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Predictors of Left Ventricular Dilatation in Young Adults (from the Bogalusa Heart Study)

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Abstract

Left ventricular (LV) dilatation may be an early sign of cardiac decompensation progressing to LV dysfunction. Determinants of LV dilatation in young asymptomatic adults are unknown. Five hundred six asymptomatic subjects (mean age 32 ± 3 years) enrolled in the Bogalusa Heart Study underwent echocardiographic examination. LV dilatation (LV end-diastolic diameter >5.5 cm) as measured by M-mode echocardiography was found in 31 subjects (6%). Subjects with LV dilatation had greater body mass indexes (32 ± 9 vs 27 ± 6 kg/m^2, p <0.0001), systolic (119 ± 15 vs 112 ± 12 mm Hg, p = 0.007) and diastolic (79 ± 12 vs 75 ± 9 mm Hg, p = 0.04) blood pressures, and LV mass (230 ± 50 vs 123 ± 39 g, p <0.0001). Age, gender, race, and metabolic parameters (glucose, insulin, and lipoprotein levels) did not differ significantly between the subjects with and without LV dilatation. After correction for age, gender, and race differences, adulthood obesity (body mass index >30 kg/m^2) was associated with a threefold odds ratio (2.9, 95% confidence interval 1.4 to 6.1), and hypertension (defined as per the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) was also associated with a threefold odds ratio (3.0, 95% confidence interval 1.2 to 7.1) for an increased incidence of LV dilatation. There was an incremental increase in LV end-diastolic dimension depending on the presence of hypertension or obesity, and subjects with obesity and hypertension in adulthood had the greatest degree of LV end-diastolic dimensions. In multiple regression analyses, body mass index in childhood was the only significant predictor of LV dilatation in adulthood (odds ratio 1.47, 95% confidence interval 1.03 to 2.09). In conclusion, obesity beginning in childhood and obesity and hypertension in young adulthood are predictors of LV dilatation in an otherwise healthy young adult population.

Studies of patients with coronary heart disease have confirmed the concept of left ventricular (LV) dilatation as a precursor of heart failure.[1–3] Furthermore, cardiac enlargement is associated with increased morbidity and mortality in otherwise healthy middle-aged and elderly subjects.[4,5] The prevalence and the risk factors for LV dilatation in young patients without symptomatic ischemic heart disease or heart failure are not known. We investigated the relation of LV end-diastolic dimensions and known cardiovascular risk factors in a group of patients free of congestive heart failure or myocardial infarction in a population study of young adults.

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Methods

The Bogalusa Heart Study is a long-term epidemiologic study of the natural history of cardiovascular disease in children and young adults from the semi-rural, biracial (65% white, 35% black) community of Bogalusa, Louisiana. The population and study design of the Bogalusa Heart Study have been previously described.[6,7] Five hundred six subjects (age range 20 to 38 years; 71% white, 39% men) who had echocardiographic examinations of the heart in adulthood in addition to other risk factor measurements in childhood and adulthood were included in the study.

Informed consent was obtained from all participants, and the protocols were reviewed by the institutional review board of the Tulane University Health Science Center.

All examinations essentially followed the same previously described protocols.[7,8] Subjects were instructed to fast for 12 hours before screening, with compliance ascertained by interview on the morning of the examination. Height and weight were measured twice to ±0.1 cm and to ±0.1 kg, respectively, and the average values were used to calculate body mass index (BMI) as a measure of overall adiposity.

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

Venipuncture was performed after confirmation of a 12-hour fast. Serum total cholesterol and triglyceride levels were assayed using an enzymatic procedure on the Abbott VP instrument (Abbott Laboratories, North Chicago, Illinois). Serum lipoprotein cholesterol levels were analyzed by a combination of heparin-calcium precipitation and agar-agarose gel electrophoresis procedures.[8] The laboratory was monitored by the Lipid Standardization and Surveillance Program of the Centers for Disease Control and Prevention (Atlanta, Georgia). A commercial radioimmunoassay kit was used for measuring plasma immunoreactive insulin levels (Phadebas insulin kit; Pharmacia Diagnostics, Piscataway, New Jersey). Plasma glucose levels were measured as part of a multiple chemistry profile (SMA20, Laboratory Corporation of America, Burlington, North Carolina) by a glucose oxidase method.

LV dimensions were assessed by 2-dimensional M-mode echocardiography with 2.25- and 3.5-MHz transducers according to the American Society of Echocardiography's recommendations.[9] Images were recorded on standard VHS videocassette tapes by trained technicians, and repeated observations were obtained in a randomized 6% sample of subjects selected for repeat measurements 10 to 12 days apart. The measurement errors were consistent with those found in other epidemiologic studies. The coefficient of variation for inter- and intrareader variabilities for all measures of cardiac anatomy was <10%. All echocardiograms were digitized and measured on Tomtec/Freeland Cardiology Workstation digitizing systems (Tomtec/Freeland Systems, Broomfield, Colorado).

Parasternal long- and short-axis views were used for measuring LV end-diastolic and end-systolic measurements in duplicate, which were then averaged. An end-diastolic diameter of >5.5 cm was considered abnormal. LV mass was calculated on the basis of the formula recommended by Devereux.[10] Diastolic function was measured using mitral inflow velocity patterns (E/A ratio), and fractional shortening was calculated.

Data analyses were performed using SAS version 8.2 (SAS Institute Inc., Cary, North Carolina). Variables were compared between the groups with normal LV end-diastolic diameters (LVEDDs) and LV dilatation using Students' *t* test, the chi-square test, and analysis of covariance. The difference between hypertension and/or obesity groups was tested using covariant analysis. Multiple logistic regression analysis on the basis of the maximum-likelihood method was used to calculate adjusted odds ratio with 95% confidence intervals for hypertension and/or obesity compared with no hypertension and obesity with LV dilatation. Risk factors measured at the first and last examinations were used as childhood and adulthood values, respectively.

Pearson's correlation coefficients were used to assess the relations of LVEDD with risk factors. To explore the childhood predictors of LVEDD in adulthood, multiple regression analysis was performed with LVEDD as a dependent variable and risk factors measured in childhood as the independent variables, with all the variables corrected for age, gender, and race.

Results

Among 506 subjects, 31 (6%) were found to have LV dilatation. The characteristics of young adults on the basis of the risk factor variable for cardiac dilatation are listed in Table 1. Subjects with LV dilatation had higher BMIs compared with subjects without LV dilatation. Similarly, subjects with LV dilatation had on average higher systolic and diastolic blood pressures than subjects without LV dilatation. Subjects with LV dilatation also had higher serum triglyceride and low-density lipoprotein cholesterol levels and lower high-density lipoprotein cholesterol levels, although the differences were not statistically significant. Table 2 lists the correlations between LVEDD and cardiovascular risk factors in the 31 subjects. The greatest correlations were seen among BMI, systolic blood pressure, and LVEDD.

After correction for age, gender, and race differences, adulthood obesity (BMI >30 kg/m^2) was associated with a 2.9 odds ratio, and hypertension (defined as per the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure as 140/90 mm Hg or receiving medication) was also associated with a threefold odds ratio and increased incidence of LV dilatation (Table 3). Of the 31 patients, 8 were considered overweight (BMI 25 to 29 kg/m^2) and 16 were obese (BMI ≥30 kg/m^2). Seventy-two of 504 patients were hypertensive or receiving antihypertensive medications in the total sample, whereas 7 of 31 patients with LV dilatation were hypertensive or receiving antihypertensive medications. Thirteen patients were overweight or obese without having hypertension or receiving antihypertensive treatment.

There was an incremental increase in LVEDD depending on the presence of hypertension or obesity, and subjects with obesity and hypertension in adulthood had the greatest degree of LV end-diastolic dimensions (odds ratio 3.5, 95% confidence interval 1.1 to 9.3; Figure 1). As listed in Table 4, subjects with LV dilatation had greater LV mass and also had lower diastolic indexes (E/A ratio) and fractional shortening.

When childhood variables were analyzed for the adult subjects with LV dilatation, BMI was the only significant risk factor for LV dilatation (Table 5), indicating childhood obesity as the primary predictor of adult LV dilatation. Multiple regression analyses showed that BMI in childhood (Table 6) was the only significant predictor of LV dilatation, with systolic blood pressure in childhood of marginal significance.

Discussion

In the present study, obesity and hypertension emerged as 2 major independent determinants of cardiac size. The effect was even more significant when the 2 variables were concomitantly present, indicating complementary hemodynamic and potential metabolic influences on cardiac structural changes. The burden of adiposity, measured as BMI in childhood, emerged as the only significant predictor of LV dilatation. Our earlier studies also showed that obesity is the major predictor of adult increased LV mass[11] and even precedes other risk factors in development of the metabolic or insulin-resistant syndrome.[12]

These observations emphasize the adverse effects of childhood obesity and the long-term burden of obesity. Although the relation of obesity and heart disease has long been recognized,[13] a growing problem of obesity has been observed.[14] Several mechanisms by which obesity can lead to LV dilatation include the excessive vascularity of adipose tissue, an increase in total blood volume, and greater cardiac output.[3,13–15] In addition, fat cells generate cytokines and inflammatory factors that can enhance cardiac remodeling. Dilatation produces an increase in stress and compensatory hypertrophy. Diastolic dysfunction may ensue, and if wall stress remains high, systolic dysfunction may ultimately develop. In the present observations, an increase in LV mass and a trend toward abnormal diastolic function occurred, shown by decreased LV compliance and the E/A ratio. These changes are a reflection of LV myocardial structural changes.

Hypertension occurs in 60% of obese adults, and obesity is also known to be associated with increased blood pressure levels and other risk factors in childhood and adolescence, especially in Caucasians.[16–18] The co-existence of systemic hypertension and obesity causes simultaneous increases in afterload and preload,[13–15] which likely occurs beginning in childhood, at blood pressure levels much lower than recommended by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure for adults. In hypertensive obese patients, LV volume is smaller and LV wall thickness is greater than in normotensive obese subjects, suggesting a hybrid form of hypertrophy[13] that could change over time, with ultimate dilatation of the LV chamber.

This study was retrospective and observational and thus subject to limitations. However, the study indicates that obesity and high blood pressure beginning at an early age can have major consequences of increased altered cardiac size and cardiac function. The long-term follow-up of subjects would be essential to study the natural course of LV dilatation leading to overt heart failure clinically. However, there is persuasive evidence that substantial weight reduction in severely obese patients as well as patients receiving antihypertensive medications has the potential to reverse LV hypertrophy, improve cardiac Doppler-derived indexes of LV diastolic dysfunction, and reduce LV systolic dysfunction.[19,20] These findings need to be tested in asymptomatic subjects followed over time noting heart failure as an outcome, but more importantly, preventive cardiology should be instituted early in life.

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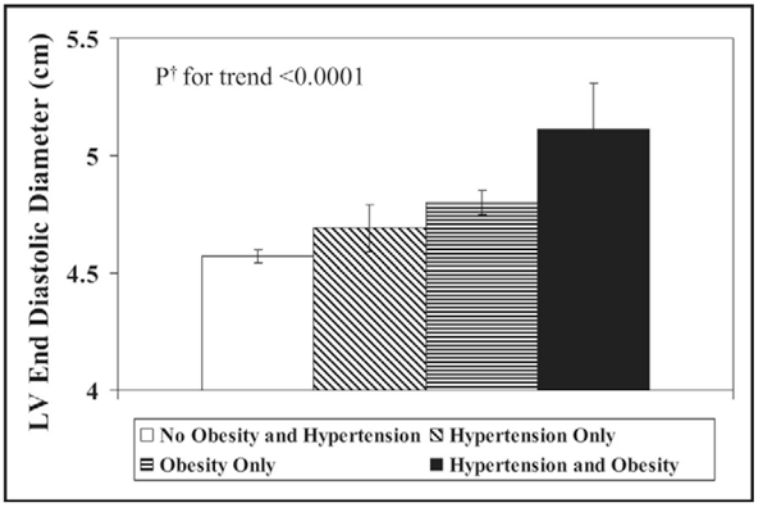

Figure 1.
Individual and combined effects of obesity and hypertension on LVEDD (note the trend with the presence of obesity). †Adjusted for race, gender, age, and high-density lipoprotein and low-density lipoprotein cholesterol.

Table 1

Characteristics of asymptomatic young adults with or without left ventricular dilatation: the Bogalusa Heart Study

Parameters‡	Normal (n = 475)	LV Dilatation* (n = 31)	Comparison p Value†
Age (yrs)	32.5 ± 1.8	32.4 ± 1.8	NS
White/men	72%/39%	71%/52%	NS/NS
BMI (kg/m^2)	27.2 ± 2.5	32.2 ± 2.9	<0.0001
Systolic BP (mm Hg)	112 ± 4	119 ± 4	0.007
Diastolic BP (mm Hg)	75 ± 3	79 ± 4	0.04
HDL cholesterol (mg/dl)	50 ± 4	46 ± 3	NS
LDL cholesterol (mg/dl)	124 ± 6	133 ± 6	NS
Triglycerides (mg/dl)	123 ± 10	128 ± 9	NS
Glucose (mg/dl)	79.5 ± 3.4	79.9 ± 3.1	NS
Insulin (μU/ml)	12.2 ± 3.5	11.7 ± 2.4	NS

*LVEDD >5.5 cm.

†BMI, BP, and metabolic parameters were adjusted for race, gender, and age when appropriate.

‡Raw mean ± SE for continuous variables, percentage for categorical variables.

BP = blood pressure; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

Table 2

Correlation between left ventricular end diastolic diameter and cardiovascular risk factors: the Bogalusa Heart Study

Cardiovascular Risk Factor	Correlation Coefficient	p Value*
BMI (kg/m^2)	0.28	< 0.0001
Systolic BP (mm Hg)	0.20	< 0.0001
Diastolic BP (mm Hg)	0.15	0.003
HDL cholesterol (mg/dl)	−0.10	0.04
LDL cholesterol (mg/dl)	0.12	0.01
Triglycerides (mg/dl)	0.06	NS
Glucose (mg/dl)	0.02	NS
Insulin (μU/ml)	0.03	NS

*Adjusted for age.

Abbreviations as in Table 1.

Table 3

Association between left ventricular dilatation and obesity and hypertension in asymptomatic young adults: the Bogalusa Heart Study

Cardiovascular Risk Factor	Adjusted OR* (95% CI)	p Value
Obesity (BMI ≥30 kg/m^2)	2.9 (1.4–6.1)	0.005
Hypertension (systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg or antihypertensive medication)	3.0 (1.2–7.1)	0.01
Obesity and hypertension	3.5 (1.1–9.3)	0.02

*Adjusted for race, gender, and age.

CI = confidence interval; OR = odds ratio; other abbreviations as in Table 1.

Table 4

Echocardiographic characteristics of asymptomatic young adults with or without left ventricular dilatation: the Bogalusa Heart Study

Parameters‡	Normal (n = 475)	LV Dilatation* (n = 31)	Comparison p Value†
LVEDD (cm)	4.6 ± 0.4	5.8 ± 0.4	< 0.0001
LV mass (g)	123 ± 39	230 ± 50	< 0.0001
E/A ratio	2.4 ±1.3	1.9 ± 0.7	0.05
Fractional shortening (%)	60.0 ± 7.0	56.0 ± 10.0	0.06

*LVEDD >5.5 cm.

†All parameters were adjusted for race, gender, and age.

‡Raw mean ± SD for continuous variables.

Table 5

Mean ± SD of risk factor variables in childhood by dilatation status: the Bogalusa Heart Study

Childhood Variable	Normal (n = 475)	LV Dilatation* (n = 31)	Comparison p Value†
Age (yrs)	11.0 ± 3.1	11.4 ± 3.9	0.551
BMI (kg/m^2)	18.2 ± 3.6	20.3 ± 4.4	0.001
Systolic BP (mm Hg)	102 ± 10	107 ± 14	0.140
LDL cholesterol (mg/dl)	89 ± 25	93 ± 26	0.895
HDL cholesterol (mg/dl)	65 ± 21	62 ± 21	0.732
Triglycerides (mg/dl)	72 ± 40	83 ± 38	0.253

p Values were adjusted for covariates when appropriate.

Abbreviations as in Table 1.

Table 6

Odds ratios of childhood risk factors for having left ventricular dilatation in adulthood by multiple logistic regression analysis: the Bogalusa Heart Study

Variable	OR	95% CI	p Value
BMI (kg/m^2)	1.47	1.03–2.09	0.034
Systolic BP (mm Hg)	1.46	0.97–2.21	0.069
LDL cholesterol (mg/dl)	1.01	0.67–1.53	0.962
HDL cholesterol (mg/dl)	1.08	0.69–1.68	0.742
Triglycerides (mg/dl)	1.23	0.81–1.86	0.331

Childhood risk factor variables were standardized to age-, race-, and gender-specific z scores.

Abbreviations as in Tables 1 and 3.