Impact of Obesity on Cardiac Geometry and Function in a Population of Adolescents

The Strong Heart Study

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OBJECTIVES
The goal here was to examine left ventricular (LV) geometry and function in a large, unselected group of adolescents with different degrees of abnormal body build, and verify whether possibly higher LV mass is compensatory for increased cardiac workload.

BACKGROUND
There is little information on how much the excess of body weight impacts LV geometry and function in populations of adolescents.

METHODS
Anthropometric, laboratory, and Doppler echocardiographic parameters of cardiac geometry and function were obtained in 460 adolescent participants (age 14 to 20 years, 245 female participants, 27 hypertensive, 10 with diabetes) from the Strong Heart Study. Body build was classified based on 85th and 95th percentiles of body mass index (BMI)-for-age charts.

RESULTS
Range of BMI was 16.3 to 56.5 kg/m² (28.8 ± 8.3 kg/m²); 114 participants (24.9%) fell within the 85th percentile of BMI distribution (normal weight [NW]), 113 (24.6%) fell between 85th and 95th percentile (overweight [OW]), and 223 (48.5%) fell above the 95th percentile (obese [OB]). Obese participants were older than OW and NW subjects (p < 0.01), without differences in heart rate. Both OW and OB had greater LV diameter and mass than NW (all p < 0.05). Left ventricular hypertrophy was more prevalent in the OB (33.5%) and OW (12.4%), as compared with NW participants (3.5%, p < 0.001), largely compensating increased cardiac workload. However, OB subjects had four-fold higher probability of carrying an LV mass exceeding values compensatory for their cardiac workload (p < 0.001), a feature associated with lower ejection fraction, myocardial contractility, and greater force developed by left atrium to complete LV filling (all p < 0.05).

CONCLUSIONS
While in OW adolescents increased levels of LV mass are appropriate to compensate their higher hemodynamic load, in OB increase in LV mass exceeds this need and is associated with mildly reduced LV myocardial performance and increased left atrial force to contribute to LV filling. (J Am Coll Cardiol 2006;47:2267–73) © 2006 by the American College of Cardiology Foundation

The American Heart Association has recently stressed the importance of obesity as a modifiable, independent risk factor for coronary artery disease, ventricular dysfunction, congestive heart failure, and cardiac arrhythmias (1). A published survey on prevalence and trends in overweight among U.S. children and adolescents (2) reported a 15.5% prevalence among 12- through 19-year-olds in 1999 to 2002 with increases of more than 10% in African Americans and Mexican Americans as compared with 1982. Overweight adolescents very often maintain overweight in adulthood (3). Similarly, adolescent obesity is strongly related to adult obesity and may progress to type 2 diabetes and/or hypertension (4). Adult obesity has been shown to be associated with increased left ventricular (LV) mass and both systolic and diastolic dysfunction (5–7), all important predictors of adverse cardiovascular outcome and identifying a pre-clinical cardiovascular disease (8). The distribution of body fat has also been shown to be an important determinant of cardiovascular phenotype in both adults (9) and adolescents (10).

Increased left ventricular mass (LVM) in overweight children and adolescents has been described to be strongly associated with increased values of systolic blood pressure and lean body mass, suggesting that left ventricular hypertrophy (LVH) often reported in obese children and adolescents might represent a compensatory response to increased cardiac workload (11). This would be consistent with the

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LV geometry and function in a large unselected population
response for increased cardiac workload. Thus, we examined
the question of whether the increase in LVM
on cardiac geometry and function in adolescents, and
the impact of increasingly severe abnormalities of body build
date, no unselected population-based study has examined
adverse outcome, independently of clear-cut LVH (13). To
associate with high-risk cardiovascular phenotype and
pensate cardiac workload, and in adults this excess is
LVM exceeds the amount that would be needed to com-
sampling frames (overall participation rate
13 tribes age 45 to 74 years were recruited from defined
communities in Arizona, Oklahoma, and North/South
Dakota. As previously described (14), 4,549 members from
three tribes age 45 to 74 years were recruited from defined
sampling frames (overall participation rate = 61%) for
baseline examination (July 1989 and January 1992). The
fourth SHS examination, conducted in 2001 to 2003,
enrolled members of large three-generation families that
included a total of 460 unselected adolescent participants
(53.2% female participants, age 14 to 20 years), who
comprise the population of the present study.

Physical examination and laboratory testing. The exam-
ination included medical history, computerized electrocar-
diogram, measurement of brachial blood pressure, fasting
glucose and insulin, glycosylated hemoglobin, lipid and
lipoprotein levels, and a 2-h, 75-g glucose tolerance test.
Blood pressure was measured after recommendations of the
Fifth Report of the Joint National Committee on Preven-
tion, Detection, Evaluation, and Treatment of High Blood
Pressure (15). Laboratory tests and anthropometric mea-
sures (weight, height, and waist circumferences) were taken
as previously reported (15). Fat-free mass and adipose body
mass were estimated by the use of an RJL impedance meter
(model B14101, RJL Equipment Co., Clinton Township,
Missouri) and equations based on total body water validated
in the American Indian population (16).

Evaluation of abnormal body weight, blood pressure, and
metabolic syndrome. Body mass index (BMI)-for-age charts developed by the National Center for Health Statis-
tics (NCHS) (17) were used to classify body weight groups.
The 85th and 95th percentiles of the normal distribution
were used to identify risk of overweight and clear-cut
overweight, respectively, according to the NCHS charts. For
convenience, we will use the term overweight to label the
NCHS “risk of overweight” class and the terms obese for the
NCHS “overweight” class. Guidelines correction was
applied (18) so that the limit separating overweight and
obesity did not exceed a BMI of 30 kg/m².

For adolescents up to 18 years of age, normal blood
pressure was assessed by using age-, gender-, and height-
specific partition values according to the Fourth Report on the
Diagnosis, Evaluation, and Treatment of High Blood
Pressure in Children and Adolescents (19). For adolescents
over 18 years of age, recommendations from the Seventh
Report of the Joint National Committee on Prevention,
Detection, Evaluation, and Treatment of High Blood
Pressure were used (20). Because single blood pressure measure-
ments were available, we did not use the terms hypertension
and pre-hypertension for children and adolescents. Devia-
tions from normal values will be called high or high-normal
casual blood pressure (21). Prevalence of metabolic syn-
drome was assessed according to Adult Treatment Panel III
criteria (22) modified for adolescent population (23).

Echocardiography. Echocardiograms were performed by
expert sonographers, according to standardized methods
and reviewed off-line using computerized review station
with digitizing tablet and monitor screen overlay for cali-
bration and performance of needed measurements (24).

Left ventricular internal dimension, septal and posterior
wall thickness were measured at end-diastole and end-
systole using American Society of Echocardiography rec-
ommendations on up to three cycles (25,26). As previously
described (27), left atrial anteroposterior diameter was
measured from the parasternal long-axis view in end-
systole, and aortic root diameter was measured at level of the
sinus of Valsalva in end-diastole.

Standard formula was used to calculate LVM (28,29),
which was normalized for body height in meters to the
allometric power of 2.7, which linearizes the relations
between LVM and height and identifies the impact of
obesity (30).

To evaluate the concentricity of LV geometry, myocardial
thickness (wall + septum) was divided by LV minor axis
diameter) to generate a relative wall thickness (RWT).
Because normal RWT increases with age (31), its raw value
was normalized to age 10 years or 46 years (RWTₐₐ) by the
following equations (31):
RWTₐ = RWT − 0.005 · (age − 10) up to age 18

RWTₐ = RWT − 0.0016 · (age − 46) above age 18

A subgroup of 92 untreated participants (56 male participants and 36 female participants; age 14 to 20 years; mean age 16.80 ± 1.40 years without obesity, diabetes, high or high-normal blood pressure or dyslipidemia was elected as the normal reference group and was analyzed to derive the gender-specific 95th percentiles to define LVH in this adolescent population (40.75 g/m².7 for male participants and 38.49 g/m².7 for female participants).

To establish whether the possible increase in LVM was consistent with the increase in cardiac workload in groups with body builds abnormalities, we calculated the individual theoretical ideal value of LVM (LVMₚ), using age-stratum specific equations generated by stroke work (systolic blood pressure times stroke volume times 0.014, in grammeters/beat), gender (male gender = 1; female gender = 2) and height in meters to the 2.7 power. Equations were (13):

LVMₚ = 39.95 + 14.61 × height + 0.65 × stroke work − 17.17 × gender, up to age 18

LVMₚ = 55.37 + 6.64 × height + 0.64 × stroke work − 18.07 × gender, above age 18

The value of LVM directly measured from echocardiograms was divided by LVMₚ and expressed in % of predicted value (Δ%LVM), as a measure of compensation for cardiac workload. Thus, a high value of Δ%LVM represented an excess of LVM relative to the value that would compensate and sustain the individual cardiac workload. For convenience, values of Δ%LVM were categorized using 5th and the 95th percentile of the distribution in the reference subgroup of 92 normal participants. Inadequately low LVM was defined as Δ%LVM <66%, while inappropriately high LVM was defined as Δ%LVM >109%.

We measured LV systolic function using a traditional assessment of LV chamber function with the shortening of LV minor axis measured at the endocardial level (endocardial shortening), and with a more complex measure of shortening at the mid-wall level (mid-wall shortening), which reflects more accurately myocardial contractile force, independent of LV concentric geometry (32), which has been demonstrated to preserve LV chamber function, when myocardial contractility is depressed (33).

Stroke volume was determined by an invasively validated Doppler method (34) and used to calculate cardiac output.

Left ventricular diastolic properties were assessed by Doppler interrogation of transmitral peak velocity at early (E) and late (A) LV filling and their ratio. Isovolumic relaxation time was measured between mitral valve closure and aortic opening. We also measured the force that left atrium develops to complete LV filling (left atrial systolic force), according to previously reported methods (35).

Statistical analysis. Statistical analyses were performed using SPSS 12.00 (SPSS Inc., Chicago, Illinois) software. Data are presented as mean ± SD for continuous variables and as proportions for categorical variables. Chi-square statistics were used to determine differences for categorical variables (with Monte Carlo method to compute exact two-tailed alpha value, when appropriate). One-way analysis of variance and analysis of covariance were used to compare continuous variables. When needed, Ryan–Einot-Gabriel-Welsch F post-hoc test was used, or main effects were compared by Sidak’s adjustment of p value (36). The p values were shown for post-hoc tests. Two-tailed p < 0.05 was considered statistically significant.

RESULTS

Clinical and metabolic characteristics. Of the 460 participants (mean age 17.36 ± 1.44 years; BMI range 16.3 to

| Table 1. Clinical Characteristics of Normal Weight, Overweight, and Obese Adolescents |
|---------------------------------|----------------|----------------|
| Age (yrs) | 16.8 ± 1.3 | 17.0 ± 1.4 | 17.7 ± 1.4* |
| Women (%) | 38.6 | 38.1 | 64.5* |
| Fat-free mass (kg) | 46.1 ± 8.1 | 53.2 ± 93† | 55.9 ± 13.8‡ |
| Adipose mass (kg) | 12.2 ± 4.3 | 22.4 ± 6.2‡ | 41.1 ± 17.1‡ |
| Waist circumference (cm) | 74.3 ± 6.9 | 87.1 ± 7.6† | 104.8 ± 16.0‡ |
| Systolic blood pressure (mm Hg) | 108.3 ± 10.1 | 115.2 ± 9.9† | 115.6 ± 11.8* |
| Diastolic blood pressure (mm Hg) | 66.3 ± 8.5 | 67.9 ± 8.9† | 71.6 ± 10.2* |
| Heart rate (beats/min) | 64.2 ± 11.5 | 65.7 ± 8.9 | 65.8 ± 11.3 |
| Cigarette smoking (%) | 25.4 | 25.7 | 24.9 |
| Alcohol drinking (%) | 56.1 | 58.4 | 54.9 |
| High-normal casual blood pressure (%) | 16.7 | 31.9† | 35.2‡ |
| High casual blood pressure (%) | 2.6 | 4.4† | 9.9‡ |
| Diabetes (%) | 0.0 | 0.9 | 1.7‡ |

One-way analysis of variance with Ryan–Einot-Gabriel-Welsch F post-hoc test. *p < 0.05 between obese and normal weight; †p < 0.05 between normal and overweight; ‡p < 0.05 between overweight and obese.
56.5 kg/m²), 113 (24.6% of study population) were overweight (38.1% female participants) and 233 (50.7% of study population) were normal weight (38.1% female participants) and 233 (50.7% of study population; 41.6% girls) and high blood pressure as well were more frequent in both strata of abnormal BMI (all p < 0.05), whereas no difference was found for RWT. One-third of obese adolescents had LVH at a mean age <18 years.

As shown in Table 4, stroke volume and cardiac output exhibited step-wise increase from normal weight to overweight and obese participants (all p < 0.05). Both ejection fraction and mid-wall shortening were mildly lower in obese adolescents than in the other groups. No differences were found in the LV filling pattern, but obese adolescents exhibited significantly higher left atrial systolic force than the other groups (p < 0.05).

No one of the 460 adolescents showed significant aortic regurgitation, while 20 participants (3.9% of study population) had mild (n = 18) or mild-to-moderate (n = 2) mitral regurgitation. Prevalence of mitral regurgitation was 2.8% in normal weight, 5.3% in overweight, and 3.9% in obese participants (p = NS). Additional analysis comparing cardiac geometry and function, after excluding patients with mitral regurgitation, confirmed our results.

### Table 2. Metabolic Characteristics of Normal Weight, Overweight, and Obese Adolescents

<table>
<thead>
<tr>
<th></th>
<th>Normal Weight (n = 114)</th>
<th>Overweight (n = 113)</th>
<th>Obese (n = 223)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fasting glucose (mg/dl)</strong></td>
<td>89.3 ± 9.6</td>
<td>90.6 ± 10.6</td>
<td>94.1 ± 24.0†</td>
</tr>
<tr>
<td><strong>Plasma insulin (IU/ml)</strong></td>
<td>11.1 ± 13.1</td>
<td>12.7 ± 8.8</td>
<td>23.5 ± 28.1†‡</td>
</tr>
<tr>
<td><strong>Hb1Ac (%)</strong></td>
<td>5.0 ± 0.2</td>
<td>5.2 ± 0.7</td>
<td>5.5 ± 1.5†‡</td>
</tr>
<tr>
<td><strong>Triacylglycerols (mmol/l)</strong></td>
<td>95.85 ± 48.01</td>
<td>105.54 ± 51.25</td>
<td>147.05 ± 60.14†‡</td>
</tr>
<tr>
<td><strong>HDL cholesterol (mmol/l)</strong></td>
<td>50.17 ± 12.57</td>
<td>49.91 ± 10.23</td>
<td>46.29 ± 12.85†‡</td>
</tr>
<tr>
<td><strong>Serum creatinine (mmol/l)</strong></td>
<td>0.80 ± 0.15</td>
<td>0.81 ± 0.13</td>
<td>0.75 ± 0.15</td>
</tr>
<tr>
<td><strong>Metabolic syndrome (%)</strong></td>
<td>2.1</td>
<td>10.6‡</td>
<td>51.1*‡</td>
</tr>
</tbody>
</table>

One-way analysis of variance with Ryan-Einot-Gabriel-Welsch F post-hoc test. *p < 0.05 between obese and normal weight; †p < 0.05 between overweight and obese; ‡p < 0.05 between normal weight and overweight.

Hb1Ac = hemoglobin 1Ac; HDL = high-density lipoprotein.

### Table 3. Cardiac Geometry in Normal Weight, Overweight, and Obese Adolescents

<table>
<thead>
<tr>
<th></th>
<th>Normal Weight (n = 114)</th>
<th>Overweight (n = 113)</th>
<th>Obese (n = 223)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LV diameter (cm)</strong></td>
<td>5.08 ± 0.39</td>
<td>5.25 ± 0.37*</td>
<td>5.31 ± 0.44†‡</td>
</tr>
<tr>
<td><strong>Aortic root (cm)</strong></td>
<td>2.97 ± 0.25</td>
<td>3.02 ± 0.25*</td>
<td>3.08 ± 0.28†‡</td>
</tr>
<tr>
<td><strong>Left atrial diameter (cm)</strong></td>
<td>3.08 ± 0.32</td>
<td>3.34 ± 0.30*</td>
<td>3.64 ± 0.46†‡</td>
</tr>
<tr>
<td><strong>Relative wall thickness</strong></td>
<td>0.27 ± 0.03</td>
<td>0.27 ± 0.03</td>
<td>0.28 ± 0.04</td>
</tr>
<tr>
<td><strong>LV mass (g)</strong></td>
<td>131.78 ± 30.15</td>
<td>148.98 ± 37.40*</td>
<td>165.03 ± 41.07‡‡</td>
</tr>
<tr>
<td><strong>LV mass index (g/m²)</strong></td>
<td>30.21 ± 5.17</td>
<td>33.04 ± 5.57*</td>
<td>35.97 ± 7.60‡‡</td>
</tr>
<tr>
<td><strong>Concentric geometry (%)</strong></td>
<td>0.5</td>
<td>1.8</td>
<td>4.4‡‡</td>
</tr>
<tr>
<td><strong>LV hypertrophy (%)</strong></td>
<td>3.5</td>
<td>12.4*</td>
<td>33.5‡‡</td>
</tr>
<tr>
<td><strong>Inappropriate LV mass (%)</strong></td>
<td>6.3</td>
<td>9.8</td>
<td>27.2‡‡</td>
</tr>
</tbody>
</table>

Analysis of covariance with Sidak’s adjustment of means for age, gender, systolic and diastolic blood pressure, heart rate, and height (as a surrogate of body growth). *p < 0.05 between normal weight and overweight; †p < 0.05 between obese and normal weight; ‡p < 0.05 between overweight and obese. LV = left ventricular.

**Cardiovascular phenotype.** Left ventricular chamber size (diameter) was similarly greater in both obese and overweight than in normal weight adolescents (Table 3). Similarly, aortic root diameter, left atrial dimension, and LVM were greater in overweight and even more in obese than in normal weight adolescents (all p < 0.05), whereas no difference was found for RWT. One-third of obese adolescents had LVH at a mean age <18 years.

As shown in Table 4, stroke volume and cardiac output exhibited step-wise increase from normal weight to overweight and obese participants (all p < 0.05). Both ejection fraction and mid-wall shortening were mildly lower in obese adolescents than in the other groups. No differences were found in the LV filling pattern, but obese adolescents exhibited significantly higher left atrial systolic force than the other groups (p < 0.05).

None of the 460 adolescents showed significant aortic regurgitation, while 20 participants (3.9% of study population) had mild (n = 18) or mild-to-moderate (n = 2) mitral regurgitation. Prevalence of mitral regurgitation was 2.8% in normal weight, 5.3% in overweight, and 3.9% in obese participants (p = NS). Additional analysis comparing cardiac geometry and function, after excluding patients with mitral regurgitation, confirmed our results.
cess of LVM relatively to their cardiac workload. The prevalence of clear-cut LVH was 12% in overweight and 34% in obese individuals (both p < 0.001 vs. normal weight control subjects), whereas a clear-cut excess of LVM was not statistically different in normal weight and overweight participants (6% and 10%, respectively), whereas it was more than four-fold higher in obese (27%) than in normal weight adolescents (p < 0.001).

**DISCUSSION**

Obesity is an increasingly common condition in industrialized and developing countries, affecting both adults (1) and children (37) and increasing the social burden due to incident cardiovascular disease. Obesity predisposes to hypertension because of concomitant metabolic and hemodynamic abnormalities leading to inadequate lowering of systemic resistance and, therefore, to more severe cardiocirculatory burden (38).

During the past two decades, we are registering an increasing incidence of overweight and obesity in adolescents (2). This increase represents a major public concern because overweight in adolescence has been associated with increased incidence of arterial hypertension, unfavorable lipid profile, diabetes, as well as increased risks of adult obesity (4). Recent studies have also reported increased prevalence of LVH in selected samples of children with or without arterial hypertension associated with increased BMI (39,40).

The present study has been carried out in a cohort of unselected adolescents from a specific ethnic group (American Indians). Even in this population-based study, the highest level of abnormality of body build (we have named conventionally obesity) was associated with worse lipid profile, glucose metabolism, and increased prevalence of metabolic syndrome.

Our findings demonstrate that, even among adolescents at a mean age under 18, severity of abnormality in body build also parallels early cardiac changes, including high prevalence of LVH and increased hemodynamic load, paralleling previous findings (30,38,39) and suggesting that increased LVM occurs to sustain the increased cardiac workload. This was apparently the case in the adolescent group with mild elevation of body weight (classified as “risk of overweight” and called for convenience “overweight” in the present study). In contrast, in the adolescent group with more severe elevation of body weight (classified as “overweight” and called for convenience “obese” in the present study), the level of increased LVM substantially exceeded the need to compensate for cardiac workload, resulting in a markedly higher prevalence of inappropriate LVM. As already demonstrated in adults, the phenotype of excess LVM was also associated with reduced LV systolic function and myocardial performance. In contrast with adults, however, traditional indexes of LV filling were normal and only studying left atrial performance could reveal a slight abnormality in the late phase of LV filling.

The demonstration that at higher stages of abnormal body weight increase in LVM is not depending on hemodynamic load in a cohort of adolescents, which has not been yet exposed for a long time to overload, reinforces the view that development of LVH also depends on non-hemodynamic factors. This is particularly interesting in the present population, not only for the young age, but also because of the relatively low prevalence of abnormal casual blood pressure, indicating that non-hemodynamic factors play a significant role in determining the inappropriate increase in LVM found in the obese subgroup. This observation, paired with the high prevalence of metabolic syndrome, exceeding 50%, in the obese adolescents, suggests that, in frankly obese participants, the increase in LVM is a response not only to substantially increased hemodynamic load but also to possible neurohormonal effects of clustered metabolic factors influencing LV growth.

**Study limitations.** There are limitations in this study that need to be highlighted. The analysis was performed in an American Indian population and whether these results can be generalized to other ethnic groups needs to be demonstrated. However, similar analyses previously performed in other ethnic groups, as Caucasians and African Americans, have suggested similar association between LVM and adiposity, independently of other cardiovascular risk factors (40–42). Also, determination of Tanner stage was not...
performed, and the relation between body maturation and cardiac geometry/function could not be investigated; however, all participants were ≥14 years of age and, therefore, most probably all post-pubertal.

Blood pressure was measured by standardized methods during a single clinical visit, instead of three distinct measurements as suggested by current guidelines, causing participants with seldom increase in blood pressure to be included in the high blood pressure group. For this reason, we decided to avoid the definition of hypertension, while using the definition of “high casual blood pressure.” We have previously shown that high casual blood pressure in children is associated with LV geometric abnormalities similar to those found in the presence of sustained hypertension (21). Eventually, the prevalence of high blood pressure/hypertension in this population is low, and any possible misclassification is unlikely to have substantially influenced the results.

Conclusions. In an unselected cohort of adolescents, participants with high values of BMI have increased values of LVM and a dramatically higher prevalence of LVH. While in overweight participants the increased levels of LVM are appropriate for their higher hemodynamic load, in obese adolescents this increase is disproportionately high and is associated with mildly reduced LV chamber and mid-wall function, and increased left atrial contribution to LV filling. Early intervention during childhood and adolescence to reduce the prevalence of obesity and prevent the transition from overweight to overt obesity might represent a crucial step in averting unfavorable cardiac phenotype present in the obese adolescents.

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