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Associations of Cardiac Structure with Obesity, Blood Pressure, Inflammation, and Insulin Resistance in African American Adolescents

Samuel S. Gidding, MD[*], **Robert A. Palermo, DO**[*], **Stephanie S. DeLoach, MD**[†], **Scott W. Keith, PhD**[‡], and **Bonita Falkner, MD**[§]

[*]Nemours Cardiac Center, Nemours Cardiac Center at A.I. duPont Hospital for Children, Wilmington, Delaware

[†]Department of Internal Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania

[‡]Division of Biostatistics, Department of Pharmacology and Experimental Therapeutics, Thomas Jefferson University, Philadelphia, Pennsylvania

[§]Division of Nephrology, Thomas Jefferson University, Philadelphia, Pennsylvania

Abstract

To determine if obesity, blood pressure, markers of inflammation, and insulin resistance are associated with cardiac structure in African American adolescents, a cross-sectional study was conducted on a cohort oversampled for high blood pressure and obesity. Measurements included: anthropometrics, blood pressure, homeostasis model assessment to assess insulin resistance, high sensitivity C-Reactive Protein, and plasma adipokines (adiponectin, Interleukin-6, Plasminogen Activator Inhibitor-1. Echocardiogram measurements were left ventricular mass index ($g/m^{2.7}$), left ventricular relative wall thickness, left atrial diameter index (mm/m) and left ventricular diastolic time intervals. Left atrial diameter index ($r^2 = 0.25$) was associated with body mass index systolic blood pressure, and female gender. Left ventricular mass index ($r^2 = 0.35$) variation was associated with body mass index systolic blood pressure, heart rate, age, and male gender. Left ventricular relative wall thickness ($r^2 = 0.05$) was associated with homeostasis model assessment. Tissue diastolic intervals were not associated with any risk factor. Inflammatory markers and adipokines were associated with body mass index but were not independently associated with any echo measures. In African American adolescents, body mass index and systolic blood pressure but not inflammatory markers or adipokines are important correlates of left atrial size and left ventricular mass.

Keywords

Obesity; Inflammation; Adolescents; Left Atrium; Left Ventricular Mass

Introduction

There are racial differences in development of cardiovascular disease, with African Americans adversely affected. Compared to Caucasians, African Americans and males have been shown to have increased left ventricular mass (LVM).[1-3] There is inconsistent data on

Address for correspondence: Samuel S. Gidding, MD, Alfred I. duPont Hospital for Children, Nemours Cardiac Center, 1600 Rockland Road, Wilmington, DE 19803, Phone: 302-651-6639, Fax: 302-651-5369, Samuel.gidding@nemours.org.

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the association of insulin resistance to LV and left atrial (LA) size.[4-6] Bibbins-Domingo et al[7] followed healthy, young adults over 20 years and found significantly more cases of heart failure in African American young adults than Caucasians. Obesity and obesity-related risk factors including high blood pressure (BP) lead to cardiovascular morbidity through inflammation and endothelial damage.[8] In African-American adults, DeLoach et al. have shown an association between body mass index (BMI) and elevated pro-inflammatory adipokine levels (tumor necrosis factor alpha (TNF-α), interleukin-6 (IL6), plasminogen activator (PAI-1) and high sensitivity c-reactive protein (CRP)), which was unrelated to BP.[9]

We recruited an African-American adolescent cohort oversampled for the presence of obesity and pre- and stage 1 hypertension to further assess early cardiovascular and metabolic co-morbidities of evolving cardiovascular risk. , We have previously shown in this cohort that both adverse cardiac structure and markers of inflammation and insulin resistance are strongly associated with intermediate as well as high risk BP and obesity phenotypes.[10] The purpose of this study was to examine in greater depth these factors and how they are associated with cardiac structure. Associations of cardiac structure with BP, BMI, a pro-inflammatory adipokine profile (low adiponectin, elevated IL6, PAI-1 and CRP), insulin resistance, and urinary sodium were investigated.

Methods

Participants

Healthy adolescents, ages 13-18 years and 47% female, were recruited through community advertisements and referral from primary care offices between 2009 and 2011 as part of a study investigating co-morbidities of obesity and elevated BP in African Americans; participants were oversampled for obesity (BMI ≥95th percentile, Centers for Disease Control United States graphs) and high risk BP defined as average BP ≥120/80 mm Hg. [11] Participants were Tanner 4 or higher. Exclusions included secondary hypertension, diabetes, renal disease, cardiovascular disease, autoimmune disease, thyroid disease, sickle cell disease, eating disorders, and use of steroids. Children with stage 2 hypertension or with a history of taking antihypertensive medication were not enrolled. Children taking behavioral medications on a stable regimen (the same dose at each study visit; n=5) were included. The most common medications taken by participants were for asthma, allergies, or birth control. The study protocol was approved by the Institutional Review Boards of Thomas Jefferson University and A. I. DuPont Hospital for Children. Written informed consent was obtained from 18-year-old participants, while consent was obtained from the parent or guardian at enrollment and assent was obtained from the child if age <18 years.

Study Procedures

Information regarding health status, medication use, and health related behaviors were obtained by self-report of each participant or guardian. Birth weight was also obtained by self-report. BMI was calculated as weight (kg) divided by height squared (m^2). Obesity was defined as BMI ≥ 95th percentile for age and gender. BP measurements were obtained by auscultation, seated, following a 10-minute rest and performed on the right arm using a cuff large enough to encircle 80% of the subject's upper arm. The average of three successive measurements of systolic BP and diastolic BP on two separate visits was used as the BP value. For adolescents with high BP, a third 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.[11] In a sub-group of adolescents, 24 hour ambulatory blood pressure monitoring (ABPM) was

conducted using the SpaceLabs™ 90207 device, an oscillometric BP monitor that has been validated in the pediatric population. All participants were Tanner stage 4 or fully mature.

Each participant underwent 2-dimensional guided echocardiography to evaluate LA diameter, LV geometry and mass. Measurements of the LA diameter, LV internal dimension, interventricular septal thickness, and posterior wall thickness during diastole were made according to methods established by the American Society of Echocardiography.[12] LA diameter was indexed by height (m). Left ventricular mass (LVM) was calculated from 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. LVM index (LVMI) was calculated as LVM/m$^{2.7}$.[11] LV hypertrophy in children and adolescents is defined as LVMI ≥95th percentile on sex specific normative LVMI data.[13] LV relative wall thickness was calculated as the ratio of twice the LV posterior wall thickness in diastole to LV internal diameter in diastole. LV geometry was assessed as normal, concentric remodeling, eccentric LV hypertrophy, or LV hypertrophy with concentric remodeling based on the presence of LVMI above or below the 95th percentile and LVRWT above or below 0.41.[14] Tissue Doppler analysis of the lateral mitral valve annulus was performed and values from sequential beats were averaged. Diastolic function was calculated as: LV diastolic time intervals (LVDTI) = E/Ea. Heart rate (HR) was calculated from the M Mode tracing. A single echocardiographer and observer (SG) performed and interpreted the data related to echocardiographic assessment. Coefficient of variation for intra-reader repeat studies (n=30) was < 8% for all variables.

Participants returned to the clinical research unit following an overnight fast. 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 indwelling venous catheter was placed and a fasting blood sample was obtained for laboratory studies. Plasma glucose concentration was analyzed with the glucose oxidase technique (YS Model 27; Glucostat, Yellow Springs, OH). Plasma insulin concentration was determined with a solid phase radioimmunoassay (Coat-a-Count; Diagnostic Products Corp, Los Angeles, CA). Insulin resistance was estimated using the homeostasis model assessment of insulin resistance (HOMA).[15] Plasma was saved from the fasting blood samples and stored at −80 degrees centigrade for later assay of adiponectin and the inflammatory cytokines high sensitivity C Reactive Protein (CRP), IL6, PAI-1 (TNF-α and Tumor Necrosis Factor-alpha receptor (TNF-αR). All assays for the cytokines were performed by ELISA in duplicate using commercially available kits. Kits for Adiponectin (total), IL-6, TNF-α, TNF-αR and CRP were obtained from (R&D Systems, Minneapolis, MN). The kits for PAI-1 were obtained from (Aniara, Mason, OH). The coefficient of variation for these assays was consistently <10% and most <6%.

Statistical analyses

Categorical variables were summarized by frequency counts and percentages. Continuously measured study variables were summarized by measures of central tendency and variability (arithmetic mean and standard deviation if approximately normally distributed or geometric mean and first and third quartiles [Q1, Q3] if substantially skewed). Substantially skewed data were natural-log transformed for all analyses. Univariate comparisons were made for study variables across groups defined by LADI tertiles and the 4 LVMI/LV relative wall thickness study groups as defined above. ANOVA F-tests were used to evaluate differences in means and Fisher's exact tests were used to evaluate differences in proportions. Adjustments were made to these p-values to help control the overall false discovery rate.[16] The significance level for all tests was set in advance at α = 0.05.

Multiple regression methods were used to fit models to each of the dependent variables LADI, LVMI, LV relative wall thickness, and LVDTI. For each, we applied a multi-stage model selection procedure. In the first stage, we regressed the dependent variable on age, gender, BMI z-score, SBP z-score, and heart rate in beats per minute (bpm). The residuals from this model were then regressed in the second stage of selection where we used the hybrid Least Angle Regression method with the Mallow's Cp criterion suggested by Efron et al. (2004)[17] to select variables that substantially contributed to predicting the dependent variable independently of the contributions from the first stage model variables. The variables considered in the second stage included HOMA, IL-6, PAI-1, adiponectin, TNF-α, TNF-αR, and CRP. The third stage entailed including the selected variables from second stage into one model with variables from stage 1. Each of the continuous variables were mean centered prior to modeling. Results on regression coefficients and 95% confidence intervals from the full models, including all variables considered, and the selected models are presented.

All statistical analyses were conducted using SAS version 9.2 (SAS Institute, Inc., Cary, NC, USA).

Results

Total enrollment for the study was 301 adolescents; complete data were available for this analysis on 280 participants. Those with incomplete data were phenotypically similar to the analyzed cohort. Forty eight percent of the participants were female; the mean age was 16 years (range 13-18 years); the lean normotensive group comprised 37% of the cohort, the lean high risk BP group 12%, the obese normal BP group 34%, and the obese high risk BP group 17%. Participant ages ranged from 13-18 years with a mean of 16 years. Gender distribution was similar with regard to obesity but there were significantly fewer females with high BP (38%, p=0.02). Age was significantly associated with BP (p=0.01). Data on echocardiographic measures are shown in Table 1. These values are generally comparable to distributions presented in the literature.

Participants were stratified into three groups (low, moderate, high) by tertiles of LADI. Study variables within each LADI group are shown in Table 2. In univariate analysis, there is a statistically significant association of LADI with BMI (p<0.01BMI z-score (p<0.01), waist circumference (p<0.01), fasting insulin (p<0.01), HOMA (p<0.01), PAI-1 (p<0.01), CRP (p<0.01), and LVMI (p<0.01).

Participants were also stratified according to LV geometry classification. Study variables for each LV geometry group are provided in Table 3. BMI and SBP are significantly associated with LVMI and geometry classification. Relationships of PAI1 and HOMA with increased LVMI were seen but the strength of these was weaker than for LADI. Other relationships of marginal significance were seen but these showed inconsistent patterns. In those with concentric geometry, LVDTI was higher suggesting these individuals may have early diastolic dysfunction.

Further analysis was performed by dividing participants based on BP and BMI designation. Obesity was significantly associated with elevated fasting insulin (p<0.01), HOMA (p<0.01), IL6 (p=0.01), PAI-1 (p<0.01), TNF-αR (p<0.01), CRP (p<0.01) and lower adiponectin (p<0.01). On the other hand, high BP was only significantly associated with elevated HOMA (p=0.01) and PAI-1 (p=0.02).

Among the obese adolescents with normal BP, 24% met echocardiographic criteria for LV hypertrophy based on LVMI >95th percentile.[13] To exclude the possibility of masked hypertension accounting for LV hypertrophy in this group, a sample of the obese normal BP

adolescents with and without LV hypertrophy were recalled for 24 hour ambulatory BP monitoring. Ambulatory BP monitoring studies were completed on 51 obese normotensive adolescents, including 23 with LV hypertrpophy and 28 without LV hypertrophy. There were no differences in BMI or average BP between those with and without LV hypertrophy. There were also no differences in any of the ambulatory BP monitoring parameters and no cases of masked hypertension were detected.

Table 4 shows results of linear regression models to identify correlates of LADI, LVMI, and LV relative wall thickness. After model selection, variation in LADI was significantly associated with BMI (β=0.13, p<0.01), female gender (β=0.08, p=0.02), and SBP z-score (β=0.05, p=0.02); and LVMI variation was significantly associated with BMI z-score (β = 3.63, p<0.01), age (β = 0.70, p<0.01), female gender (β = −3.65, p<0.01), SBP (β = 1.09, p=0.02), and inversely with HR (β = −0.13, p<0.01). Although significant in univariate models, inflammatory markers were not significantly associated with LADI or LVMI after adjustment for other variables, particularly BMI. LV relative wall thickness was weakly associated with HOMA (β = 0.02, p=0.01). For LV DTI only a weak correlation with TNF-αR was present.

Discussion

The major finding of this study is that BMI is the factor most strongly associated with LADI and LV structure in a cohort of African American adolescents. BMI is associated with a pro-inflammatory adipokine profile and HOMA. In univariate analyses, inflammatory factors and HOMA are associated with LADI and LV structure. However, after adjustment for BMI, these associations disappear. BP is also associated with heart size and geometry but to a lesser extent than BMI. HOMA has a weak relationship to LV relative wall thickness. The magnitude of these relationships to BMI and BP are similar to other epidemiologic studies in this age group.[3, 18] LV DTI was generally unrelated to cardiovascular risk factors, although a weak relationship to those with concentric geometry was seen. Ambulatory BP monitoring in a subset of the cohort with increased LV mass excluded masked hypertension as a cause. To our knowledge, this is the first study to evaluate the association of cardiovascular risk factors, inflammatory markers, adipokines, and insulin resistance with echocardiographic measurements in African American adolescents.

Enlargement of the LA in adults predicts increased cardiovascular morbidity (heart failure, stroke, atrial fibrillation) and mortality.[19, 20] LA volume index has been shown to provide similar predictability for heart failure, hospitalization, and mortality as LV ejection fraction in adults with coronary artery disease.[20] In children, BMI z-score has been reported to be independently associated with LA size.[21, 22]; and in hypertensive adults, LA size increases as a function of body size..[23] In Native American adolescents, similar relationships to LA size have been found.[24] These associations are important as data from the Bogalusa Heart Study have shown that, compared to Caucasians, African Americans are more likely to become hypertensive, with onset of hypertension occurring at a younger age.[25] Further study is needed on LADI as a marker of cardiac target organ injury at a young age.

LV hypertrophy is a manifestation of target organ injury detectable in children with hypertension.[11] LV hypertrophy is associated with BMI and BP and associations similar to those found in this study have been previously published.[3,24] A recent study has shown that higher birth weight is also associated with increased LVM.[26] In this study, no significant associations of birth weight with LVM were detected (data not shown). However our data on birth weight were obtained by self-report of the parent, guardian, or participant and were not verified in birth records. Moreover, the birth weight could not be recalled in 30% of the participants. Therefore, associations of birth weight with cardiac mass could not be

determined in our African American adolescent cohort. Among African American adults with LV hypertrophy, there is a significant increase in cardiovascular mortality, independent of BMI and BP.[27] The adolescent participants with high BP in this study did not have clinically confirmed hypertension and most had average BP levels in the range of prehypertension. The results of this study demonstrate that BMI and BP related target organ injury to the heart occurs early in life in association with modest elevations in BP.

Correlates of LV relative wall thickness have not been studied in younger generally healthy individuals. Most studies that examine these cardiac parameters have been in children with chronic hypertension or severe obesity; these children have significantly increased LV relative wall thickness and abnormal cardiac geometry, particularly those with hypertension.[28-30] Elevated BP at night on ambulatory monitoring may contribute to concentric remodeling. A recent population-based Italian study showed a relationship of elevated triglyceride to HDL ratio (a marker of insulin resistance), with LV relative wall thickness.[31] Body adiposity may also be correlated with LV relative wall thickness.[32] In our cohort, where adolescents with severe obesity and chronic hypertension were excluded, we found a weak relationship of LV relative wall thickness with insulin resistance estimated by HOMA. Collectively, these studies suggest chronic exposure to severe obesity and/or hypertension may have a significant impact on LV relative wall thickness. Among adolescents with less severe BP elevation or obesity, insulin resistance may also have a subtle impact.

Pulsed-wave Tissue Doppler Imaging is used to assess ventricular function by measuring regional systolic and diastolic myocardial velocities.[33] LVDTI assessment of diastolic function is load independent compared to conventional pulsed wave Doppler measurement. In this study no significant associations with BP, BMI, or other risk markers were identified. LVTDI was increased in those with concentric geometry suggesting that diastolic function may be affected in those with excess LV wall thickness for a given degree of LV mass. These findings are consistent with those of Border et al.[33] We did not find associations with BP or BMI as in other studies in cohorts with more severe hypertension or obesity.[28, 34] Using different measures of diastolic function than in this study, the Strong Heart Study uncovered associations of adverse diastolic function with obesity and metabolic syndrome in Native American adolescents.[24]

Limitations

Because the study is based on a cross-sectional design, only associations can be examined. Children at the extremes of the blood pressure and BMI distributions were excluded. Prospective studies that examine adolescents longitudinally are needed to determine the factors that predict increasing LADI and unfavorable LV geometry; inflammatory markers, adipokines, and insulin resistance might emerge as determinants if subsequent progression in LADI and LV geometry. More sophisticated echocardiographic function such as speckle tracking techniques might add additional cardiac function information. The sample size of this study is relatively small and limited to one ethnic group, thus statistical power and generalizability may be limited. Because the cohort was oversampled for obesity and elevated blood pressure we compared the distribution of BMI and BP to the most recent National Health And Nutrition Examination Survey, and found that average BMI and BP were higher than those distributions. Thus, prevalence of adverse LV geometry and distribution of LA size are skewed compared to the general African-American adolescent population.

Conclusions

Obesity and obesity development are strongly associated with future hypertension, thus, the inflammatory milieu associated with obesity described in this study could contribute to injury to the microcirculation, a more rapid rise in BP with aging, and further cardiac end organ injury.[35, 36] Obesity is associated with an increase in cardiac index and a hyperdynamic circulation.[37] Whether these consequences are sufficient by themselves or are mediated by other obesity-associated metabolic changes is difficult to assess from current clinical studies. Regardless, the evolution of adverse cardiac structure begins in youth. Further longitudinal studies will be important to better understand the complex mechanism of adverse changes in LV geometry and LA size in African-Americans and other ethnic groups.

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Abbreviations

LVM(I)	left ventricular mass (index)
LA(DI)	left atrium (diameter index)
BP	blood pressure
BMI	body mass index
TNF-α (R)	tumor necrosis factor alpha (receptor)
IL-6	interleukin-6
PAI-1	plasminogen activator
CRP	high sensitivity C-reactive protein
LVDTI	LV diastolic time intervals
HR	heart rate
HOMA	homeostasis model assessment

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Table 1
Echocardiogram data summary by gender

Variable	Mean (SD) or Geometric Mean [Q1, Q3]		
	All Subjects (N = 280)	Male (N = 148)	Female (N = 132)
Aortic Root (cm)	2.59 (0.31)	2.67 (0.31)	2.51 (0.30)
Left Atrium (cm)	3.34 (0.51)	3.36 (0.49)	3.33 (0.53)
Left Vent Dimension/Diastole (cm)	4.86 (0.49)	5.03 (0.42)	4.66 (0.49)
Left Vent Posterior Wall Thickness/Diastole (cm)	0.87 (0.16)	0.90 (0.15)	0.83 (0.16)
Intraventricular Septal Thickness/Diastole (cm)	0.83 (0.13)	0.88 (0.13)	0.78 (0.12)
Left Ventricular Shortening Fraction (%)	36.32 (5.28)	35.53 (5.41)	37.21 (4.99)
Left Ventricular Mass (gm)	143.07 (41.85)	160.60 (40.94)	123.40 (33.35)
MV E (m/sec)	0.97 (0.56)	0.99 (0.75)	0.94 (0.18)
E' (m/sec) ‡	0.18 [0.15, 0.20]	0.18 [0.15, 0.20]	0.17 [0.15, 0.20]
DTI Ratio	5.66 (1.48)	5.55 (1.41)	5.79 (1.55)

‡Data natural log transformed: geometric means with [first quartile, third quartile] presented

Table 2

Data summary by tertile-based categories (low, moderate, high) of left-atrial diameter index (LADI)

Variable	Categorical Variables: Frequencies (Percents) Continuous Variables: Mean (SD) or Geometric Mean [Q1,Q3]			
	Low LADI ≤ 1.87 (N = 94)	**Moderate 1.87 < LADI ≤ 2.12 (N = 93)**	**High LADI > 2.12 (N = 93)**	**3-way p-value †**
Age (yrs)	16.18 (1.64)	16.14 (1.69)	16.30 (1.72)	0.82
Gender Female	39 (41.5%)	41 (44.1%)	52 (55.9%)	0.19
BP ≥120/80	26 (27.7%)	25 (26.9%)	29 (31.2%)	0.82
Heart Rate (bpm) ‡	70.8 [64, 78]	69.7 [64, 76]	71.8 [64, 80]	0.02
Height (m)	1.71 (0.08)	1.68 (0.09)	1.67 (0.10)	0.01
BMI (kg/m^2) ‡	24.32 [20.44, 27.33]	28.04 [24.89, 32.39]	33.32 [28.58, 39.46]	<.01
BMI z-score	0.78 (1.01)	1.45 (0.91)	1.94 (0.88)	<.01
Waist Circumference (cm) ‡	78.16 [70.00, 87.00]	85.71 [75.00, 97.40]	96.99 [85.00, 114.0]	<.01
SBP (mmHg) ‡	112.05 [104.3, 121.0]	112.56 [104.7, 120.0]	115.04 [108.7, 122.7]	0.19
SBP z-score	−0.23 (0.96)	−0.08 (0.97)	0.20 (0.92)	0.02
DBP (mmHg) ‡	63.52 [59.00, 69.67]	61.50 [56.83, 67.00]	62.21 [57.67, 67.00]	0.25
DBP z-score	−0.27 (0.60)	−0.37 (0.70)	−0.33 (0.66)	0.58
Heart rate (bpm) ‡	70.82 [64.0, 78.0]	69.75 [64.0, 76.0]	71.85 [64.0, 80.0]	0.44
HOMA (mg/dl) ‡	1.55 [0.98, 2.21]	1.79 [1.05, 3.38]	2.32 [1.33, 3.52]	0.02
Adiponectin (ug/ml) ‡	6.24 [4.30, 9.30]	5.27 [3.90, 8.20]	5.15 [3.45, 8.65]	0.10
IL6 (pg/ml) ‡	2.78 [1.90, 3.90]	3.06 [2.10, 4.20]	2.95 [2.10, 4.10]	0.61
PAI1 (ng/ml)	50.43 (24.87)	58.86 (27.55)	69.21 (25.63)	<.01
TNF-α (pg/ml) ‡	8.88 [7.30, 10.60]	8.01 [7.10, 8.90]	8.22 [6.75, 9.55]	0.25
TNF-αR (pg/ml) ‡	0.88 [0.70, 1.10]	0.93 [0.80, 1.20]	0.96 [0.80, 1.20]	0.35
hsCRP (mg/dl) ‡	0.51 [0.20, 1.10]	0.77 [0.30, 1.70]	1.13 [0.40, 3.50]	<.01
LVMI (g/[height in m^2.7)	30.59 (7.06)	34.95 (7.13)	38.27 (7.96)	<.01
LV RWT (cm/m of height) ‡	0.36 [0.32, 0.41]	0.35 [0.31, 0.41]	0.35 [0.30, 0.39]	0.43
DTI Ratio	5.39 (1.23)	5.71 (1.49)	5.89 (1.66)	0.10

† Fishers exact test (categorical) or ANOVA F-test (continuous): any groups different (3-way comparison test)

‡ Data natural log transformed: geometric means with [first quartile, third quartile] presented

Table 3
Data Summary by LV Geometry and LV mass index groupings

Variable>	Categorical Variables: Frequencies (Percents) Continuous Variables: Mean (SD) or Geometric Mean [Q1,Q3]				
	Normal (N = 161)	Concentric Remodeling (N = 32)	Eccentric LVH (N = 58)	Concentric LVH (N = 29)	p-value†
Age (yrs)	16.01 (1.69)	16.40 (1.79)	16.40 (1.70)	16.71 (1.34)	0.13
Gender Female	78 (48.4%)	18 (56.3%)	24 (41.4%)	12 (41.4%)	0.58
BP ≥120/80	31 (19.3%)	8 (25.0%)	26 (44.8%)	15 (51.7%)	<.01
Heart rate	71.3 [64, 80]	73.3 [66, 78]	68.6 [62, 78]	69.0 [62, 72]	0.02
Height (m)	1.68 (0.09)	1.67 (0.09)	1.69 (0.09)	1.72 (0.10)	0.25
BMI (kg/m^2) ‡	26.49 [21.97, 31.86]	25.99 [20.69, 32.01]	34.26 [28.26, 42.59]	30.71 [23.79, 37.51]	<.01
BMI z-score	1.19 (1.03)	1.01 (1.16)	2.04 (0.77)	1.62 (0.94)	<.01
Waist Circumference (cm) ‡	82.00 [71.00, 91.75]	82.77 [70.05, 95.24]	99.94 [84.50,118.10]	92.30 [75.50,110.50]	<.01
SBP (mmHg) ‡	110.98 [105.0,118.00]	113.09 [104.0,120.44]	116.87 [108.3,126.00]	118.77 [109.7,127.33]	0.01
SBP z-score	−0.22 (0.84)	0.02 (1.06)	0.26 (1.04)	0.32 (1.11)	0.01
DBP (mmHg) ‡	61.78 [57.67, 67.00]	62.86 [58.67, 67.00]	62.80 [57.67, 69.00]	64.71 [60.00, 69.67]	0.33
DBP z-score	−0.35 (0.64)	−0.27 (0.60)	−0.33 (0.76)	−0.21 (0.61)	0.71
Heart rate (bpm) ‡	71.38 [64.0, 80.0]	73.31 [66.0, 78.0]	68.6 [62.0, 78.0]	69.0 [62.0, 72.0]	0.18
HOMA (mg/dl) ‡	1.67 [0.99, 2.71]	1.97 [1.29, 3.40]	2.30 [1.38, 3.92]	2.11 [1.23, 3.26]	0.04
Adiponectin (ug/ml) ‡	5.77 [4.00, 8.70]	5.87 [3.65, 9.69]	5.37 [3.80, 7.50]	4.37 [2.65, 7.50]	0.35
IL6 (pg/ml) ‡	2.94 [2.00, 4.10]	2.54 [2.00, 3.40]	3.21 [2.20, 4.90]	2.79 [1.95, 3.90]	0.44
PAI1 (ng/ml)	56.60 (25.04)	53.19 (29.45)	69.81 (27.05)	62.13 (30.75)	0.03
TNF-α (pg/ml) ‡	8.48 [7.00, 9.90]	8.28 [7.30, 10.10]	8.51 [6.85, 9.90]	7.57 [6.75, 8.90]	0.46
TNF-αR (pg/ml) ‡	0.92 [0.70, 1.10]	0.91 [0.60, 1.10]	0.97 [0.80, 1.20]	0.86 [0.70, 1.05]	0.48
hsCRP (mg/dl) ‡	0.66 [0.20, 1.70]	0.87 [0.30, 1.95]	1.18 [0.60, 3.15]	0.65 [0.24, 1.77]	0.04
LVMI (g/[height in $m^{\wedge 2.7}$)	30.24 (5.24)	31.04 (5.15)	43.10 (3.63)	45.61 (5.26)	
LV RWT (cm/m of height) ‡	0.32 [0.29, 0.36]	0.46 [0.42, 0.48]	0.34 [0.32, 0.38]	0.47 [0.42, 0.49]	
DTI Ratio	5.38 (1.35)	6.39 (1.76)	5.69 (1.50)	6.43 (1.33)	0.01

LVMI: left ventricular mass index; LV RWT: left ventricular relative wall thickness.

High LVMI: ≥36.9 (females), 39.4 (males); High LVRWT: ≥ 0.41

†Fishers exact test (categorical) or ANOVA F-test (continuous): any groups different (4-way comparison test)

‡Data natural log transformed: geometric means with [first quartile, third quartile] presented

Table 4

Full and reduced linear regression models of cardiac measurements

	Left Ventricular Mass Index				Left Atrium Diameter Index				Left Ventricular Relative Wall Thickness			
	Full (R^2 = 0.36)		Reduced (R^2 = 0.35)		Full (R^2 = 0.26)		Reduced (R^2 = 0.25)		Full (R^2 = 0.06)		Reduced (R^2 = 0.05)	
Variable	**β**	**p**	**β**	**p**	**β**	**p**	**β**	**p**	**β**	**p**	**β**	**p**
Intercept	36.21	<.01	36.14	<.01	1.95	<.01	1.95	<.01	0.36	<.01	0.36	<.01
Age	0.76	<.01	0.70	<.01	>−.01	0.75	>−.01	0.81	0.005	0.10	<.01	0.12
Gender	−3.81	<.01	−3.65	<.01	0.08	0.03	0.08	0.02	0.002	0.85	<.01	0.91
BMI z-score	3.79	<.01	3.63	<.01	0.12	<.01	0.13	<.01	−0.01	0.71	−0.01	0.36
SBP z-score	0.97	0.04	1.09	0.02	0.04	0.03	0.05	0.02	0.01	0.11	0.01	0.14
Heart rate	−0.12	<.01	−0.13	<.01	>−.01	0.37	>−.01	0.47	<.01	0.80	>−.01	0.98
log HOMA	0.91	0.17			>−.01	0.97			0.02	0.01	0.02	0.01
log IL6	0.67	0.37			0.01	0.77			−0.01	0.57		
PAI1	>−.01	0.86			<.01	0.28			>−.01	0.33		
Adiponectin	0.13	0.30			0.01	0.29			>−.01	0.49		
log TNF-α	−1.69	0.13			−0.03	0.58			0.01	0.69		
log TNF-αR	−1.23	0.31			−0.10	0.05	−0.09	0.07	−0.01	0.40		
log hsCRP	−0.32	0.43			0.01	0.66			>−.01	0.86		