High Risk Blood Pressure and Obesity Increase the Risk for Left Ventricular Hypertrophy in African-American Adolescents

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Objective To examine the relative effects of high blood pressure (HBP) and obesity on left ventricular mass (LVM) among African-American adolescents; and if metabolic or inflammatory factors contribute to LVM.

Study design Using a 2 × 2 design, African-American adolescents were stratified by body mass index percentile (body mass index <95th percentile = non-obese; ≥95th percentile = obese) and average blood pressure (BP) (normal BP <120/80 mm Hg; HBP ≥120/80). Glucose, insulin, insulin resistance, lipids, and inflammatory cytokines were measured. From echocardiography measures of LVM, calculated LVM index (LVMI) ≥95th percentile defined left ventricular hypertrophy (LVH).

Results Data included 301 adolescents (48% female), mean age 16.2 years, 51% obese, and 29% HBP. LVMI was highest among adolescents with both obesity and HBP. The multiplicative interaction of obesity and HBP on LVH was not significant (OR = 2.35, $P = .20$) but the independent additive associations of obesity and HBP with log-odds of LVH were significant; obesity OR = 3.26, $P < .001$; HBP OR = 2.92, $P < .001$. Metabolic and inflammatory risk factors were associated with obesity, but had no independent association with LVMI. Compared with those with average systolic BP (SBP) <75th percentile, adolescents with SBP from the 75th percentile to 90th percentile had higher LVMI (33.2 vs 38.7 g/m$^{2.7}$, $P < .001$) and greater LVH (18% vs 43%, $P < .001$), independent of obesity.

Conclusions Prevalence of LVH is highest among African-American adolescents with average BP ≥120/80 mm Hg and obesity. There also is an independent association of LVMI with BP, beginning at the 75th SBP percentile. *(J Pediatr 2013;162:94-100)*.

The prevalence of high blood pressure (HBP) among adolescents is increasing, in concert with the childhood obesity epidemic, and the increases of both HBP and obesity are greater among minority children.[1] Although long-term outcome data following onset of prehypertension or hypertension in childhood are limited, a few recent reports, based on longitudinal data extending from childhood into adulthood, provide some evidence that HBP in the young can be linked to premature cardiovascular events in adulthood, particularly among minority groups. Childhood hypertension is associated with an increase in premature death among Native Americans.[2] The CARDIA study reported that HBP with high body mass index (BMI) in young African-American adults is associated with subsequent premature heart failure.[3] HBP in childhood has also been associated with increased risk of coronary artery disease in adult life.[4]

Measures of target organ damage, especially cardiac hypertrophy indicate a significant increase in risk for cardiovascular events among adult patients with hypertension. Longitudinal data, although limited, indicate that both childhood obesity and HBP are associated with higher left ventricular mass (LVM) in young adulthood.[5] Several reports describe left ventricular hypertrophy (LVH), based on echocardiographic measurements, in some adolescents with untreated primary hypertension. In these reports, obesity is commonly present among adolescents with hypertension and LVH.[6-8] Metabolic factors associated with obesity such as insulin resistance[9] and inflammation[10] are components of the metabolic syndrome and could have an effect on cardiovascular growth or injury in the young. Dietary patterns expressed as a high ratio of sodium to potassium is also associated with greater LVM even among healthy young adults.[11]

The excess risks related to hypertension among African-Americans begin in the young. The prevalence of prehypertension in boys is higher in non-Whites compared with Whites.[12] The progression from prehypertension to hypertension is accelerated in adult African-Americans,[13] and among adults, both HBP and high BMI contribute to LVH.[14] Considering these overall observations, we conducted a study to examine the relationships of blood pressure (BP) and BMI with cardiac mass at a young age in

ABPM	Ambulatory BP measurements	LVM	Left ventricular mass
BMI	Body mass index	LVMI	LVM index
BP	Blood pressure	N-HBP	Non-obese HBP
DBP	Diastolic BP	N-NBP	Non-obese normal BP
HBP	High BP	O-HBP	Obese HBP
HOMA	Homeostasis model assessment	O-NBP	Obese normal BP
hsCRP	High sensitivity C Reactive Protein	PAI-1	Plasminogen activator inhibitor-1
LV	Left ventricle	SBP	Systolic BP
LVH	Left ventricular hypertrophy	TNF-αR	Tumor necrosis factor-α receptor

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African-Americans. The purpose of our study was to determine if the associations of obesity and HBP with left LVM are additive or if there is a synergistic relationship between obesity and HBP that results in an effect on LVM that is greater than additive. Our study was designed to test the hypothesis: adolescents with the clinical phenotype of obesity plus HBP have greater left ventricular mass index (LVMI) compared with adolescents without obesity or without HBP. Our study was also designed to examine the association of other metabolic risk factors, including insulin resistance, and biomarkers of inflammation with LVM independent of obesity.

Methods

Healthy African-American adolescents (ages 13-18 years) were recruited in Philadelphia, PA and Wilmington DE, between 2009 and 2011, through primary care practices in the Departments of Family Medicine and Pediatrics at Thomas Jefferson University and from community primary care practices. Non-obese and obese (BMI ≥95th percentile) adolescents were enrolled, as were adolescents with normal blood pressure (BP) (average BP <120/80 mm Hg) and adolescents with HBP (average systolic BP [SBP] ≥120 mm Hg or average diastolic BP [DBP] ≥80 mm Hg). Using a 2 × 2 factorial design, participants were stratified into 4 different groups predetermined on the basis of BMI and BP status: non-obese normal BP (N-NBP), non-obese HBP (N-HBP), obese normal BP (O-NBP), and obese HBP (O-HBP). Electronic records in the primary care practices were utilized in screening for potential participants with HBP. Exclusion criteria included known secondary hypertension, diabetes, renal disease, cardiovascular disease, autoimmune disease, thyroid disease, sickle cell disease, eating disorders, and use of steroids. Adolescents with stage 2 hypertension and adolescents with suspected secondary hypertension based on medical history and urinalysis were also excluded. The study protocol was approved by the Institutional Review Board of Thomas Jefferson University and the A. I. DuPont Hospital for Children. Written informed consent was obtained from 18-year-old participants, while for adolescents age <18 years, consent was obtained from the parent or guardian at enrollment and assent was obtained from the child.

Data on health status, medication use, and health related behaviors were obtained by self report of each participant or guardian (for younger adolescents). Clinical assessment consisted of BP and anthropometric measurements (height, weight, and waist circumference). BMI was calculated as weight (kg) divided by height squared (m^2), and obesity was defined as BMI ≥95th percentile according to the Centers for Disease Control and Prevention criteria for children (http://www.cdc.gov/obesity/childhood/defining.html), which are derived from population-standardized BMI Z-scores based on age, sex, and BMI. All BP measurements in this study were obtained by research staff trained in child BP measurement methodology. On each adolescent participant, BP measurements were obtained, by auscultation with an aneroid device, following a 10-minute rest period. During both rest period and BP measurement, the adolescent remained in a seated position with his/her back supported and feet flat on the floor. Measurements were performed on the right arm, supported at heart level, using a cuff with a width that was at least 40% of the measured arm circumference and was large enough to encircle 80% of the subject's upper arm.[15] The average of 3 successive measurements of SBP and DBP on 2 separate visits was used as the BP value for each participant. For adolescents with HBP, a third separate set of BP measurements were obtained to ensure that the average of all BP measurements were ≥120 systolic or ≥80 diastolic mm Hg. BP percentiles were also calculated based on population-standardized BP Z-scores.[15] Adolescents invited for screening based on a record of recent elevated BP in their medical record, but who during BP screening by study staff had an average BP <120/80 mm Hg were not enrolled.

Echocardiography was performed for determination of LVM, which was measured by 2-dimensional guided M-mode echocardiography. A trained technician obtained measurements of the left ventricular internal dimension, interventricular septal thickness, and posterior wall thickness during diastole. LVM was calculated from measurement of the left ventricle (LV) using the equation LVM (g) = 0.81 (1.04 [interventricular septal thickness + posterior wall thickness + LV end diastolic internal dimension])^3 − (LV end diastolic internal dimension)^3 + 0.06.[16] According to the methods of de Simone et al,[17] LVM was corrected for height by dividing LVM by height in $m^{2.7}$ to calculate a LVMI. LVH in children and adolescents is defined as LVMI ≥95th percentile on sex-specific normative LVMI data published by Khoury et al.[18] A single echo technician performed the echocardiographic measurements and an investigator (S.G.) blinded to the adolescent's BP measurements interpreted the data. Intra-reader reproducibility of LVM measurement showed a correlation of 0.97 for repeat samples with a mean difference in LVM of 2 g between readings.

On a separate visit, participants returned to the clinical research unit following an overnight fast for an oral glucose tolerance test. Each participant saved the first morning voided urine sample (with the time interval from the previous void) and brought the sample to the visit. An in-dwelling venous catheter was placed and a fasting blood sample was obtained for glucose, insulin, and lipid profile. Following the ingestion of 75 g of glucose solution (Glucola; Ames Diagnostics, Elkhart, Indiana), blood samples were then obtained at 30, 60, and 120 minutes post-ingestion and assayed for plasma glucose and insulin concentrations. Plasma glucose concentration was analyzed with the glucose oxidase technique (YS model 27; Glucostat, Yellow Springs, Ohio). Plasma insulin concentration was determined with a solid phase radioimmunoassay (Coat-a-Count; Diagnostic Products Corp, Los Angeles, California). Coefficients of variation for intra- and inter-assay variability for glucose and insulin assays were <5%. Insulin resistance was estimated using the homeostasis model assessment (HOMA) of insulin