **Results:** Overall, 142 participants were included, 50 (35%) with normal weight, 39 (28%) overweight, and 53 (37%) obesity. The diastolic diameter of the left ventricular and interventricular septum, and diameter of the left atrium and LV mass were significantly higher in children with obesity compared to those with normal weight. No significant differences in the conventional indicators of LV systolic and diastolic function were found between groups. Significant differences in the regional myocardial deformation between the three groups were observed. Mean global longitudinal myocardial deformation was smaller in patients with obesity (−20.9% vs. −23.5%, $p < 0.05$) compared to children with normal weight. **Conclusions:** The childhood obesity was associated with altered myocardial deformation, even in the presence of normal ejection fraction. Myocardial deformation evaluation is relevant in the assessment of pediatric patients with obesity.

Key words: Childhood obesity. Myocardial function. Echocardiography. Myocardial deformation. Speckle tracking. Mexico.

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Date of reception: 20-09-2018

Date of acceptance: 13-12-2018

DOI: 10.24875/ACME.M19000051

Available online: 06-05-2019

Arch Cardiol Mex (Eng). 2019;89(3):202-211

www.archivoscardiologia.com

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Resumen

Objetivo: El propósito de este estudio fue evaluar los cambios tempranos en la función miocárdica en niños con sobrepeso y obesidad, sin hipertensión arterial. **Métodos:** Estudio transversal en el que se incluyeron 150 participantes de ambos sexos entre 6 y 15 años. Se realizaron evaluaciones antropométricas, bioquímicas y de función ventricular mediante métodos ecocardiográficos convencionales y análisis de deformación miocárdica con ecocardiografía bidimensional speckle tracking. La comparación global entre los grupos de estudio (niños con peso normal, sobrepeso y obesidad) se llevó a cabo con la prueba de análisis de varianza (ANOVA) de una vía y análisis post hoc con corrección de Bonferroni para las comparaciones múltiples, y se consideró a los niños con peso normal como grupo de referencia. **Resultados:** La muestra final fue de 142 participantes, 50 (35%) con peso normal, 39 (28%) con sobrepeso y 53 (37%) con obesidad. El diámetro diastólico del ventrículo izquierdo (VI) y el septum interventricular, y el diámetro de la aurícula izquierda (AI) y la masa del VI fueron significativamente más altos en el grupo con obesidad en comparación con el grupo con peso normal. No se observaron diferencias significativas en los indicadores convencionales de la función sistólica y diastólica ventricular izquierda. Se observaron diferencias significativas en la deformación miocárdica regional entre los tres grupos. La media de deformación miocárdica longitudinal global fue más baja en los pacientes con obesidad (-20.9% vs. -23.5% ; $p < 0.05$) en comparación con los niños con peso normal. **Conclusiones:** La obesidad infantil se asoció a alteraciones en la deformación miocárdica, incluso en presencia de fracción de expulsión normal. La evaluación de la deformación miocárdica es relevante en los pacientes pediátricos con obesidad.

Palabras clave: Obesidad infantil. Función miocárdica. Ecocardiografía. Deformación miocárdica. Speckle tracking. México.

Introduction

Childhood obesity is a public health problem that has been increasing over the past three decades in the world¹. In Mexico, the combined prevalence of obesity and overweight at school age is 33.2% (15.3 and 17.9%, respectively), according to the 2016 National Health and Nutrition Survey².

Excess weight can affect different organs and systems, with serious consequences, such as hypertension, diabetes mellitus, dyslipidemia, fatty liver, and psychosocial problems, among others³. In addition, early development of arteriosclerotic lesions such as fibrous plaques and fatty stretch marks in the aorta and coronary arteries has been observed in children with obesity, which increases the risk of myocardial infarction in adulthood⁴⁻⁸.

Echocardiographic studies in adults with obesity have demonstrated structural and functional alterations, such as left atrium (LA) and left ventricle (LV) dilation, as well as LV hypertrophy and global dysfunction⁹. Through the evaluation of myocardial deformation, early LV functional alterations have been able to be detected in the presence of a normal ejection fraction (left ventricular ejection fraction [LVEF])^{10,11}. However, in the children's population, early changes in the myocardial function associated with obesity have been less studied¹²⁻¹⁶. Detection of early subclinical alterations is essential for cardiovascular risk secondary prevention strategies to be implemented and to reduce the expenses deriving from health care at later ages¹⁷.

The purpose of this study was to identify early changes in the myocardial function in children with overweight and obesity and without hypertension, through evaluation of longitudinal myocardial deformation (strain) with the speckle tracking echocardiographic method.

Methods

Study population

A cross-sectional study was conducted that included 150 participants of both genders, aged between 6 and 15 years, who were recruited through a call addressed to children of workers of the National Institute of Cardiology "Ignacio Chávez" *Instituto Nacional de Cardiología Ignacio Chávez* (INCICH) and pupils of elementary schools from the Southern area of Mexico City, between July 2015 and February 2017. The participants attended the INCICH Socio-medical Research area for initial assessment and eligibility criteria confirmation. Participants with underweight, hypertension, congenital heart diseases, diabetes mellitus, renal disease, neoplasms or systemic inflammatory diseases were excluded from the study. Once non-echocardiographic eligibility criteria were confirmed, the participants were scheduled for echocardiographic assessment at the INCICH pediatric echocardiography department.

The study was approved by the INCICH Research and Ethics Committees. Informed consent was obtained from parents or legal guardians, as well as assent of the child to participate in the study.

Assessments

Anthropometry. Weight and height assessment was carried out in accordance with the guidelines described by the International Society for the Advancement of Kinanthropometry for anthropometric evaluation¹⁸, with the child without shoes and dressed in a light gown. For weight measurement, a mechanical column scale (SECA 700), with a precision of 0.05 kg and maximum capacity of 220 kg, was used. Height was evaluated with a stadiometer (SECA 220), with a measurement range of 60-200 cm and 1-mm precision. The Z-score for body mass index was calculated and classified with the World Health Organization growth standards specific for age and gender¹⁹. Overweight was defined as a Z-score $> +1$ standard deviations (SD), and obesity as a Z-score $> +2$ SD.

Blood pressure. Blood pressure was measured in the left arm on three occasions, with intervals of 3 min between each measurement, and with the child at rest for not < 10 min, in a sitting position before the first evaluation. A previously-calibrated mercury sphygmomanometer and a bracelet according to the child's age were used, following the recommendations for manual blood pressure measurement in the pediatric patient²⁰. The presence of hypertension was defined as the average of three measurements of systolic, diastolic blood pressure, or both, equal to or above percentile 95 + 5 mmHg for gender, age, and height²⁰.

Biochemical evaluation. After a 12-h fasting, serum glucose, triglycerides (TG), total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, atherogenic index, serum creatinine, and uric acid levels were measured.

Echocardiography. The acquisition of images and measurements during post-processing was carried out by three echocardiography expert physicians, trained and certified in the technique, using an echocardiographic Philips iE33 xMatrix equipment, in the M, two-dimensional (2D), three-dimensional (3D), pulsed, continuous and color Doppler modalities, as well as tissue Doppler imaging (TDI), using 5 and 7 MHz transducers. LA and LV, LV mass (LVm), 3D LVm, LVEF, LV shortening fraction, 3D LVEF, 3D LV end-diastolic volume, transmitral flow pulsed-wave Doppler and myocardial performance indexes measurements, with their respective Z-scores, were carried out with TDI^{21,22}. The Z-scores for LV dimension and function measurements, adjusted to the body surface area, were calculated taking as reference a USA population of children and adolescents²¹, since so far there are no standards for the Mexican population.

Post-processing for myocardial deformation analysis and 3D volumetric quantification was performed on the workstation with the QLAB 10.3.1 program (Phillips Healthcare®2001-2014). 2D echocardiography with the speckle tracking technique was used. Tracing was performed with the block matching method.

LV overall longitudinal deformation was obtained as an average of chambers 4, 3, and 2 apical projections^{23,24}. The capture of images was carried out automatically followed by manual correction of the assessed region. Measurements accepted by the equipment software, or those that were not accepted by the software but that could be manually corrected (less than two segments) were considered adequate. A proper acoustic window and precise synchronization with the child's breathing pattern, which would avoid oscillation of the heart within the chest, was necessary for correct 2D image acquisition.

Statistical analysis

The sample size was calculated considering a clinically relevant minimal difference of 2.3% (-18.2 ± 2.0 vs. -20.5 ± 2.3) for LV myocardial longitudinal strain between children with obesity and normal weight, as reported by Mangner et al.¹². In addition, a two-tailed alpha of 5%, 95% power, and a non-response rate of 20% were considered, with a total of 58 children (28 per group) being calculated. Due to the inclusion of three groups in the present study (children with normal weight, overweight, and obesity), the estimated total sample size was $28 \times 3 = 84$.

The results are presented as means $\pm$ SD for continuous variables and as absolute and relative frequencies for categorical variables. For the overall comparison of continuous variables between study groups (children with normal weight, overweight, and obesity), a one-way analysis of variance (ANOVA) was used. Bonferroni's *post hoc* analysis with correction was used for multiple between-group comparisons of the continuous variables that showed a significant difference in the overall comparison, with the children with normal weight being considered as the reference group. For the comparison of categorical variables, Pearson's Chi-square test was used. The echocardiographic indicators that showed a significant difference between groups on the bivariate analysis were subsequently tested in a covariance analysis, including age, height, and gender as covariates. Adjusted means were presented with the corresponding 95% confidence intervals. A difference was considered statistically significant when $p < 0.05$.

Table 1. General characteristics of the population by study group

	Patients with normal weight (n = 50)	Patients with overweight (n = 39)	Patients with obesity (n = 53)	p-value*
Age (years)	9.4 ± 2.5	9.4 ± 1.8	9.8 ± 1.8	0.511
BMI (kg/[height] ²)	16.9 ± 1.7	20.6 ± 1.8 [‡]	25.6 ± 3.7 [†]	<0.001
BMI Z-score (kg/[height] ²)	0.05 ± 0.6	1.4 ± 0.3 [‡]	2.6 ± 0.4 [†]	<0.001
SBP (mmHg)	94 ± 10.7	97 ± 7.6	97 ± 20.9	0.587
DBP (mmHg)	62 ± 8.2	64 ± 5.7	63 ± 13.8	0.687
Glu (mg/dL)	90 ± 6.2	90 ± 4.1	91 ± 5.9	0.359
TC (mg/dL)	160 ± 24.2	163 ± 26.7	164 ± 27.7	0.646
HDL (mg/dL)	58 ± 12.7	49 ± 11.4 [‡]	45 ± 8.7 [†]	<0.001
LDL (mg/dL)	95 ± 22.1	104 ± 24.6	109 ± 24.7 [†]	0.025
TGL (mg/dL)	77 ± 34.3	95 ± 39.9	132 ± 49.2 [†]	<0.001

BMI: body mass index; DBP: diastolic blood pressure; Glu: glucose; HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; SBP: systolic blood pressure; TC: total cholesterol; TGL: triglycerides.

Values are presented as means for continuous variables with their standard deviation.

*Overall comparison between groups with the ANOVA test.

[†]p < 0.05 for the comparison of the obesity group versus normal weight group.

[‡]p < 0.05 for the comparison of the overweight group versus normal weight group.

Results

A total of 150 patients were recruited, out of which eight were excluded from the study, two for incomplete data, three for diagnosis of congenital heart disease on the echocardiographic study, and three due to an inadequate acoustic window, which did not allow quality image acquisition. The final sample comprised 142 participants, 77 females and 65 males, 50 with normal weight (35%), 39 with overweight (28%), and 53 with obesity (37%). Mean age and gender distribution were similar between groups. There were no significant differences in blood pressure between the three groups (Table 1).

HDL cholesterol mean serum concentration was significantly lower in children with obesity than in those with normal weight (45 mg/dL vs. 58 mg/dL; p < 0.05). In addition, LDL cholesterol (109 mg/dL vs. 95 mg/dL; p < 0.05) and TG means (132 mg/dL vs. 77 mg/dL; p < 0.05) were significantly higher in children with obesity in comparison with those with normal weight. In the group of children with overweight, there was a significant difference only in HDL cholesterol concentrations, which were lower in this group than in children with normal weight (49 mg/dL vs. 58 mg/dL; p < 0.05). No significant differences were observed in the glucose serum levels between the three groups (Table 1).

When the echocardiographic dimensions obtained on M mode were compared, there were significant

differences between the three groups in the LV diastolic diameter, the interventricular septum, and the LA diameter; however, no differences were observed in the Z-score for neither of these dimensions (Table 2). After the *post hoc* analysis, the overweight group showed a higher mean LV diastolic diameter, in comparison with the group with normal weight, with no significant differences in the remaining parameters assessed. In turn, LA diastolic diameter and interventricular septum, LA diameter and LVm means were significantly higher in the group with obesity in comparison with the group with normal weight. In the latter group, not only a significant difference in LVm was observed but also in the corresponding Z-score.

Regarding the 3D echocardiographic evaluation, a significantly higher mean diastolic volume (57.2 vs. 44.9 cm³; p < 0.05) and 3D LVm (90.7 vs. 60.8 g; p < 0.05) were observed in the group with obesity in comparison with the normal weight group. In turn, the group with overweight showed a higher 3D LVm mean than the normal weight group (76.8 vs. 60.8 g; p < 0.05) (Table 2).

No significant differences were observed in the means of LV systolic and diastolic function conventional indicators between groups (Table 3).

Regarding the study of myocardial regional strain, there were significant differences between all three groups in eight of the 17 ventricular segments evaluated²⁵. A lower mean myocardial deformation was

Table 2. LV dimensions, mass and 3D measurements by study group

	Patients with normal weight (n = 50)	Patients with overweight (n = 39)	Patients with obesity (n = 53)	p-value*
LV (mm)	25.9 ± 3.3	26.8 ± 4.8	28.9 ± 5.0 [†]	0.003
LV Z-score	0.94 ± 0.85	0.95 ± 0.94	0.84 ± 1.04	0.811
LVDD (mm)	39.1 ± 3.8	41.7 ± 4.3 [‡]	42.2 ± 4.3 [†]	<0.001
LVDD Z-score	-0.5 ± 0.66	-0.27 ± 0.75	-0.55 ± 0.91	0.213
LVSD (mm)	24.7 ± 2.8	26.1 ± 3.7	26.6 ± 5.0	0.068
LVSD Z-score	-0.2 ± 0.82	-0.23 ± 0.77	-0.18 ± 0.92	0.973
IVSD (mm)	6.7 ± 1.2	7.0 ± 1.4	7.5 ± 1.5 [†]	0.013
IVSD Z-score	0.27 ± 0.77	0.35 ± 0.71	0.19 ± 1.5	0.804
PWD mm	7.6 ± 1.2	6.6 ± 1.0	8.3 ± 1.3	0.756
PWD Z-score	0.38 ± 0.7	0.33 ± 0.88	0.40 ± 0.7	0.725
LV mass (g)	75.6 ± 25.9	83.1 ± 24.2	104.4 ± 29.1 [†]	<0.001
LV mass Z-score	-0.78 ± 1.1	-0.48 ± 1.1	0.28 ± 1.1 [†]	<0.001
LV mass (g/m ²)	66 ± 20.6	66 ± 12.5	71.3 ± 13.5	0.211
3D LVED vol. (cm ³)	44.9 ± 15.9	50.7 ± 15.1	57.2 ± 24.9 [†]	0.010
3D LV mass (g)	60.8 ± 21.4	76.8 ± 22.8 [‡]	90.7 ± 31.3 [†]	<0.001

IVSD: interventricular septum diameter in diastole; LA: left atrium; LV: left ventricle; LVDD: left ventricle diastolic diameter; LVED Vol.: left ventricle end-diastolic volume; LVSD: left ventricle systolic diameter; PWD: posterior wall diastolic diameter.

Values presented in means for continuous variables with their standard deviation.

*Overall comparison between groups with the ANOVA test.

[†]p < 0.05 for the comparison of the group with obesity versus normal weight group.

[‡]p < 0.05 for the comparison of the group with overweight versus normal weight group.

observed in ventricular segments 4, 7, 10, 13, 14, 15, 16, and 17 in the group with obesity in comparison with the normal weight group, whereas in the group with overweight, only ventricular segments 13, 14, 16, and 17 showed a lower myocardial strain mean in comparison with the normal weight group. Mean myocardial global longitudinal strain was lower both in patients with obesity (-20.9 vs. -23.5%; p < 0.05) and in those with overweight (-21.9 vs. -23.5; p < 0.05), in comparison with the children with normal weight (Table 4).

The differences found between the groups of children with obesity and normal weight in LV dimensions and 3D LVm and 3D diastolic volume continued to be statistically significant after being adjusted for age, gender, and height. Similarly, myocardial deformity in all four affected ventricular segments of patients with overweight (13, 14, 16, and 17) and in 6 of the 8 compromised segments in the group of patients with obesity (4, 7, 13, 14, 16, and 17), maintained a significant difference in comparison with the group with normal weight after adjusting for age, gender, and height (Table 5).

Discussion

The combined prevalence of obesity and overweight in Mexico continues to be high, and it affects up to one-third of children older 5 than years, without significant changes being observed when the 2012 and 2016 National Health and Nutrition Surveys are compared².

Obesity and overweight almost epidemic proportions in Mexican children are attributed to cultural, economic, demographic, and environmental changes in recent years. Although genetic and hormonal disorders are risk factors for the development of obesity and overweight, dietary factors in Mexican children are more important, such as the widespread consumption of sugary and carbonated drinks instead of water, accessibility to densely energetic foods at low price, high consumption of saturated fats with low protein and fiber intake, as well as a sedentary lifestyle, with a marked decrease in the practice of physical activity outdoors²⁶. Low birth weight, breastfeeding period short duration, poverty, migration from rural to urban areas, mistaken concepts

Table 3. Indicators of left ventricular systolic and diastolic function by study group

	Patients with normal weight (n = 50)	Patients with overweight (n = 39)	Patients with obesity (n = 53)	p-value*
LVEF (%)	64.5 ± 4.6	65.2 ± 5.1	64.1 ± 5.9	0.608
3D LVEF (%)	62.1 ± 7.2	66.9 ± 18.8	63.8 ± 7.1	0.173
LV SF (%)	36.4 ± 6.9	37.8 ± 7.0	38.0 ± 8.6	0.537
M E/A ratio	1.7 ± 0.3	2.1 ± 1.7	1.7 ± 0.8	0.120
M E/A ratio Z-score	-0.24 ± 0.31	0.03 ± 0.77	-0.21 ± 0.82	0.207
Left lat. Tei	0.40 ± 0.08	0.41 ± 0.07	0.45 ± 0.42	0.662
Left lat. Tei Z-score	0.38 ± 0.79	2.1 ± 9.4	0.55 ± 1.1	0.214
Left med. Tei	0.38 ± 0.08	0.4 ± 0.1	0.41 ± 0.12	0.282
Left med. Tei Z-score	0.34 ± 0.86	0.59 ± 1	0.68 ± 1.3	0.304

Left lat. Tei: left lateral Tei index; Left med. Tei: left medial Tei index; LV SF: left ventricular shortening fraction; LVEF: left ventricular ejection fraction; M E/A: mitral E/A-waves ratio.

Values are presented as means for continuous variables with their standard deviation.

*Overall comparison between groups with the ANOVA test.

Table 4. LV myocardial segmental and global longitudinal strain by study groups

Segment	Patients with normal weight (n = 50)	Patients with overweight (n = 39)	Patients with obesity (n = 53)	p-value*
1	-21 ± 5.7	-23 ± 6.8	-20 ± 8.1	0.149
2	-19 ± 2.9	-20 ± 5.7	-19 ± 4.4	0.378
3	-19 ± 4.1	-20 ± 4.7	-18 ± 4.5	0.156
4	-21 ± 4.3	-22 ± 5.4	-18 ± 5.5 [†]	0.005
5	-24 ± 4.7	-25 ± 5.7	-22 ± 3.7	0.117
6	-23 ± 3.6	-23 ± 5.6	-21 ± 8.1	0.144
7	-22 ± 5.7	-24 ± 6.4	-18 ± 5.5 [†]	<0.001
8	-23 ± 4.8	-24 ± 6.2	-22 ± 5.1	0.140
9	-22 ± 3.7	-22 ± 5.7	-21 ± 5.0	0.249
10	-22 ± 5.2	-22 ± 6.1	-19 ± 5.1 [†]	0.017
11	-23 ± 4.1	-21 ± 4.7	-21 ± 4.7	0.262
12	-24 ± 4.4	-22 ± 6.0	-22 ± 5.9	0.297
13	-24 ± 5.5	-19 ± 6.1 [‡]	-19 ± 4.8 [†]	<0.001
14	-26 ± 4.7	-23 ± 5 [‡]	-23 ± 3.9 [†]	0.001
15	-26 ± 5.2	-24 ± 5.1	-23 ± 4.3 [†]	0.015
16	-24 ± 3.9	-21 ± 3.9 [‡]	-20 ± 5 [†]	<0.001
17	-25 ± 3.7	-21 ± 3.9 [‡]	-21 ± 3.8 [†]	<0.001
GLS (%)	-23.5 ± 2.2	-21.9 ± 2.6 [‡]	-20.9 ± 2.2 [†]	<0.001

GLS: global longitudinal strain.

Values are presented as means for continuous variables with their standard deviation.

*Overall comparison between groups with the ANOVA test.

[†]p < 0.05 for the comparison of the group with obesity versus normal weight group.

[‡]p < 0.05 for the comparison of the group with overweight versus normal weight group.

Table 5. Age-, gender-, and height-adjusted means for selected indicators of LV dimensions, mass, volume, and myocardial longitudinal strain by study groups

	Patients with normal weight (n = 50)	Patients with overweight (n = 39)	Patients with obesity (n = 53)	p-value*
LV dimensions, mass, and two/three-dimensional volumes				
LA (mm)	26.1 (25, 27.3)	26.9 (25.6, 28.2)	28.7 (27.6, 29.8) [†]	0.009
LVDD (mm)	39.2 (38.3, 40.1)	42 (41, 43.1) [‡]	41.8 (41, 42.7) [†]	<0.001
IVSD (mm)	6.7 (6.3, 7.1)	7.0 (6.6, 7.5)	7.4 (7.1, 7.8) [†]	0.036
3D LV mass (g)	65.8 (59.7, 71.9)	77.2 (70.3, 84.1)	85.8 (79.9, 91.6) [†]	<0.001
LVED vol. (cm ³)	45.1 (40.1, 50.2)	51.2 (45.5, 57)	56.5 (51.7, 61.4) [†]	0.009
LV myocardial strain				
Segment				
4	-21.8 (-23.3, -20.3)	-22.3 (-24, -20.5)	-18.8 (-20.2, -17.3) [†]	0.003
7	-22.9 (-24.6, -21.1)	-24.1 (-26.1, -22.1)	-18.6 (-20.3, -16.9) [†]	<0.001
10	-22.3 (-23.9, -20.7)	-22.2 (-24, -20.3)	-19.5 (-21, -18)	0.028
13	-23.8 (-25.3, -22.3)	-19.8 (-21.5, -18) [‡]	-19.7 (-21.2, -18.3) [†]	<0.001
14	-25.9 (-27.2, -24.7)	-23.3 (-24.7, -21.9) [‡]	-24.4 (-25.6, -23.2)	0.022
15	-25.9 (-27.3, -24.5)	-24.4 (-26, -22.8)	-23.6 (-24.9, -22.2)	0.079
16	-23.9 (-25.2, -22.7)	-21.4 (-22.8, -19.9) [‡]	-21.0 (-22.2, -19.8) [†]	0.004
17	-25.2 (-26.3, -24.1)	-21.8 (-23.1, -20.6) [‡]	-21.4 (-22.4, -20.3) [†]	<0.001
GLS (%)	-23.3 (-24, -22.6)	-21.9 (-22.7, -21.1) [‡]	-21.0 (-21.7, -20.4) [†]	<0.001

GLS: global longitudinal strain; IVSD: interventricular septum diameter in diastole; LA: left atrium; LV: left ventricle; LVDD: left ventricle diastolic diameter; LVED Vol.: left ventricle end-diastolic volume.

Values presented as means (95% confidence intervals).

*For the comparison between groups of height-, gender-, and age-adjusted means using the analysis of covariance.

[†]p < 0.05 for the comparison of the group with obesity versus normal weight group.

[‡]p < 0.05 for the comparison of the group with overweight versus normal weight group.

about health, parental obesity, globalization, and industrialization add up to the aforementioned factors.

To allow early and timely diagnosis of obesity-associated changes in the cardiovascular system, advanced echocardiography techniques have been used to support decisions and behaviors adopted regarding the prevention, treatment, and control of excess weight.

In the adult population, changes in the dimensions of the left cavities resulting from obesity have been reported, including LA and LV dilation, LV hypertrophy with an increase in the interventricular septum and posterior wall dimensions^{9,27}; however, in children with overweight and obesity there is no such extensive documentation on heart structural and functional alterations.

Experimental studies have shown that hypercholesterolemia may cause LV hypertrophy through several mechanisms, which include increased endothelin one concentration, intracellular signaling activation in

cardiomyocytes and increased oxidative stress^{28,29}, as well as systolic and diastolic dysfunction related to alterations in calcium intracellular homeostasis³⁰. Vitarelli et al.⁴ reported an inverse relationship between LDL cholesterol levels and myocardial deformation in patients with hypercholesterolemia with and without obesity and were of greater importance in the latter group. In the present study, we observed significantly higher LDL cholesterol levels and greater involvement of myocardial strain in the group of patients with obesity in comparison with the group with overweight; however, the association between LDL cholesterol and myocardial deformation was not analyzed. On the other hand, a low level of HDL cholesterol is considered a significant risk factor for the development of cardiovascular disease in adult life³¹. Recently, an increased TG/HDL cholesterol ratio was shown to be associated with an unfavorable cardiovascular and metabolic profile³². In

the present study, significantly higher TG and lower HDL cholesterol concentrations were observed in the group of children with obesity, in comparison with the children with normal weight (Table 1).

The results of our study demonstrated significant subclinical changes in LV geometry and ventricular function in children with overweight and obesity and without hypertension. The number of compromised echocardiographic indicators was higher in the group of patients with obesity.

Kibar et al., in a study in adolescents aged between 10 and 16 years, reported LA and LV dimensions significantly larger in the group with obesity in comparison with adolescents with normal weight¹⁶; however, these measurements remained within the normal limits for age. Although most measurements assessed in the present study remained within normal limits for age, significant changes were observed in the comparison between groups. The group with overweight showed a significantly higher mean for the LV diastolic diameter in comparison with the group with normal weight. In turn, in the children with obesity, not only a significantly higher mean was observed for LV diastolic diameter but also for interventricular septum diameter, LVm and LA, even after adjusting for age, gender, and height in the covariance analysis (Table 5), given that these are factors that might have an impact on cardiac dimensions. These results demonstrate the impact that the degree of body fat accumulation has on the changes experienced by the LV, with a larger number of alterations in children with obesity than in those with overweight. We consider that early interventions are required in patients with overweight, to avoid their progression to obesity and the increased cardiovascular risk this entails.

The characteristic LVm increase observed in obese patients is associated with the mechanical stress imposed by afterload sustained increase, which in the long term can lead to subendocardial fiber damage and cause regional functional alterations³³. With 3D echocardiography, we observed not only a larger LVm but also a higher LV diastolic volume in the group with obesity, in comparison with the group with normal weight.

We did not observe alterations or significant differences with regard to LV systolic function conventional indicators between the groups, which was consistent with observations reported by other authors^{13,16}. We know that conventional echocardiographic methods lack sufficient sensitivity to detect ventricular function early changes associated with obesity¹⁰. This is attributed to Simpson modified method-assessed LVEF inability to accurately detect early changes in the ventricular

function in patients with obesity. Kibar and Di Salvo failed to find significant differences in LV diastolic function as assessed with mitral flow Doppler or TDI between patients with obesity and normal weight^{13,16}. Similarly, we did not observe significant differences in the LV diastolic function in the group of children with obesity when compared with the normal weight group.

Echocardiographic indicators' Z-scores were calculated considering a reference population from the US, which might have affected the sensitivity of these standards to detect alterations associated with obesity in this sample of Mexican children. However, echocardiographic indicator raw values (before being standardized to Z-scores) showed significant differences between groups, which were maintained after being adjusted for age, gender, and height. This highlights the importance of constructing reference standards for the Z distribution of specific echocardiographic indicators for each population.

The assessment of myocardial deformation in obese patients using 2D speckle tracking echocardiography is relatively new³⁴. Barbosa et al., using this echocardiographic method, found a significantly lower myocardial longitudinal strain in patients with obesity, in comparison with subjects of normal weight matched by age and gender, in spite of no differences existing in LVEF¹⁵. In turn, Kibar et al. also reported a reduction in myocardial regional deformation in the septal and lateral wall, using 2D speckle tracking, in patients with obesity and normal LVEF¹⁶. The present study demonstrated significant differences in myocardial longitudinal strain means between the groups with obesity (−20.9 vs. −23.5; $p < 0.05$) and overweight (−21.9 vs. −23.5; $p < 0.05$), when compared with the group with normal weight, without a LVEF decrease being observed. The number of LV compromised segments was larger in the group of children with obesity than in those with overweight, with apical, and middle segments being mainly affected. These results maintained their statistical significance even after being adjusted for age, gender, and height in the analysis of covariance (Table 5). Recently, Balderrábano reported 34 severely obese adolescents, out of which 52% already had a LVEF < 55%, and 78.9% had abnormal myocardial longitudinal strain values evaluated by 2D speckle tracking echocardiography³⁵. With this previous observations, we consider that 2D speckle tracking echocardiography is an important tool in the monitoring of the subclinical functional alterations the myocardium suffers in relation to overweight and obesity severity and evolution time³⁶.

It is of the utmost importance for the reference ranges for the values derived from the measurement of

myocardial deformity by 2D speckle tracking echocardiography at pediatric age to be established. These reference ranges allow the application of the technique to clinical practice. However, most studies in pediatrics still have an inconsistent methodology and small sample sizes³⁷. In this regard, the fact that meta-analyses that report reference ranges in the pediatric population have chosen studies where even less 50% of patients had global longitudinal strain determined as an average of the measurement in all three (4-, 3-, and 2-chamber) apical projections stands out²³. In addition, it cannot be definitively concluded that demographic variables do not influence on myocardial deformity data obtained at pediatric age²³. The wide reference range reported for myocardial deformity values led us to consider a group of healthy patients as the control group in our study, and significant differences were found in myocardial longitudinal strain means between the groups with obesity (-20.9 vs. -23.5 ; $p < 0.05$) and overweight (-21.9 vs. -23.5 ; $p < 0.05$), when compared to the normal weight group. Among the findings of the current study, we highlight the presence of early changes in myocardial deformity in obese and overweight children before they become apparent with conventional assessment methods. Studies with larger sample sizes and standardized methodology will be required in the future.

The dissemination and application of prevention measures aimed at modifying the diet and at the adoption of healthy lifestyle habits have great importance in the pediatric population, taking into account the increase in childhood obesity in recent decades. According to the results obtained in the present investigation, intervention measures and treatment should be early and timely started in overweight children, since as it was demonstrated in this work, they already present incipient changes, to avoid the appearance of more severe myocardial function alterations than those the child with obesity already has³⁸.

Overweight and obesity treatment in pediatrics is mainly based on non-pharmacological measures and should include not only the adoption of a balanced and healthy diet that meets the nutritional needs of the child, with adequate control of servings and decreased consumption of sugary drinks and foods of high caloric content and low nutritional value but also the practice of regular physical activity and reduction of sedentary activities³⁹. Pharmacological therapy in obese children is rather limited and is frequently associated with adverse effects⁴⁰.

Our group continues the follow-up of these patients, which have been incorporated into a program of primary prevention strategies. Currently, we are carrying out

a study that has as its main goal to assess the effect of a nutrition and physical activity education program on indicators of cardiac function and structure and cardiovascular risk markers in school children with overweight and obesity. The results of this still ongoing study are expected show the relevance of lifestyle changes as a priority measure for the control of overweight and obesity and cardiovascular risk management in the pediatric population.

2D speckle tracking echocardiography could be a useful tool to assess the impact of lifestyle modifications on global and regional myocardial LV function in patients with overweight and obesity.

Limitations of the study

The sample size was not representative of the Mexican pediatric population, which limits the generalization of the obtained data.

Conclusions

The present study demonstrated the presence of alterations in the left cavities' dimension and in myocardial longitudinal strain in children with obesity who were not hypertensive, even in the presence of normal LVEF. These results support the increasing usefulness of myocardial deformation assessment with 2D speckle tracking echocardiography in the early diagnosis of LV function alterations in this population.

With a smaller number of alterations in LV dimensions and function, overweight patients should be the main target in the implementation of excess weight secondary prevention measures and treatment to prevent its progression to obesity and the consequent deterioration of ventricular function.

Studies are required for the assessment of the possible regression of functional alterations acquired by the LV in patients with obesity and overweight once treatment is started and secondary prevention measures have been adopted.

Conflicts of interest

None.

Funding

The present investigation has not received specific aid from public or commercial sector agencies or non-profit entities.

Ethical disclosures

Protection of people and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained written informed consent of the patients and/or subjects mentioned in the article.

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