Increased left ventricular mass in obese adolescents


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Received 8 October 2003; revised 8 March 2004; accepted 18 March 2004

Aims An increase of left ventricular mass (LVM) has been reported in obese adolescents in previous studies using echocardiography. The aim of our study was to determine the extent of the increase in LVM and correlation to other risk factors using cardiac magnetic resonance imaging in obese and lean adolescents.

Methods and results Nineteen obese and 20 lean adolescents were recruited. Following resting blood pressure measurements and blood sampling for insulin, triglycerides, and cholesterol levels, all subjects underwent cardiac magnetic resonance examination to assess LVM.

LVM adjusted for body height was 16% greater in obese compared to lean adolescents (median 66 g/m², p = 0.0042). Obese subjects had higher resting systolic blood pressures than controls (median 115 vs. 110 mmHg, p = 0.0077) and higher fasting triglyceride and insulin levels. HDL-cholesterol levels were lower in the obese group compared with the lean group.

Conclusions Obese adolescents had a higher LVM than age-matched lean subjects, which correlated mainly with body mass index and systolic blood pressure. These findings add to the established cardiovascular risk profile of obese adolescents.

KEYWORDS
Obesity; Paediatrics; Myocardium; Magnetic resonance imaging; Blood pressure

Introduction

Obesity is becoming an epidemic threat for the individual and society. The increasing prevalence of overweight children and adolescents is likely to have a great impact on the future cardiovascular health of these subjects.1,2 Increased left ventricular mass (LVM), hypertension, insulin resistance, and secondary hyperinsulinaemia and dyslipidaemia are recognised cardiovascular complications of obesity.3 Many of these factors have traditionally been considered to lead to serious health consequences in the adult population, but ample evidence suggests that these pathologic events begin in the young.3-5 Moreover, recent results suggest that obesity accelerates the progression of coronary atherosclerosis in young men.6

Left ventricular hypertrophy, as detected by echocardiography, has been clearly established as an independent risk factor for cardiovascular morbidity and mortality.7 It has also been suggested that obesity in both adults and children is an important determinant of LVM.8 Furthermore, elevated blood pressure and hyperinsulinaemia have also been shown to contribute to increased LVM in adults.9,10 The extent to which these factors are associated to LVM in adolescents is less known. Few studies have examined total LVM more accurately, that is, by means of cardiovascular magnetic resonance (CMR) imaging, in paediatric subjects. To our knowledge, only Lorenz11 has reported LVM values in children and young adults ranging in age from 7 to 20 years. However, this group was rather small (n = 8) and...
gender was not stated. Since an increase of LVM in obese adolescents has been reported in previous studies using echocardiography, we proposed to determine the extent of LVM using CMR and its correlation to other risk factors. Therefore, we measured LVM (both absolute and normalised for height) by means of CMR in obese adolescents and compared these results with those of age-matched lean adolescents. In addition, we sought to investigate the relationship between LVM, blood pressure, fasting lipids, and insulin levels.

**Methods**

**Study population and design**

Nineteen obese adolescents (9 females) were recruited from the outpatient department of Paediatrics at the Queen Silvia Children’s Hospital, Gothenburg. Excess weight and obesity were defined according to the standard definition of the international obesity task force. BMI-SD (standard deviation) adjusted for gender and age was also calculated. The results obtained in the obese adolescents were compared with those of 20 normotensive lean adolescents (11 females) with normal BMI for age. These lean control subjects were randomly selected from two schools in the surrounding Gothenburg area. They had permission from their parents and were selected within the same age range as the obese subjects (11–17 years of age). A paediatrician assessed sexual maturation in all adolescents based on Tanner staging principles. The study was approved by the regional ethics review board of Sahlgrenska University Hospital.

**Lipid and serum measurements**

On the first visit after enrolment, blood samples were drawn after an overnight fast from both groups of adolescents. Fasting total cholesterol, HDL-cholesterol, and triglyceride concentrations were analysed using enzymatic methods (Roche Diagnostics, Mannheim, Germany). LDL-cholesterol was calculated using the Freiwald equation. Fasting serum insulin was analysed with a radioimmunochemical method (Pharmacia & Upjohn Diagnostics AB, Uppsala, Sweden) and fasting blood glucose was analysed using an enzymatic method.

**Blood pressure measurements**

At the second scheduled visit, blood pressure was assessed after 30 min of rest. In obese adolescents, the arm cuff was dimensioned to the arm circumference.

**CMR investigation**

CMR was performed with a 1.5-T scanner (Magnetom Vision Plus, Siemens, Erlangen, Germany) and phased-array body coil. The adolescents were studied in supine position. Standard scout images were used to locate the orthogonal planes of the heart. Short-axis scans were planned from the four-chamber view using the end-diastolic cardiac phase. Contiguous 10-mm slices covering a region that extended from more than 2 cm proximal to the atrioventricular valve plane to beyond the apex were acquired using 2D short-axis, single-slice, multiphase, segmented k-space cine gradient-echo images with phase-sharing. Seven k-lines were acquired each heartbeat. Images were obtained during breath holding at the end-expiratory position. The sequence parameters were: TR 80 ms, TE 4.8 ms, FA 30°, slice thickness 10 mm, rectangular field of view 320–380 (depending on the size of the adolescent) with a matrix of 256. With these parameters, one breath hold took 19 heartbeats. The number of phases obtained per cardiac cycle was 15–19 depending on the heart rate, giving a temporal resolution of 40–50 ms.

At the time of the study newer sequences, such as steady-state free precession, were not available at our institution. It has been shown that LVM is measured more accurately using these new techniques and that these techniques produce small, but significantly higher, left ventricular volume measurements. The reproducibility is, however, similar. However, given that both groups of adolescents were examined and their data analysed using the same machine and software, the between-group comparisons were not affected.

The first frame in each series was determined as the end-diastolic frame and the image with the smallest ventricular volume was defined as the end-systolic frame. None of the children had valvular disease. Two independent observers manually traced the endocardial and epicardial contours of the end-diastolic and end-systolic frames of the left ventricle, one using Argus software (Siemens) and the other using Scion image (www.scioncorp.com). All short-axis slices showing left ventricular myocardium were analysed. The most basal image plane included in the measurement showed the left ventricular (LV) wall only in end-diastole and the end-systolic frame of this slice was excluded since this frame depicted the left atrium due to the translational motion of this slice. The papillary muscles were defined as part of the LVM in those slices where they were contiguous with the ventricular wall, otherwise they were excluded. LVM was obtained by multiplying the mean wall volume of the end-diastolic and end-systolic frames by the specific weight of cardiac muscle (1.05 g/ml). The parameters of global left ventricular function were end-diastolic and end-systolic volume, ejection fraction, and cardiac output. The interobserver difference for LVM was 1.7 ± 4.2%.

**Statistics**

Statistical analyses were performed with Statview. Data are presented as medians and ranges. To detect a mean relative LV mass difference of 10 g/m (relative to height) with an expected SD of approximately 10–11, with alpha established at 5% and a power of >80% to identify this difference, we estimated (SPSS, Sample Power) that a group size of 40 adolescents (20 in each group) would be needed. The Student t-test for unpaired comparisons was used to identify statistically significant differences between obese and control groups, respectively. For relative LVM (normalised for height), two-way analysis of variance (ANOVA) was used with group (obese/lean) and gender (male/female) as independent factors. The Mann–Whitney U test for unpaired comparisons was used for continuous variables with a non-normal distribution. The relationship between two variables was assessed from bivariate scatter plots and the rank correlation coefficient was calculated according to Spearman. A multiple forward stepwise linear regression analysis was performed with LVM normalised for height as the dependent variable. All variables with a significant (p < 0.05) univariate association to LVM were added to the model: gender, age, BMI, HDL-cholesterol, systolic and diastolic blood pressure. All tests used were two-sided and a p value of less than 0.05 was considered statistically significant.
Results

Obese adolescents were more than 3 SD above reference BMI and significantly heavier compared to the lean group (Table 1). This lean group was 0.4 SD heavier than a reference value obtained from a large sample (Table 1). There was no difference in terms of puberty staging (based on Tanner principles) between the obese and lean group. On a scale of 1–5, the presence of pubic hair was 3 in both groups (median, range 1–5). For males, genital development was 2.5 and 3.0 for obese and control groups, respectively (range 1–5 for both). For females, breast staging demonstrated similar median values, 3.2 and 3.0 for the obese and lean groups, ranging from 2 to 5 and from 1 to 5 for the obese and lean groups, respectively. Five out of 9 obese and 6 out of 11 lean females had reached menarche.

Obese adolescents had higher resting systolic and diastolic blood pressures than lean subjects and higher fasting triglyceride and insulin levels (Table 1). Fasting blood glucose was normal in all subjects. LDL-cholesterol concentrations were similar in both groups, whereas HDL-cholesterol levels were lower in the obese group (see Fig. 1).

LVM, expressed in both absolute and normalised terms (height-adjusted), was significantly greater in obese versus lean adolescents (Table 2, Fig. 2). With two-way ANOVA analysis, both gender and group (obese/lean) were shown to be independently related to relative LVM ($p = 0.05$ and $p = 0.0048$, respectively). Although our study group is rather small, we observed a pronounced difference in normalised LVM between obese and lean girls (Table 3). Lean female and male adolescents also differed statistically in terms of normalised LVM, albeit to a lesser degree (Table 3). Left ventricular mass adjusted for height correlated significantly with BMI, HDL, and systolic and diastolic blood pressures ($r = 0.62, p < 0.0001; r = -0.41, p = 0.0091; r = 0.57, p = 0.0002; r = 0.34, p = 0.038$), while weak correlations were found for insulin, triglycerides, and LDL ($r = 0.28, p = 0.08; r = 0.26, p = 0.11; r = 0.20, p = 0.22$, respectively). Multiple regression analysis with inclusion of gender, age, and the statistically significant variables from prior analysis revealed that, besides age and gender, BMI (regression coefficient $= 0.60, SE = 0.25, p = 0.0267$) and systolic blood pressure (regression coefficient $= 0.41, SE = 0.16, p = 0.0165$) remained independently correlated with LVM normalised for height. Finally, both groups of adolescents showed a normal ejection fraction, approximately 65% (Table 2).

Discussion

This study establishes and confirms that obese adolescents have a greater left ventricular myocardial mass

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Table 1  Demographic, haemodynamic, lipid and metabolic variables in lean and obese adolescents

<table>
<thead>
<tr>
<th>Variable</th>
<th>Obese adolescents ($n = 19$)</th>
<th>Lean adolescents ($n = 20$)</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (F/M)</td>
<td>9/10</td>
<td>11/9</td>
<td>0.53</td>
</tr>
<tr>
<td>Age (years)</td>
<td>14 (11–17)</td>
<td>13 (12–16)</td>
<td>0.53</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78.0 (63.7–96.8)</td>
<td>51.2 (35.0–59.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.62 (1.49–1.80)</td>
<td>1.60 (1.41–1.80)</td>
<td>0.34</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.8 (26.4–41.7)</td>
<td>19.6 (16.2–23.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI-SD (kg/m²)</td>
<td>3.11 (2.29–3.97)</td>
<td>0.42 (–0.61–1.83)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>115 (104–133)</td>
<td>110 (84–117)</td>
<td>0.0077</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>67 (51–84)</td>
<td>62 (49–72)</td>
<td>0.0072</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>4.2 (2.9–5.3)</td>
<td>4.1 (3.1–5.9)</td>
<td>0.94</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.1 (0.5–2.9)</td>
<td>0.7 (0.4–1.5)</td>
<td>0.007</td>
</tr>
<tr>
<td>HDL (mmol/l)</td>
<td>1.1 (0.6–1.9)</td>
<td>1.4 (1.0–2.0)</td>
<td>0.004</td>
</tr>
<tr>
<td>LDL (mmol/l)</td>
<td>2.5 (1.3–3.4)</td>
<td>2.4 (1.1–2.6)</td>
<td>0.57</td>
</tr>
<tr>
<td>Insulin (mU/l)</td>
<td>18.0 (5.8–38.0)</td>
<td>5.9 (3.7–18.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>B-glucose (mmol/l)</td>
<td>4.9 (4.2–5.3)</td>
<td>5.0 (4.5–5.7)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Data are expressed as medians and range. Gender is indicated by number. Blood samples were taken after 12 h fasting. BMI is body mass index and BMI-SD is standard deviation of BMI adjusted for age and gender.
than age-matched lean subjects. The difference, as determined with CMR, was 16%, which was highly statistically significant \( p < 0.0042 \) despite the small sample sizes. Increased LVM was correlated mainly with body mass index and systolic blood pressure. This finding adds another important factor to the already established health risk profile of these young obese individuals, given the high risk of increased LVM, as shown in adults.

**Noninvasive assessment of LVM**

In order to estimate individual risk for an obese child, it is necessary to have a reliable method of LVM assessment. CMR is well suited as a non-invasive approach for assessing many cardiac variables in the young and it provides highly reproducible and accurate LVM measurements,\(^4\) as confirmed by our high interobserver concordance. The claim that very accurate LVM measurements can be obtained using the CMR technique is further supported by the excellent agreement between height-adjusted LVM for the lean

### Table 2 Absolute and body height-adjusted left ventricular mass in lean and adolescent subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Obese adolescents ((n = 19))</th>
<th>Lean adolescents ((n = 20))</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular mass (absolute weight, g)</td>
<td>123 (90–172)</td>
<td>105 (53–168)</td>
<td>0.0146</td>
</tr>
<tr>
<td>Left ventricular mass (height-adjusted, g/m)</td>
<td>76 (59–96)</td>
<td>66 (36–93)</td>
<td>0.0042</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>67 (56–74)</td>
<td>63 (58–73)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Data are expressed as medians and range.

### Table 3 Gender differences in left ventricular mass (LVM) normalised for height

<table>
<thead>
<tr>
<th></th>
<th>LVM (g/m)</th>
<th>(p)-Value obese vs. lean</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Obese adolescents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females ((n = 9))</td>
<td>75 (59–94)</td>
<td>0.004</td>
</tr>
<tr>
<td>Males ((n = 10))</td>
<td>78 (62–96)</td>
<td>0.28</td>
</tr>
<tr>
<td><strong>Controls</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females ((n = 11))</td>
<td>63 (36–70)</td>
<td></td>
</tr>
<tr>
<td>Males ((n = 9))</td>
<td>67 (60–93)</td>
<td>*</td>
</tr>
</tbody>
</table>

Data are expressed as medians and range.

*Denotes statistically significant difference between male and female lean adolescents \((p = 0.03)\).
In the adult patient, increased LVM and LV hypertrophy in adults, LVM is related to body size and surface area, height, and different powers of height. Correlations have been shown between LVM and body fat mass and LVM. In support of this view, Daniels et al. demonstrated in children and adolescents that fat-free mass was a strong determinant of LVM. Furthermore, their study showed no association between fat mass and LVM. In support of this view, Daniels et al. showed in children and adolescents that fat-free mass determined 75% of the variation in LVM. Indexing or normalising LVM to height offers some advantages. Daniels et al. demonstrated in children and adolescents that the correlation of height with LVM was similar to that of body surface area with LVM in both genders. The use of height adjustment of LVM is also more valid in obese patients, inasmuch as increased LVM may go undetected if indexed to body surface area (see above). Furthermore, Urbina et al. demonstrated in the Bogalusa Heart study that linear growth and height correction are major determinants of cardiac growth in children. Therefore, we feel confident in our assumption of relating LVM to body height, avoiding any possible confounding effect on LVM by relating it to body surface area.

Clinical significance

In the adult patient, increased LVM and LV hypertrophy are strongly implicated in the development of cardiovascular disease. As a predictor of LV hypertrophy and increased cardiovascular risk, augmented LVM may already be present early in life, particularly in association with obesity. Indeed, our results demonstrate clearly an increased LVM in obese adolescents compared with lean controls, indicating that these obese subjects already have an increased risk for future cardiovascular disease. There is no clear definition of LV hypertrophy in children and adolescents, albeit the figure of 51 g/m²² calculated for adults — and associated with a significant increase in cardiovascular risk in hypertensive patients — can be used as guidance. This figure, however, was obtained for adults using echocardiographic investigations. Although there are no data for adolescents on the cutoff limit of LV hypertrophy estimated from CMR, Daniels et al. have calculated echocardiographic criteria for LV hypertrophy (absolute and height-adjusted) in children and adolescents, based on the 95th percentile. One has to bear in mind, though, that this assumption is based on two different techniques for estimating LVM and, given the fact that CMR is more accurate in determining LVM than echocardiography, the cutoff limit for LV hypertrophy may even be somewhat lower. Further studies in both overweight and obese young subjects are warranted to more precisely identify the cutoff value for LV hypertrophy, which would facilitate early identification of increased LVM as a risk factor and its modification. This may be particularly important in young females, given our finding of a pronounced difference in normalised LVM, close to 20%, between obese and lean female adolescents.

Normalisation of left ventricular mass to body shape

In adults, LVM is related to body size and univariate correlations have been shown between LVM and body surface area, height, and different powers of height. As a result, LVM is commonly indexed to body surface area, thus allowing comparisons between subjects of different size. Estimation of LVM in obese subjects may therefore present a challenge, given that indexing to body surface area may normalise and thus incorrectly grossly underestimate LVM measurements. By combining echocardiographic data with body composition measurements in adults, Whalley et al. were able to demonstrate that fat-free mass was a strong determinant of LVM. Furthermore, their study showed no association between fat mass and LVM. In support of this view, Daniels et al. showed in children and adolescents that fat-free mass determined 75% of the variation in LVM. Indexing or normalising LVM to height offers some advantages. Daniels et al. demonstrated in children and adolescents that the correlation of height with LVM was similar to that of body surface area with LVM in both genders. The use of height adjustment of LVM is also more valid in obese patients, inasmuch as increased LVM may go undetected if indexed to body surface area (see above). Furthermore, Urbina et al. demonstrated in the Bogalusa Heart study that linear growth and height correction are major determinants of cardiac growth in children. Therefore, we feel confident in our assumption of relating LVM to body height, avoiding any possible confounding effect on LVM by relating it to body surface area.

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Influence of metabolic factors on LVM

The present study demonstrated a clustering of metabolic and cardiovascular risk factors in obese adolescents. There was a significant positive correlation between LVM and systolic blood pressure and a negative correlation with HDL-cholesterol concentration. With regression analysis, systolic blood pressure, in addition to age, gender, and BMI, remained an independent contributing factor to LVM. These results suggest that these young obese individuals have a salient risk factor profile.

Conclusions

In summary, we demonstrated increased LVM in obese adolescents using CMR and determined that the increase in LVM correlated mainly with body mass index and systolic blood pressure. These findings add yet another factor to the already increased cardiovascular risk burden in these obese subjects. Given the cardiovascular risk associated with LV hypertrophy, the goal of reducing body weight and cardiovascular risk in obese adolescents must be taken seriously.

Acknowledgements

We are grateful for all the help provided by the staff of the Department of Paediatrics, Obesity Section, Queen Silvia Children’s Hospital, and the staff of the Depart-
ment of Clinical Physiology and Radiology, CMR section, Sahlgrenska University Hospital.

All authors contributed to the design of the study, interpretation of results and preparation of the manuscript. P. Friberg, A. Allansdotter-Johnsson, and S. Marild were the principal investigators responsible for subject recruitment, performance, and analysis of the magnetic resonance studies and the main drafting of the manuscript. R. Ahl and H. Arheden took part in methodology development and reproducibility calculations. A. Ambri, A. Johansson, D. Holmgren, H. Wahlander, and J. Framme helped with the recruitment and examination of subjects.

References