Childhood Adiposity as a Predictor of Cardiac Mass in Adulthood
The Bogalusa Heart Study
Xiangrong Li, MD, MSPH; Shengxu Li, MD; Eralp Ulusoy, MD; Wei Chen, MD, PhD; Sathanur R. Srinivasan, PhD; Gerald S. Berenson, MD

Background—The association between left ventricular hypertrophy, an independent predictor of cardiovascular (CV) morbidity and mortality, and CV risk factors has been well documented in childhood and in adulthood. However, information on the relationship between left ventricular mass (LVM) in adults and longitudinal measurements of CV risk factors from childhood to adulthood is limited.

Methods and Results—LVM was obtained with 2D M-mode echocardiography in a community-based sample of 467 young adults (71% white and 29% black) aged 20 to 38 years who were examined an average of 6 times for CV risk factors from childhood to adulthood. The average follow-up period was 21.5 years. The cumulative burden of each risk factor was calculated as the area under the curve for each individual. Compared with whites, blacks had greater LVM (indexed to height$^{27}$; $P<0.05$). In multiple regression analyses, adiposity (measured as body mass index) in childhood, adiposity and systolic blood pressure in adulthood, and the cumulative burden of adiposity and systolic blood pressure from childhood to adulthood were significant predictors of LVM index in young adults.

Conclusions—These observations, by showing that adiposity beginning in childhood is a consistent predictor of LVM in young adults, underscore the importance of obesity in the development of left ventricular hypertrophy and the need for early prevention. (Circulation. 2004;110:3488-3492.)

Key Words: ventricles ▪ adiposity ▪ blood pressure

It is now well known that cardiovascular (CV) risk factors are identifiable in childhood and are predictive of adult CV risk.$^{1-4}$ Longitudinal epidemiological studies have shown the utility of different traditional risk factors measured from childhood to adulthood in predicting subclinical CV changes in adults.$^{5-9}$ Among the subclinical measures, left ventricular mass (LVM) assessed by 2D M-mode echocardiography is recognized as an important and powerful predictor of CV morbidity and mortality, independent of other traditional risk factors.$^{10-12}$

The association between LVM and CV risk factors has been well documented in childhood and in adulthood.$^{13-18}$ Previously, we have shown that increased adiposity and blood pressure are the 2 major factors that lead to excessive cardiac growth beyond that of normal growth in children.$^{15}$ Similar findings were also observed in adults.$^{17}$ However, information linking childhood CV risk factor variables and their cumulative burden since childhood to LVM in young adults is lacking. Such information is vitally important for CV risk assessment beginning in youth. Longitudinal data from the Bogalusa Heart Study, a biracial (black-white) community-based investigation of the natural history of CV disease beginning in childhood,$^{2,3,15}$ provide a unique opportunity to examine the influence of traditional CV risk factors measured from childhood to adulthood on LVM measured in young adults.

Methods

Study Population
Between 1973 and 1996, 7 cross-sectional surveys of children aged 4 to 17 years and 5 surveys of young adults aged 18 to 38 years who participated as children were conducted in the biracial (65% white, 35% black) community of Bogalusa, La. This panel design, which was based on repeated cross-sectional examinations conducted approximately every 3 to 4 years, resulted in multiple observations during childhood and young adulthood and allowed an evaluation of the cumulative burden of risk factor variables beginning in childhood. During the last 6 months of the 1995 to 1996 survey of young adults (n=1420), M-mode echocardiography examination was performed on 467 subjects (71% white, 39% male) aged 20 to 38 years (average age 32.6 years) who were previously examined 2 to 12 times (average 6 times) since childhood. Compared with the rest of the study cohort, those who had echocardiography measurements had similar race, gender, and risk factor profiles ($P=0.19$ to 0.80), except that the latter group was 4 years older than the former ($P<0.001$). The average follow-up period was 21.5 years.
Written informed consent was obtained from parents or guardians in childhood and from the participants in adulthood. The Institutional Review Board of the Tulane University Health Sciences Center approved the protocol.

Examinations
All examinations followed essentially the same protocols. Subjects were instructed to fast for 12 hours before the screening, with compliance ascertained by interview on the morning of the exami-
nation. Height and weight were measured twice to within ±0.1 cm and ±0.1 kg, respectively, and the average values were used to calculate body mass index (BMI; kg/m²) as a measure of overall adiposity.

Replicate blood pressure measurements were obtained on the right arm of the subjects in a relaxed, sitting position. Arm measurements, length and circumference, were made during the examination to ensure proper cuff size. Systolic and diastolic blood pressure levels were recorded as the first, fourth (in children), and fifth (in adults) Korotkoff phases with mercury sphygmomanometers. Blood pressure levels were reported as the mean of 6 replicate readings taken by each of 2 randomly assigned and trained observers.

Laboratory Analysis
During 1973 to 1986, cholesterol and triglycerides levels were measured by the use of chemical procedures with a Technicon AutoAnalyzer II (Technicon Instrument Corp) according to the laboratory manual of the Lipid Research Clinics Program. Since 1987, these variables were determined with the Abbott VP instrument (Abbott Laboratories) by enzymatic procedures. Both chemical and enzymatic procedures met the performance requirements of the Lipid Standardization Program of the Centers for Disease Control and Prevention (CDC), Atlanta, Ga, which routinely monitors the accuracy of measurements of total cholesterol, triglycerides, and HDL cholesterol concentrations. Measurements on CDC-assigned quality control samples showed no consistent bias over time within or between surveys. Serum lipoprotein cholesterol were analyzed with a combination of heparin-calcium precipitation and agar-agarose gel electrophoresis procedures.

Left Ventricular Mass
LVM was assessed by 2D M-mode echocardiography with 2.25- and 3.5-MHz transducers according to the American Society of Echocardiography recommendations. Images were recorded on standard VHS videocassette tapes. All echocardiograms were digitized and measured on Tomtec/Freeland Cardiology Workstation digitizing systems (Tomtec/Freeland Systems). The coefficient of variation for interreader and intrareader variability for all measures of cardiac anatomy was <10%. LVM was calculated on the basis of the formula recommended by Devereux. The index of LVM to height²/³ (g/m³) was used to adjust for body size.

Statistical Methods
All data analyses were performed with SAS version 8.2. A general linear model was used to examine the race and gender differences of risk factor variables and LVM index, adjusted for covariates where appropriate. Whenever race-gender interaction was present, separate models were used by race or gender. The area under the curve (AUC) of serial measurements of each risk factor was used as a measure of cumulative risk burden from childhood to adulthood; its computation has been described previously in detail. Age was centered by subtracting 17.0, which was the average value of age in the total sample, to eliminate colinearity between the first- and second-order terms of age. Risk factors measured at the first and last examinations were used as childhood and adulthood values, respectively.

Pearson correlation coefficients were used to assess the relationships of LVM index to risk factors measured since childhood, with risk factors and LVM index standardized to race-, gender-, and age-specific z-scores; risk factor AUC values were standardized to race-, gender-, and average age-specific z-scores. LVM index and triglycerides were log-transformed before standardization. To ex-
Obesity affects the cardiac muscle through multiple mechanisms.\textsuperscript{30} Obesity alone can cause chronic volume overload and related greater cardiac output.\textsuperscript{31,32} Both hemodynamic and metabolic factors related to obesity can cause structure-function changes of the myocardium that result in increased LVM. Furthermore, hypertension associated with obesity affects the cardiac muscle through multiple mechanisms.\textsuperscript{33–35} Obesity-related oxidative stress, inflammation, and activation of the renin-angiotensin system can induce cardiac remodeling with increased cardiac myocyte and connective tissue matrix accumulation.\textsuperscript{33–35}

The causality of the observed association between childhood adiposity and adulthood LVM cannot be established by this observational study. Persistence of adiposity over time plays a role in this regard. Among CV risk factors, childhood BMI was highly correlated with adulthood BMI over a 21-year period ($r=0.54$, $P<0.001$). Nevertheless, as mentioned previously, the association of obesity with LVM in childhood has been established cross-sectionally\textsuperscript{13,14} and, more importantly, longitudinally.\textsuperscript{15}

In the present study, systolic blood pressure, either in adulthood or as a cumulative burden from childhood, was also an independent predictor of adult LVM index. Subjects with higher systolic blood pressure in childhood tended to have higher levels of LVM in adulthood, although the association was marginal ($P=0.086$) after adjustments for BMI and other covariates (Table 3). The adverse effect of elevated blood pressure to increase LVM is well documented.

### TABLE 1. Mean±SD of LVM Index in Adulthood and Risk Factors Measured Since Childhood

<table>
<thead>
<tr>
<th>Risk Factor Variables</th>
<th>White</th>
<th>Black</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male (n=128)</td>
<td>Female (n=206)</td>
<td>Male (n=56)</td>
</tr>
<tr>
<td>LVM, g/m$^2$</td>
<td>30.1±8.9</td>
<td>31.3±12.3</td>
<td>32.3±12.5</td>
</tr>
<tr>
<td>BMI, kg/m$^2$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childhood</td>
<td>18.1±3.4</td>
<td>18.2±3.7</td>
<td>17.7±4.0</td>
</tr>
<tr>
<td>Adulthood</td>
<td>27.7±4.6</td>
<td>26.1±6.2</td>
<td>27.4±7.5</td>
</tr>
<tr>
<td>AUC</td>
<td>25.6±4.3</td>
<td>23.1±4.7</td>
<td>24.5±5.1</td>
</tr>
<tr>
<td>SBF, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childhood</td>
<td>102.0±9.6</td>
<td>100.6±9.3</td>
<td>103.9±13.6</td>
</tr>
<tr>
<td>Adulthood</td>
<td>114.7±10.4</td>
<td>107.6±11.1</td>
<td>119.0±11.4</td>
</tr>
<tr>
<td>AUC</td>
<td>112.6±7.6</td>
<td>107.3±6.6</td>
<td>114.8±6.2</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childhood</td>
<td>87.0±23.3</td>
<td>89.0±26.0</td>
<td>84.4±20.0</td>
</tr>
<tr>
<td>Adulthood</td>
<td>136.3±32.8</td>
<td>121.9±30.5</td>
<td>120.5±50.1</td>
</tr>
<tr>
<td>AUC</td>
<td>110.4±21.0</td>
<td>105.1±20.9</td>
<td>99.9±28.3</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childhood</td>
<td>62.8±17.9</td>
<td>62.4±21.9</td>
<td>68.8±20.1</td>
</tr>
<tr>
<td>Adulthood</td>
<td>41.5±9.8</td>
<td>51.4±12.5</td>
<td>50.7±20.3</td>
</tr>
<tr>
<td>AUC</td>
<td>45.5±8.7</td>
<td>54.0±8.9</td>
<td>57.1±13.9</td>
</tr>
<tr>
<td>TG, mg/dL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childhood</td>
<td>72.1±39.2</td>
<td>79.8±47.0</td>
<td>61.9±28.5</td>
</tr>
<tr>
<td>Adulthood</td>
<td>153.5±147.8</td>
<td>118.0±111.1</td>
<td>130.2±138.8</td>
</tr>
<tr>
<td>AUC</td>
<td>94.3±37.0</td>
<td>85.8±30.7</td>
<td>76.5±26.1</td>
</tr>
</tbody>
</table>

NS indicates nonsignificant; AUC, AUC divided by follow-up years; SBF, systolic blood pressure; and TG, triglycerides.

*Only in females; †only in blacks; ‡only in whites.

$P$ values were adjusted for covariates where appropriate.

### TABLE 2. Pearson Correlation Coefficients of LVM Index in Young Adults With Risk Factors Measured Since Childhood

<table>
<thead>
<tr>
<th>Time Measured</th>
<th>BMI</th>
<th>Systolic Blood Pressure</th>
<th>HDL Cholesterol</th>
<th>LDL Cholesterol</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Childhood (4–17 years)</td>
<td>0.172†</td>
<td>0.153*</td>
<td>−0.011</td>
<td>0.078</td>
<td>0.056</td>
</tr>
<tr>
<td>Adulthood (20–38 years)</td>
<td>0.292†</td>
<td>0.222†</td>
<td>−0.073</td>
<td>0.060</td>
<td>0.093</td>
</tr>
<tr>
<td>Cumulative burden (AUC)</td>
<td>0.248†</td>
<td>0.193†</td>
<td>−0.052</td>
<td>0.072</td>
<td>0.083</td>
</tr>
</tbody>
</table>

AUC indicates AUC divided by follow-up years.

Race-, gender-, and age-specific $z$-scores were used for LVM index and risk factors.

* $P<0.01$; † $P<0.001$. 

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both cross-sectionally and longitudinally, in childhood and in adulthood.\textsuperscript{13–18,27,28} Taken together, these data, along with intervention studies,\textsuperscript{36,37} indicate that obesity and elevated blood pressure are the 2 major determinants acting in concert to develop increased cardiac mass.

The observed greater LVM in blacks than in whites has been documented in several studies\textsuperscript{15–18,26,28,38,39}; however, the racial difference in LVM (Table 1) disappeared when further adjusted for BMI and systolic blood pressure (data not shown). Higher levels of blood pressure occur even in childhood in blacks, which can be detected with automatic instruments but are difficult to detect with indirect measurements by mercury sphygmomanometry.\textsuperscript{40} Additionally, the developing greater adiposity in blacks, especially black females, compared with whites partly accounts for this black-white difference in LVM. Also, blacks likely carry a greater blood pressure load over a day due to a smaller decline in nocturnal blood pressure.\textsuperscript{41,42}

In conclusion, adiposity beginning in childhood plays an important role in the development of left ventricular hypertrophy. Furthermore, adiposity and systolic blood pressure may act in concert in this regard. Information from the present study, along with other accumulating evidence showing that childhood risk factors persist over time and are predictive of CV risk in adulthood, underscores the importance of childhood risk factors in the evolution of CV risk.\textsuperscript{5–9} Importantly, the reversibility of left ventricular hypertrophy by intervention\textsuperscript{36,37} indicates that early prevention and intervention will benefit those who are at increased CV risk beginning in childhood. With the continuing secular increases in overweight and obesity in epidemic proportion and parallel increases in blood pressure levels being noted in children,\textsuperscript{43,44} it becomes incumbent to begin prevention and intervention early in life to reduce or slow the progression of underlying changes occurring in the heart and vascular tree.\textsuperscript{45}

### Acknowledgments

This study was supported by grants AG-16592 from the National Institute on Aging, HL-38844 from the National Heart, Lung, and Blood Institute, HD-043820 from the National Institute of Child Health and Human Development, and 0160261B from the American Heart Association. The Bogalusa Heart Study is a joint effort of many investigators and staff members whose contributions are gratefully acknowledged. We especially thank subjects for their long-term participation in this study.

### References


![Image of graph showing the relationship between BMI and LVM index](Image)

**TABLE 3. Multiple Regression of LVM Index in Young Adults on Risk Factor Variables Measured Since Childhood**

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>Childhood</th>
<th>Adulthood</th>
<th>Cumulative Burden (AUC)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(\beta)</td>
<td>(P)</td>
<td>(\beta)</td>
</tr>
<tr>
<td>BMI</td>
<td>0.122</td>
<td>0.019</td>
<td>0.231</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.089</td>
<td>0.086</td>
<td>0.127</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>0.025</td>
<td>0.630</td>
<td>0.043</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>0.024</td>
<td>0.635</td>
<td>-0.024</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.040</td>
<td>0.470</td>
<td>0.021</td>
</tr>
</tbody>
</table>

\(\text{AUC}\) indicates \(\text{AUC}\) divided by follow-up years. Race-, gender-, and age-specific \(\text{z}\)-scores were used for LVM index and risk factor variables.


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Circulation. 2004;110:3488-3492; originally published online November 22, 2004;
doi: 10.1161/01.CIR.0000149713.48317.27
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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