

Pediatric and Adolescent Heart Disease

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/m ² (28.8 ± 8.3 kg/m ²); 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

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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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Manuscript received October 18, 2005; revised manuscript received December 5, 2005, accepted December 13, 2005.

Abbreviations and Acronyms

BMI	=	body mass index
LV	=	left ventricle/ventricular
LVH	=	left ventricular hypertrophy
LVM	=	left ventricular mass
LVM _p	=	predicted left ventricular mass
NCHS	=	National Center for Health Statistics
RWT	=	relative wall thickness
RWT _a	=	age-adjusted relative wall thickness
SHS	=	Strong Heart Study
Δ%LVM	=	percent of predicted left ventricular mass

notion that up to 82% to 86% of variability of LVM can be explained by phenotypic variations in body size and cardiac workload (12). There are conditions, however, in which LVM exceeds the amount that would be needed to compensate cardiac workload, and in adults this excess is associated with high-risk cardiovascular phenotype and adverse outcome, independently of clear-cut LVH (13). To date, no unselected population-based study has examined the impact of increasingly severe abnormalities of body build on cardiac geometry and function in adolescents, and resolved the question of whether the increase in LVM reported in clinical settings represents a compensatory response for increased cardiac workload. Thus, we examined LV geometry and function in a large unselected population of adolescents with different degrees of abnormal body size.

METHODS

Study population. The Strong Heart Study (SHS) is a longitudinal study of cardiovascular risk factors and prevalent and incident cardiovascular disease in American Indian communities in Arizona, Oklahoma, and North/South Dakota. As previously described (14), 4,549 members from 13 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 examination included medical history, computerized electrocardiogram, 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 Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (15). Laboratory tests and anthropometric measures (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 Statistics (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 measurements were available, we did not use the terms hypertension and pre-hypertension for children and adolescents. Deviations from normal values will be called high or high-normal *casual* blood pressure (21). Prevalence of metabolic syndrome 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 calibration 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 recommendations 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 (RWT_a) by the following equations (31):

$$RWT_a = RWT - 0.005 \cdot (\text{age} - 10) \text{ up to age 18}$$

$$RWT_a = RWT - 0.0016 \cdot (\text{age} - 46) \text{ above age 18}$$

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 ($40.75 \text{ g/m}^{2.7}$ for male participants and $38.49 \text{ g/m}^{2.7}$ 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 (LVM_p), 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):

$$LVM_p = 39.95 + 14.61 \times \text{height} + 0.65 \times \text{stroke work} - 17.17 \times \text{gender, up to age 18}$$

$$LVM_p = 55.37 + 6.64 \times \text{height} + 0.64 \times \text{stroke work} - 18.07 \times \text{gender, above age 18}$$

The value of LVM directly measured from echocardiograms was divided by LVM_p and expressed in % of predicted value ($\Delta\%LVM$), as a measure of compensation for cardiac workload. Thus, a high value of $\Delta\%LVM$ represented an excess of LVM relative to the value that would compensate and sustain the individual cardiac workload. For convenience, values of $\Delta\%LVM$ 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 $\Delta\%LVM < 66\%$, while inappropriately high LVM was defined as $\Delta\%LVM > 109\%$.

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 \pm 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

	Normal Weight (n = 114)	Overweight (n = 113)	Obese (n = 223)
Age (yrs)	16.8 ± 1.3	17.0 ± 1.4	$17.7 \pm 1.4^*$
Women (%)	38.6	38.1	64.5*
Fat-free mass (kg)	46.1 ± 8.1	$53.2 \pm 9.3^\ddagger$	$55.9 \pm 13.8^{*\ddagger}$
Adipose mass (kg)	12.2 ± 4.3	$22.4 \pm 6.2^\ddagger$	$41.1 \pm 17.1^{*\ddagger}$
Waist circumference (cm)	74.3 ± 6.9	$87.1 \pm 7.6^\ddagger$	$104.8 \pm 16.0^{*\ddagger}$
Systolic blood pressure (mm Hg)	108.3 ± 10.1	$115.2 \pm 9.9^\ddagger$	$115.6 \pm 11.8^*$
Diastolic blood pressure (mm Hg)	66.3 ± 8.5	$69.7 \pm 8.9^\ddagger$	$71.6 \pm 10.2^*$
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.

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

	Normal Weight (n = 114)	Overweight (n = 113)	Obese (n = 223)
Fasting glucose (mg/dl)	89.3 ± 9.6	90.6 ± 10.6	94.1 ± 24.0*†
Plasma insulin (IU/ml)	11.1 ± 13.1	12.7 ± 8.8	23.5 ± 28.1*†
Hb1Ac (%)	5.0 ± 0.2	5.2 ± 0.7	5.5 ± 1.5*†
Triacylglycerols (mmol/l)	95.85 ± 48.01	105.54 ± 51.25	147.05 ± 60.14*†
HDL cholesterol (mmol/l)	50.17 ± 12.57	49.91 ± 10.23	46.29 ± 12.85*†
Serum creatinine (mmol/l)	0.80 ± 0.15	0.81 ± 0.13	0.75 ± 0.15
Metabolic syndrome (%)	2.1	10.6‡	53.1*†

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.

56.5 kg/m²), 113 (24.6% of study population) were overweight (38.1% female participants) and 233 (50.7% of study population) were obese (67.8% female participants); high-normal casual blood pressure was present in 110 adolescents (23.9% of study population; 41.6% girls) and high blood pressure in 27 (5.8% of study population, 35.5% girls). Diabetes was diagnosed in 10 (2.2% of study population, 1 female participant). Four hypertensive participants and three with diabetes were on treatment.

Obese adolescents were slightly older and more frequently female patients than normal weight and overweight adolescents (Table 1). Both overweight and obese participants had greater adipose mass, fat-free mass, and waist circumference, and similarly higher blood pressure than normal weight adolescents (all p < 0.05). No differences between groups were found in smoking habit or alcohol drinking. High-normal and high casual blood pressure and diabetes as well were more frequent in both strata of abnormal BMI (all p < 0.005).

Obese adolescents had significantly higher values of fasting glucose, plasma insulin, hemoglobin 1Ac, and more unfavorable lipid profile (higher total triglycerides and lower high-density lipoprotein). In contrast, overweight adolescents exhibited a metabolic profile similar to normal weight participants. Obesity was associated with a markedly higher prevalence of metabolic syndrome (Table 2).

Cardiovascular phenotype. Left ventricular chamber size (diameter) was similarly greater in both obese and over-

weight 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.

APPROPRIATENESS OF INCREASED LV MASS. No overweight or obese participant had values of LVM inadequately low for their cardiac workload. In contrast, while LVM index was progressively higher in overweight and obese adolescents, only obese participants exhibited ex-

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

	Normal Weight (n = 114)	Overweight (n = 113)	Obese (n = 223)
LV diameter (cm)	5.08 ± 0.39	5.25 ± 0.37*	5.31 ± 0.44†
Aortic root (cm)	2.97 ± 0.25	3.02 ± 0.25*	3.08 ± 0.28†‡
Left atrial diameter (cm)	3.08 ± 0.32	3.34 ± 0.30*	3.64 ± 0.46†‡
Relative wall thickness	0.27 ± 0.03	0.27 ± 0.03	0.28 ± 0.04
LV mass (g)	131.78 ± 30.15	148.98 ± 37.40*	165.03 ± 41.07†‡
LV mass index (g/m ^{2.7})	30.21 ± 5.17	33.04 ± 5.57*	35.97 ± 7.60†‡
Concentric geometry (%)	0.5	1.8	4.4†‡
LV hypertrophy (%)	3.5	12.4*	33.5†‡
Inappropriate LV mass (%)	6.3	9.8	27.2†‡

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.

Table 4. Cardiac Function in Normal Weight, Overweight, and Obese Adolescents

	Normal Weight (n = 114)	Overweight (n = 113)	Obese (n = 223)
Stroke volume (ml)	73.11 ± 10.44	76.53 ± 10.80*	79.51 ± 12.80†‡
Cardiac output (l/min)	4.82 ± 0.91	5.14 ± 0.96*	5.31 ± 1.12†‡
Ejection fraction (%)	61.10 ± 4.68	60.13 ± 4.98	59.43 ± 4.75†
Stress-corrected mid-wall shortening (%)	116.27 ± 9.18	115.28 ± 9.64	113.55 ± 10.26†
Mitral E peak (cm/s)	95.27 ± 12.92	94.56 ± 9.70	98.65 ± 12.81
Mitral A peak (cm/s)	48.19 ± 15.12	47.58 ± 14.23	48.45 ± 17.32
Mitral E/A ratio	2.10 ± 0.55	2.09 ± 0.45	2.13 ± 0.40
Isovolumic relaxation time (ms)	78.69 ± 11.43	79.56 ± 12.61	79.64 ± 11.92
Left atrial systolic force (kdynes)	4.77 ± 2.14	5.11 ± 2.38	6.01 ± 2.88†‡

Analysis of covariance with Sidak's adjusted 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.

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.

Acknowledgments

The authors would like to thank the Indian Health Service facilities, the Strong Heart Study participants, and the participating tribal communities for the extraordinary cooperation and involvement that made this study possible.

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REFERENCES

- Klein S, Burke LE, Bray GA, et al. American Heart Association Council on Nutrition, Physical Activity, and Metabolism; American College of Cardiology Foundation. Clinical implications of obesity with specific focus on cardiovascular disease: a statement for professionals from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation* 2004;110:2952-67.
- Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among U.S. children and adolescents, 1999-2000. *JAMA* 2002;288:1728-32.
- Guo SS, Roche AF, Chumlea WC, Gardner JD, Siervogel RM. The predictive value of childhood body mass index values for overweight at age 35 y. *Am J Clin Nutr* 1994;59:810-9.
- Guo SS, Wu W, Chumlea WC, Roche AF. Predicting overweight and obesity in adulthood from body mass index values in childhood and adolescence. *Am J Clin Nutr* 2002;76:653-8.
- Alpert MA, Lambert CR, Terry BE, et al. Influence of left ventricular mass on left ventricular diastolic filling in normotensive morbid obesity. *Am Heart J* 1995;130:1068-73.
- de Simone G, Devereux RB, Mureddu GF, et al. Influence of obesity on left ventricular midwall mechanics in arterial hypertension. *Hypertension* 1996;28:276-83.
- Mureddu GF, de Simone G, Greco R, Rosato GF, Contaldo F. Left ventricular filling in arterial hypertension. Influence of obesity and hemodynamic and structural confounders. *Hypertension* 1997;29:544-50.
- Devereux RB, Alderman MH. Role of preclinical cardiovascular disease in the evolution from risk factor exposure to development of morbid events. *Circulation* 1993;88:1444-55.
- de Simone G, Devereux RB, Kizer JR, et al. Body composition and fat distribution influence systemic hemodynamics in the absence of obesity: the HyperGEN study. *Am J Clin Nutr* 2005;81:757-61.
- Daniels SR, Khoury PR, Morrison JA. Utility of different measures of body fat distribution in children and adolescents. *Am J Epidemiol* 2000;152:1179-84.
- Daniels SR, Kimball TR, Morrison JA, Khoury P, Witt S, Meyer RA. Effect of lean body mass, fat mass, blood pressure, and sexual maturation on left ventricular mass in children and adolescents. Statistical, biological, and clinical significance. *Circulation* 1995;92:3249-54.
- de Simone G, Devereux RB, Kimball TR, et al. Interaction between body size and cardiac workload: influence on left ventricular mass during body growth and adulthood. *Hypertension* 1998;31:1077-82.
- de Simone G, Verdecchia P, Pede S, Gorini M, Maggioni AP. Prognosis of inappropriate left ventricular mass in hypertension: the MAVI study. *Hypertension* 2002;40:470-6.
- Lee ET, Welty TK, Fabsitz R, et al. The Strong Heart study: a study of cardiovascular disease in American Indians: design and methods. *Am J Epidemiol* 1990;131:1141-55.
- Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V). The fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V). *Arch Intern Med* 1993;153:154-83.
- Stolarczyk LM, Heyward VH, Hicks VL, Baumgartner RN. Predictive accuracy of bioelectric impedance in estimating body composition of Native American women. *Am J Clin Nutr* 1994;59:964-70.
- Kuczmarski RJ, Ogden CL, Guo SS, et al. 2000 CDC growth charts for the United States: methods and development. *Vital Health Stat* 2002;246:1-190.
- Must A, Dallal GE, Dietz WH. Reference data for obesity: 85th and 95th percentiles of body mass index (wt/ht²) and triceps skinfold thickness (erratum appears in: *Am J Clin Nutr* 1991;54:773). *Am J Clin Nutr* 1991;53:839-46.
- National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics* 2004;114:555-76.
- Chobanian AV, Bakris GL, Black HR, et al. National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003;289:2560-72.
- de Simone G, Mureddu GF, Greco R, et al. Relations of left ventricular geometry and function to body composition in children with high casual blood pressure. *Hypertension* 1997;30:377-82.
- National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002;106:3143-421.
- De Ferranti SD, Gauvreau K, Ludwig DS, Neufeld EJ, Newburger JW, Rifai N. Prevalence of the metabolic syndrome in American

- adolescents: findings from the Third National Health and Nutrition Examination survey. *Circulation* 2004;110:2494-7.
24. Devereux RB, Roman MJ, de Simone G, et al. Relations of LV mass to demographic and hemodynamic variables in American Indians—the Strong Heart Study. *Circulation* 1997;96:1416-23.
 25. Sahn DJ, De Maria A, Kisslo J, Weyman A. The Committee on M-mode Standardization of the American Society of Echocardiography—recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation* 1978;58:1072-83.
 26. Schiller NB, Shah PM, Crawford M, et al. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr* 1989;2:358-67.
 27. Ilercil A, O'Grady MJ, Roman MJ, et al. Reference values for echocardiographic left ventricular measurements in urban and rural populations of differing ethnicity: the Strong Heart Study. *J Am Soc Echocardiogr* 2001;14:606-11.
 28. Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy—comparison to necropsy findings. *Am J Cardiol* 1987;56:450-8.
 29. Daniels SR, Meyer RA, Liang YC, Bove KE. Echocardiographically determined left ventricular mass index in normal children, adolescents and young adults. *J Am Coll Cardiol* 1988;12:703-8.
 30. de Simone G, Daniels SR, Devereux RB, et al. Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight. *J Am Coll Cardiol* 1992;20:1251-60.
 31. de Simone G, Daniels SR, Kimball TR, et al. Evaluation of concentric left ventricular geometry in humans: evidence for age-related systematic underestimation. *Hypertension* 2005;45:64-8.
 32. de Simone G, Devereux RB, Roman MJ, et al. Assessment of left ventricular function by the midwall fractional shortening/end-systolic stress relation in human hypertension. *J Am Coll Cardiol* 1994;23:1444-51.
 33. de Simone G, Devereux RB, Celentano A, Roman MJ. Left ventricular chamber and wall mechanics in the presence of concentric geometry. *J Hypertens* 1999;17:1001-6.
 34. Dubin J, Wallerson DC, Cody RJ, Devereux RB. Comparative accuracy of Doppler echocardiographic methods for clinical stroke volume determination. *Am Heart J* 1990;120:116-23.
 35. Chinali M, de Simone G, Liu JE, et al. Left atrial systolic force and cardiac markers of pre-clinical disease in hypertensive patients: the HyperGEN study. *Am J Hypertens* 2005;18:898-904.
 36. Dawson B, Trapp RP. *Statistical Methods for Multiple Variables in Basic & Clinical Biostatistics*. 3rd edition. New York, NY: McGraw-Hill/Appleton & Lange, 2000:245-9.
 37. Williams CL, Hayman LL, Daniels SR, et al. Cardiovascular health in childhood: a statement for health professionals from the Committee on Atherosclerosis, Hypertension, and Obesity in the Young (AHOY) of the Council on Cardiovascular Disease in the Young, American Heart Association. *Circulation* 2002;106:143-60.
 38. Palmieri V, de Simone G, Arnett DK, et al. Relation of various degrees of body mass index in patients with systemic hypertension to left ventricular mass, cardiac output, and peripheral resistance (the Hypertension Genetic Epidemiology Network study). *Am J Cardiol* 2001;88:1163-8.
 39. Friberg P, Allansdotter-Johnsson A, Ambring A, et al. Increased left ventricular mass in obese adolescents. *Eur Heart J* 2004;25:987-92.
 40. Hanevold C, Waller J, Daniels S, Portman R, Sorof J. International Pediatric Hypertension Association. The effects of obesity, gender, and ethnic group on left ventricular hypertrophy and geometry in hypertensive children: a collaborative study of the International Pediatric Hypertension Association. *Pediatrics* 2004;113:328-33.
 41. Li X, Li S, Ulusoy E, Chen W, Srinivasan SR, Berenson GS. Childhood adiposity as a predictor of cardiac mass in adulthood: the Bogalusa Heart study. *Circulation* 2004;110:3488-92.
 42. Gutin B, Treiber F, Owens S, Mensah GA. Relations of body composition to left ventricular geometry and function in children. *J Pediatr* 1998;132:1023-7.