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# Hemodynamic overload and intra-abdominal adiposity in obese children: Relationships with cardiovascular structure and function

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Left ventricular function

**Abstract** *Background and aims:* Childhood obesity promotes adverse changes in cardiovascular structure and function. This study evaluated whether these changes are related to intra-abdominal adiposity and associated cardiometabolic risk or to body-size induced hemodynamic overload.

*Methods and results:* 55 obese children/adolescents and 35 healthy-weight controls underwent carotid, cardiac and abdominal ultrasound to assess carotid artery intima-media thickness (IMT), diameter, distension and stiffness, left ventricular (LV) dimension, mass and function and extent of intra-abdominal adiposity.

As compared to controls with healthy BMI, obese children had higher systolic blood pressure (BP), stroke volume and lower total peripheral resistance ($P < 0.001–0.0001$), higher plasma triglycerides, glycated hemoglobin, insulin and HOMA-IR index ($P = 0.01–<0.0001$), higher carotid IMT, diameter and distension ($P < 0.005–0.0005$), higher LV diameter, wall thickness and mass ($P < 0.001–0.0001$), and impaired LV diastolic function assessed by myocardial longitudinal performance ($P < 0.005$). In entire population, independent determinants of carotid diameter, LV diameter, wall thickness and mass were fat-free mass (or stroke volume, respectively) and BP. Carotid distension was determined by carotid diameter and BP, and carotid IMT by carotid diameter, BP, HDL-cholesterol and glycated hemoglobin. LV diastolic performance was inversely related to preperitoneal fat thickness and plasma insulin levels.

*Conclusions:* Obese youths present signs of impaired lipid and glucose metabolism, hyperdynamic circulation and cardiovascular changes. Increase in LV dimensions and mass and in carotid diameter and distension seems to reflect adaptation to body-size induced increase in hemodynamic load, changes in LV diastolic performance a negative impact of intra-abdominal adiposity and associated metabolic risk, and increase in IMT both adaptive remodeling and metabolic risk.


## Introduction

The prevalence of childhood obesity has dramatically increased in the past 30 years, and this escalation is becoming a public health problem. Obesity in childhood increases the probability of being obese as adult [1] and represents a risk for adulthood cardiovascular morbidity and mortality [2]. Adult obesity is associated with number of cardiovascular structural and functional abnormalities that were recognized as established biomarkers of

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cardiovascular risk, and that include increased carotid intima-media thickness (IMT) and arterial stiffness, impaired endothelial function, left ventricular (LV) hypertrophy, LV diastolic and systolic dysfunction [3]. Some of these alterations were described also in obese children and adolescents, yet the results of different studies are conflicting [4–7]. Furthermore, the pathophysiologic mechanisms linking childhood obesity to cardiovascular abnormalities have not been clearly established as some studies indicate that obesity *per se* [7–10], rather than the associated risk factors, like insulin resistance or dyslipidemia, is an independent predictor of some adverse cardiovascular changes. This could be explained by the fact that obesity is accompanied by an important hemodynamic adaptation that is necessary to statisfy the metabolic demand of an expanded body mass and that could induce remodeling of cardiovascular system [8,11].

To assess whether the cardiovascular alterations in childhood obesity are related to total and intra-abdominal adiposity and associated cardiometabolic risk or to a body-size induced hyperdynamic circulation, the present study compared several structural and functional cardiovascular measures between obese (body mass index [BMI] $\geq$ 95th percentile for age and sex) [12] and healthy-weight children and adolescents, and it tested the cross-sectional associations of these measures with body size, lean and fat mass, hemodynamic parameters, extent of intra-abdominal adiposity [13,14], and indices of insulin resistance and impaired glucose and lipid metabolism.

**Table 1** Characteristics of study population.

| | Healthy BMI | Obese | *P* |
|---|---|---|---|
| N | 35 | 55 | |
| Female:Male | 16:19 | 23:32 | 0.59 |
| Age (years) | 13.4 ± 1.9 | 12.8 ± 1.9 | 0.19 |
| Tanner stage | 3.17 ± 1.23 | 2.94 ± 0.96 | 0.36 |
| Weight (kg) | 56 ± 12 | 79 ± 17 | <0.0001 |
| Height (cm) | 161 ± 12 | 160 ± 11 | 0.57 |
| BMI (kg/m$^2$) | 21.5 ± 2.6 | 30.8 ± 4.8 | <0.0001 |
| z-score of BMI | 0.64 ± 0.59 | 2.16 ± 0.32 | <0.0001 |
| Waist circumference (cm) | 80 ± 11 | 98 ± 14 | <0.0001 |
| FFM (kg) | 42.1 ± 11.0 | 47.2 ± 10.6 | <0.005 |
| Fat mass (kg) | 14.3 ± 5.4 | 32.0 ± 11.6 | <0.0001 |
| Maximal SC abdominal fat (mm) | 16.9 ± 10.9 | 35.8 ± 10.2 | <0.0001 |
| Maximal preperitoneal fat (mm) | 11.5 ± 3.6 | 16.2 ± 4.1 | <0.0001 |
| Visceral fat (mm) | 25.9 ± 9.4 | 42.9 ± 13.1 | <0.0001 |
| Systolic BP (mmHg) | 110 ± 10 | 116 ± 9 | <0.0001 |
| Diastolic BP (mmHg) | 66 ± 6 | 67 ± 7 | 0.51 |
| Pulse pressure (mmHg) | 43 ± 9 | 49 ± 8 | <0.0005 |
| Mean BP (mmHg) | 81 ± 7 | 83 ± 7 | 0.01 |
| Heart rate (bpm) | 68 ± 10 | 69 ± 12 | 0.79 |
| HDL-cholesterol (mmol/L) | 1.3 ± 0.3 | 1.2 ± 0.3 | 0.14 |
| LDL-cholesterol (mmol/L) | 1.8 ± 0.6 | 2.7 ± 0.7 | <0.0001 |
| Triglycerides (mmol/L) | 0.5 [0.4] | 0.9 [0.6] | 0.001 |
| Fasting glucose (mmol/L) | 4.7 ± 0.5 | 4.5 ± 0.6 | 0.11 |
| HbA1c (%) | 5.2 [0.5] | 5.4 [0.5] | 0.01 |
| Fasting insulin (pmol/L) | 57 [31] | 112 [96] | <0.0001 |
| HOMA IR index | 1.1 [0.5] | 2.1 [1.6] | <0.0001 |

SC: subcutaneous.
*P** value after adjustment for sex and Tanner stage.

## Method

### *Study population*

Study population consists of 55 obese children and adolescents and 35 controls with healthy BMI that had similar age, gender distribution and Tanner stage (Table 1).

### *Study protocol*

The protocol of the study followed the principles of the Declaration of Helsinki and was approved by the institutional ethics committee. Parents of study subjects gave informed consent to participate.

### Carotid ultrasound

Carotid ultrasound was performed by a single operator (CM) on the right CCA using an ultrasound scanner equipped with a linear 10 MHz probe (MyLab 70, Esaote, Genova, Italy) and implemented with a previously validated radiofrequency-based tracking system of the arterial wall that allows a real-time measurement of far-wall common carotid artery (CCA) intima-media thickness (IMT), diameter and distension over the cardiac cycle (QIMT® and QAS®). From the distension curves, beta-stiffness index was automatically calculated [15]. Peripheral blood pressure (BP) needed for calibration of distension curves was measured at the left brachial artery (Omron, Kyoto, Japan) during each acquisition. All radiofrequency-derived measures were averaged over 6 consecutive cardiac beats, and the values used for statistical analysis represent a mean of three consecutive acquisitions. Mean circumferential wall stress was calculated by Lamé's equation as the product of mean BP and mean luminal radius (radius = diameter/2) divided by a far-wall IMT. Intra-individual variability of QIMT and QAS measurements in our laboratory was previously tested [15].

### Cardiac ultrasound

Cardiac images were obtained with a standard ultrasound system (MyLab 70, Esaote, Genova, Italy) equipped with a 3.5-MHz, phased-array probe. Conventional B-mode, M-mode and Doppler echocardiography were used for the assessment of LV mass, mean wall thickness, relative wall thickness, ejection fraction (biplane Simpson's method), Doppler-derived stroke volume (SV) and total peripheral resistance (TPR) as recommended [16,17]. LV mass was normalized for body height (LV mass index, gram/meter$^{2.7}$).

LV longitudinal velocities at mitral annular levels, both at septal and lateral sides, were measured by color-guided pulsed-wave tissue Doppler in the apical four-chamber view. From spectral traces, peak systolic longitudinal velocity (Sa), peak longitudinal velocities during early diastolic filling (Ea) and during atrial contraction (Aa) were measured and averaged over 5 consecutive cardiac cycles,