ORIGINAL ARTICLES

Echocardiographic Systolic and Diastolic Function Parameters Are Not Significantly Altered in Isolated Pediatric Excess Weight

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Abstract

Given the increasing burden pf pediatric excess weight, we employed echocardiography to assess the presence and extent of cardiac disfunction in a cohort of excess weight children compared to normal weight controls.

46 excess weight children and 28 normal weight controls underwent clinical examination, standard transthoracic echocardiography, and Tissue Doppler Imaging (TDI). Recorded parameters were normalized when possible.

Fractional shortening was normal in all subjects. A minority of participants (all of whom had excess weight) exhibited an ejection fraction of under 55%. M-mode and TDI systolic function parameters were mostly normal. There were conflicting results with respect to some diastolic function parameters (early diastolic flow propagation velocity, isovolumic relaxation time), but generally the diastolic function was also within normal limits.

Standard echocardiographic systolic and diastolic function parameters do not appear to be significantly altered in isolated pediatric excess weight. However, a thorough examination is advised in these children, as subtle changes may be identified in some, signaling a need for closer follow-up.

Keywords: pediatric, children, excess weight, echocardiography, systolic function, ejection fraction, diastolic function.

Rezumat

Dat fiind nivelul ridicat al excesului ponderal în populația pediatrică, am utilizat ecografia cardiacă pentru a identifica prezența și gradul disfuncției cardiace într-o cohortă de copii cu exces ponderal comparativ cu copii cu greutate corporală normală.

Pentru 46 de copii cu exces ponderal și 28 cu greutate normală s-au efectuat examen clinic, ecografie cardiacă standard și evaluare prin Doppler tisular (TDI).

Fracția de scurtare a fost normală. Un număr mic de participanți (toți cu exces ponderal) au prezentat o fracție de ejecție a ventriculului stâng de sub 55%. Parametrii sistolici de mod M și TDI au fost în mare parte normali. Au existat rezultate discordante în ceea ce privește anumiți parametri de funcție diastolică (velocitatea de propagare a fluxului transmitral, timpul de relaxare izovolumică), însă în general funcția diastolică s-a menținut, de asemenea, în limite normale.

Parametrii ecocardiografici standard de funcție sistolică și diastolică nu par să se modifice semnificativ în excesul ponderal pediatric izolat. Cu toate acestea, se recomandă o examinare riguroasă a acestor copii, deoarece modificări subtile pot fi prezente în anumite cazuri, indicând necesitatea unei dispensarizări atente.

Cuvinte cheie: pediatric, copii, exces ponderal, ecografie cardiacă, funcție sistolică, fracție de ejecție, funcție diastolică.

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INTRODUCTION

Obesity is a classic risk factor for heart disease and the relationship between the two has been extensively studied in adults[1]. The rationale for assessing possible effects of excess weight on cardiac function in children stems from the unique opportunity to obtain data from a population that will not typically exhibit additional, confounding risk factors. The possibility that these individuals could potentially develop premature cardiovascular disease also warrants attention.

Echocardiography presents itself as a widely accessible, non-invasive tool that can easily provide the necessary information. Given the increasing burden of pediatric excess weight, we employed echocardiography to assess the presence and extent of cardiac dysfunction in a cohort of excess weight children compared to normal weight controls.

METHOD

Patients under 18 years of age who presented to the pediatrics or pediatric cardiology departments of „Dr. V. Gomoiu" Clinical Hospital for Children in Bucharest between 2016 and 2018 were evaluated for enrollment in the study. Excess weight (overweight or obese), otherwise healthy children and normal weight, healthy controls were included, subject to parent and adolescents signing a dedicated consent form. Weight status was assessed according to the Centers for Disease Control and Prevention (CDC) criteria[2] using an online calculator[3] and defined as: healthy weight (5th percentile up to the 85th percentile, included in the control arm), overweight (85th to less than the 95th percentile) or obese (equal to or greater than the 95th percentile), both enrolled in the excess weight arm. Body surface area (BSA) was calculated using the Du Bois method[4]. Each visit comprised clinical examination, routine blood tests, total serum cholesterol and triglyceride levels, 12-lead ECG, 24 hour ambulatory blood pressure monitoring (ABPM) and echocardiography. Excess weight children were then scheduled for clinical visits at 6-month intervals and were followed up for one year.

Standard transthoracic echocardiography (2D, M-mode, colour and spectral Doppler) and Tissue Doppler Imaging were performed. A minimum of 2 consecutive cardiac cycles (usually 3 or 4) were recorded. We determined cardiac and great vessel dimensions, systolic and diastolic function parameters and performed an assessment of heart valves.

2D-guided M-mode was employed to calculate fractional shortening (FS) and the ejection fraction using Teichholz's formula. Left atrial volume was calculated using the area-length method. Left ventricular (LV) end-diastolic and end-systolic volumes were determined using the biplane disc›s summation technique. LV ejection fraction was also calculated using the modified Simpson method. We calculated stroke volume and cardiac output. Diastolic function assessment was carried out by documenting mitral inflow and early diastolic flow propagation velocity (Vp). We employed tissue Doppler imaging (TDI) to record both systolic and diastolic velocities of mitral annular motion.

Stroke volume and cardiac output were normalized to body surface area and height to its age-specific allometric power[5]. MAPSE was normalized using an online calculator[6,7], avaliable at https://www.pedz.de/en/heart.html (accessed May 26th 2020). Ratios (ejection fraction, E/A, E/Vp) were not indexed. All other parameters were normalized to body surface area using the Z-score calculator provided by Boston Children's Hospital[8].

Table 1. Baseline participant characteristics

Category	Excess weight	Control	P value
Fasting plasma glucose Mean (mg/dl) ±SD	93.02 ± 8.75	90.61 ± 8.11	NS
Lipid profile			
Modified[a] total cholesterol (%)	64.9	26.9	<0.01
Modified[a] triglycerides (%)	50	20	<0.05
HTN prevalence (ABPM[b] (%)	14.3	4	NS
Metabolic syndrome[c] (%)	21.1	0	<0.05

SD, standard deviation. NS, not significant. HTN, arterial hypertension. ABPM, ambulatory blood pressure monitoring.
[a] borderline or high, according to[10]
[b] ABPM results were interpreted using the 2014 US recommendations[11]
[c] according to the International Diabetes Federation (IDF) criteria[12]

RESULTS

46 excess weight (overweight or obese), otherwise healthy children (mean age 10.31 ± 3.1, range 2-16) and 28 normal weight, healthy controls (mean age 13.06 ± 3.58, range 4-17) were enrolled in the study. 91.3% of participants in the excess weight arm were obese according to the CDC criteria. Baseline participant characteristics are depicted in Table 1; further details regarding blood pressure data may be found elsewhere[9] we sought to identify the prevalence of abnormally high BP levels (based on auscultatory measurements and ambulatory blood pressure monitoring-ABPM.

Ejection fraction and fractional shortening

Valid data regarding the ejection fraction was available in 71 participants (95.94%) using the Teichholz formula and 66 participants (89.1%) using Simpson's biplane method.

Fractional shortening was above 25% in all subjects. Mean values of left ventricular ejection fraction (LVEF) were similar between groups using the Teichholz formula; mean values in the experimental groups (M=60.41, SD=5.64) were slightly lower compared to the control group (M=64.23, SD=5.87) when using Simpson's biplane method, t(51.9)= -2.62, p=0.011, C.I. [-6.74,-0.89]. A minority of participants (all of whom had excess weight) exhibited an ejection fraction of under 55% (Table 2). The difference became statistically significant when employing Simpson's biplane method (17.5% of excess weight children had mildly reduced LVEF (<55%) as opposed to none in the control arm, p=0.037).

Table 2. Left ventricular ejection fraction in the excess weight and normal weight groups. Percentages are derived from total valid measurements in all participants, regardless of weight status

	Teichholz		Simpson's biplane	
	EW	NW	EW	NW
LVEF <50%, n (%)	0 (0%)	0 (0%)	1 (1.51%)	0 (0%)
LVEF 50-54.9%, n (%)	2 (2.81%)	0 (0%)	6 (9.09%)	0 (0%)
LVEF 55-59.9%, n (%)	1 (1.4%)	0 (0%)	13 (19.69%)	4 (6.06%)
LVEF 60-69.9%, n (%)	15 (21.12%)	9 (12.67%)	18 (27.27%)	19 (28.78%)
LVEF ≥70%, n (%)	25 (35.21%)	19 (26.76%)	2 (3.03%)	3 (4.54%)

LVEF, left ventricular ejection fraction. EW, excess weight. NW, normal weight.

M-mode parameters

In most cases MAPSE was either normal or higher. For both MAPSE and TAPSE the mean Z score value was slightly higher in the excess weight group, however the difference did not reach statistical significance.

Cardiac output

Mean stroke volume and cardiac output were lower in excess weight children compared to controls when normalizing to BSA or BSA to its age-specific allometric power[5] (Tables 3 and 4). Non-indexed cardiac output values were either normal or slightly lower than the accepted normal value for age in all participants. Interestingly, both left and right non-indexed ventricular outputs were more frequently lower than the accepted normal value for age in the control group (p=0.024 and p=0.037, respectively).

Tissue Doppler parameters

None of the participants exhibited systolic dysfunction identified by means of a reduced lateral or septal S. There were however significant numbers of supranormal values (Z score above +2), in the control arm

Table 3. Comparison of mean stroke volume and cardiac output, normalized to body surface area

	Excess weight M (SD)	Controls M (SD)	Statistical analysis
Stroke volume normalized to body surface area	28.97 (5.83)	34.49 (7.77)	t(66)= -3.3 P=0.001 95% C.I. [-8.8,-2.21]
Cardiac index	2.49 (0.57)	2.9 (0.91)	t(39.6)= -2.1 P=0.041 95% C.I. [-0.81,-0.01]

M, mean. SD, standard deviation.

Table 4. Comparison of mean stroke volume and cardiac output, normalized to body surface area to its age-specific allometric power for individuals under 18 years of age[5]

	Excess weight M (SD)	Controls M (SD)	Statistical analysis
Stroke volume normalized to body surface area$^{0.82}$	31.12 (6.44)	36.83 (8.73)	t(66)= -3.1 P=0.003 95% C.I. [-9.38,-2.03]
Cardiac output normalized to body surface area$^{0.53}$	3 (0.72)	3.4 (1.06)	t(66)= -1.87 P=0.065 95% C.I. [-0.84,-0.02]

M, mean. SD, standard deviation.

in particular: 38.5% of normal weight children exhibited supranormal lateral S values as opposed to 13.6% of excess weight children, p=0.037. The percentage of supranormal septal S values was similar between groups (aprox. 23%). Mean lateral S standard deviation values were significantly higher in the control group (M=1.7, SD=1.15) when compared to excess weight participants (M=0.87, SD=1.15), t(68)= -2.87, p=0.005, C.I. [-1.39,-0.25].

Diastolic function

Main parameters and mean values are shown in Table 5.

Mitral inflow (E/A, DT) was normal in all participants and measurements were similar between groups. On average, the isovolumic relaxation time (IVRT) was slightly longer in normal weight children (M=69.48, SD=11.7) when compared to excess weight participants (M=62.73, SD=14.06), t(70)=2.09, p=0.04, C.I. [0.31,13.18]. A total of 28 participants (14 normal weight, 51.85% of group, and 14 excess weight, 31.11%) demonstrated a slight increase in IVRT (normal range 31 – 68ms, applicable for individuals less than 20 years of age[13]).

Mean septal and lateral e' and E/e' ratio values have been depicted in Table 5. No difference was found between groups (septal E/e' (t(66)=1.15, p=0.257, C.I. [-0.25,0.94]) and lateral E/e' (t(68)=1.82, p=0.073, C.I. [-0.03,0.76]). Only 2 participants demonstrated a corresponding Z score of over +2 for septal E/e', one of them also exhibiting an increased lateral E/e' Z score. The latter was the only to have a (septal) E/e' ratio of over 15. Both children were excess weight.

18 participants from both groups exhibited reduced (below 55cm/s[13,14]) early diastolic flow propagation velocity (Vp). Of these, 8 (19.51% of the respective group) were excess weight and 10 (38.46%) were normal weight. Only one of them (overweight) also exhibited an abnormal E/Vp ratio (>2.58). Vp was similar between groups, t(68)=1.78, p=0.078, C.I. [-0.82,14.85].

No signs of left atrial pressure elevation were recorded, and the estimated pulmonary artery pressure was normal in all participants.

Table 5. Mean values of main left ventricular diastolic function parameters in the entire study population at baseline, by age group

	2 – 5 years	6 – 9 years	10 – 13 years	14 – 18 years	Total
E-wave (m/s)	1.02 (±0.10)	0.99 (±0.13)	0.88 (±0.11)	0.87 (±0.10)	0.92 (±0.13)
A-wave (m/s)	0.63 (±0.04)	0.62 (±0.13)	0.59 (±0.11)	0.57 (±0.09)	0.60 (±0.11)
E/A	1.59 (±0.17)	1.66 (±0.35)	1.54 (±0.31)	1.56 (±0.28)	1.58 (±0.31)
DT (ms)	105.6 (±23.78)	136.9 (±23.92)	134.63 (±24.76)	148.55 (±27.22)	137.21(±27.28)
IVRT	51.40 (±7.03)	63.23 (±14.78)	65.20 (±13.66)	71.05 (±9.03)	65.26 (±13.47)
Vp	73.68 (±10.81)	65.67 (±14.49)	66.77 (±17.53)	60.13 (±14.42)	65.11 (±15.79)
E/Vp	1.42 (±0.28)	1.61 (±0.47)	1.41 (±0.39)	1.52 (±0.33)	1.50 (±0.40)
e' lateral septal	13.68 (±1.80)	12.67 (±2.23)	13.43 (±1.37)	12.98 (±2.74)	13.10 (±2.07)
E/e' septal	7.35 (±0.55)	8.26 (±3.1)	6.56 (±0.66)	7 (±1.51)	7.24 (±2.03)
e' lateral lateral	18.32 (±2.85)	17.73 (±3.61)	19.19 (±2.68)	19.17 (4.12)	18.68 (±3.5)
E/e' lateral	5.59 (±0.96)	5.88 (±1.65)	4.66 (±0.84)	4.72 (±0.88)	5.11 (±1.28)

DT, deceleration time. IVRT, isovolumic relaxation time. Vp, early diastolic flow propagation velocity

DISCUSSION

Most previous studies have identified some degree of diastolic dysfunction in obese children[15-20]. Some authors have demonstrated changes in standard mitral inflow parameters (E/A, DT)[16,18,20] or pulmonary venous flow[15], but combined parameters using TDI (E/e', E'/A') appear to be more sensitive. Existing evidence is less convincing when it comes to systolic function. While there are papers which have reported minor subclinical changes in some systolic function parameters (myocardial performance index, stroke volume)[21,22], many others report no difference from normal weight children[18-20].

In our study LV systolic function (assessed by various means) was mainly preserved across both groups. Although a significantly higher proportion of excess weight children had a slightly lower ejection fraction (below 55%, Simpson's biplane method), other systolic function parameters (MAPSE, lateral and septal peak systolic tissue velocities) were normal or supranormal. Interestingly, with respect to peak systolic tissue velocities, there was a higher number of supranormal values in the normal weight group, although this did not reach statistical significance. Arguably, this data may suggest minimal impairment of LV function in some excess weight children that could potentially be demonstrated by more sensitive tests. Supporting this is the fact that both indexed stroke volume and cardiac output were higher in normal weight children.

Diastolic function was also normal when assessed using standard echocardiographic parameters (E/A, DT). With respect to combined mitral inflow and TDI parameters, E/e' was abnormal in only 2 participants, both having excess weight. Only the septal E/e' was abnormal in one participant, who also exhibited a low Vp and increased E/Vp; as for the other, both septal and lateral E/e' were abnormal, but no changes were noted using color M mode. It is thus difficult to appreciate genuine diastolic disfunction. LV ejection fraction, as well as other systolic function parameters, were normal in both cases.

Early diastolic flow propagation velocity (Vp) was reduced in some cases without a corresponding increase in E/Vp ratio (with the single exception described above). Calculating E/Vp may thus be a more accurate method of evaluating LV diastolic function.

Finally, a significant number of children from both groups exhibited a longer IVRT when using age-appropriate (age under 20) cutoff values. This finding is difficult to interpret, as other diastolic function parameters were mainly normal and there was no echocardiographic evidence of an increase in left atrial pressure. Previous work[13] suggests limited applicability of IVRT in children because of close correlation with heart rate, which is both higher and overly variable in this population (with age, emotional context etc.).

In this study, both systolic and diastolic function parameters were normal in most cases regardless of weight status. We were unable to exclude a minimal degree of left ventricular systolic impairment that could potentially be demonstrated by means of myocardial strain imaging or cardiac magnetic resonance. The few cases which exhibited modified diastolic function parameters are difficult to interpret, as these changes were not consistent, thus causing us to question true diastolic dysfunction in these children. Vp and IVRT do not seem to be well suited for diastolic function assessment in children based on our data.

These findings do not align with some of the previously published data as discussed above. This could be since our excess weight group included overweight as well as obese children. Moreover, participants in both groups were quite young (in the excess weight arm the average age was 10, while the youngest participant was only 3 years old), thus limiting the time of exposure to excess weight. It is indeed possible that more definite changes may appear in older children with a more severe weight issue. Measurements performed in this study are however mostly standard, at least for adult studies. Incorporating calculating the ejection fraction with a volumetric method, systolic and diastolic mitral annular velocities, analysis of the mitral inflow pattern and combined TDI parameters into a dedicated assessment protocol is not difficult, may yield minor changes in some individuals and can be augmented with more complex parameters if needed.

CONCLUSION

Standard echocardiographic systolic and diastolic function parameters do not appear to be significantly altered in isolated pediatric excess weight. However, a thorough examination (ideally following a standardized protocol) is advised in these children, as subtle changes may be identified in some, signaling a need for closer follow-up in these cases.

Compliance with ethics requirements:

The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well

as the national law. Informed consent was obtained from all the patients included in the study.

References

1. Ortega, F. B., Lavie, C. J. & Blair, S. N. Obesity and cardiovascular disease. Circulation Research 118, 1752–1770 (2016).
2. Kuczmarski, R. J. et al. 2000 CDC growth charts for the United States: Methods and development. Vital Heal. Stat. Ser. 11 Data from Natl. Heal. Surv. Natl. Heal. Nutr. Exam. Surv. Hisp. Heal. Nutr. Exam. Surv. 11, 1–190 (2002).
3. Centers for Disease Control and Prevention. BMI Percentile Calculator for Child and Teen. Centers for Disease Control and Prevention (2019). Available at: https://www.cdc.gov/healthyweight/bmi/calculator.html. (Accessed: 29th April 2020)
4. Du Bois, D. & Du Bois, E. F. A formula to estimate the approximate surface area if height and weight be known. 1916. Nutrition 5, 303–311; discussion 312 (1989).
5. De Simone, G. et al. Stroke volume and cardiac output in normotensive children and adults: Assessment of relations with body size and impact of overweight. Circulation 95, 1837–1843 (1997).
6. Gräfe, D. Ped(z) Pediatric Calculator. Available at: https://www.pedz.de/en/heart.html. (Accessed: 26th May 2020)
7. Koestenberger, M. et al. Left ventricular long-axis function: Reference values of the mitral annular plane systolic excursion in 558 healthy children and calculation of z-score values. Am. Heart J. 164, 125–131 (2012).
8. Boston Children's Hospital. BCH Z-Score Calculator. Available at: http://zscore.chboston.org/. (Accessed: 26th May 2020)
9. Rădulescu, C. R. et al. Ambulatory blood pressure monitoring greatly improves diagnostic accuracy in excess and normal weight children. Rom. J. Pediatr. 69, 103–107 (2020).
10. Grundy, S. M. et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 139, E1082–E1143 (2019).
11. Flynn, J. T. et al. Update: Ambulatory blood pressure monitoring in children and adolescents: A scientific statement from the American Heart Association. Hypertension 63, 1116–1135 (2014).
12. Zimmet, P. et al. The metabolic syndrome in children and adolescents - An IDF consensus report. Pediatr. Diabetes 8, 299–306 (2007).
13. Lai, W. W., Mertens, L. L., Cohen, M. S. & Geva, T. Echocardiography in Pediatric and Congenital Heart Disease: From Fetus to Adult. Echocardiography in Pediatric and Congenital Heart Disease: From Fetus to Adult (Wiley-Blackwell, 2009). doi:10.1002/9781444306309
14. Lancellotti, P. & Cosyns, B. The EACVI Echo Handbook. (Oxford University Press, 2016). doi:10.1093/med/9780198713623.001.0001
15. Harada, K., Orino, T. & Takada, G. Body mass index can predict left ventricular diastolic filling in asymptomatic obese children. Pediatr. Cardiol. 22, 273–278 (2001).
16. Sharpe, J. A. et al. Impact of Obesity on Diastolic Function in Subjects ≤16 Years of Age. Am. J. Cardiol. 98, 691–693 (2006).
17. Mehta, S. K., Richards, N., Lorber, R. & Rosenthal, G. L. Abdominal obesity, waist circumference, body mass index, and echocardiographic measures in children and adolescents. Congenit. Heart Dis. 4, 338–347 (2009).
18. Dhuper, S., Abdullah, R. A., Weichbrod, L., Mahdi, E. & Cohen, H. W. Association of obesity and hypertension with left ventricular geometry and function in children and adolescents. Obesity 19, 128–133 (2011).
19. Harris, K. C. et al. Biophysical properties of the aorta and left ventricle and exercise capacity in obese children. Am. J. Cardiol. 110, 897–901 (2012).
20. Mangner, N. et al. Childhood obesity: Impact on cardiac geometry and function. JACC Cardiovasc. Imaging 7, 1198–1205 (2014).
21. Ingul, C. B., Tjonna, A. E., Stolen, T. O., Stoylen, A. & Wisloff, U. Impaired cardiac function among obese adolescents: Effect of aerobic interval training. Arch. Pediatr. Adolesc. Med. 164, 852–859 (2010).
22. Mahfouz, R. A., Dewedar, A., Abdelmoneim, A. & Hossien, E. M. Aortic and pulmonary artery stiffness and cardiac function in children at risk for obesity. Echocardiography 29, 984–990 (2012).