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Relationship Between Elevated Arterial Stiffness and Increased LV Mass in Adolescents and Young Adults

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Abstract

Objective—To determine whether arterial stiffness relates to left ventricular mass (LVM) in adolescents and young adults.

Study design Demographic, anthropometric, laboratory, echo, carotid ultrasound and arterial stiffness were measured in 670 subjects 10–24 yrs (35% male, 62% non-Caucasian). Global stiffness index (GSI) was calculated from 5 measures of carotid stiffness, augmentation index, brachial distensibility and pulse wave velocity (1 point if $\geq 95^{\text{th}}$ for subjects with BMI $< 85^{\text{th}}$). Stiff arteries (S=73) were defined as GSI $\geq 95^{\text{th}}$. Differences between flexible (F=597) and S groups were evaluated by t-tests. Models were constructed to determine if GSI was an independent determinant of LVM index (LVM/ht^{2.7}) or relative wall thickness (RWT).

Results—S group had more adverse CV risk factors, higher LVM index and RWT ($p \leq 0.05$) with a trend for abnormal cardiac geometry. Independent determinants of LVM index were higher GSI, age, BMI, SBP, HR, HbA1c, male sex, and sex-by-HR interaction ($r^2 = 0.52$; $p \leq 0.05$). GSI was also an independent determinant of RWT.

Conclusions—Increased arterial stiffness in adolescents and young adults is associated with LVM index independently of traditional CV risk factors. Screening for arterial stiffness may be useful to identify high risk adolescents and young adults.

Keywords

Arterial Stiffness; Cardiac hypertrophy; Pediatrics

Arteries stiffen with normal aging(1) but accelerated vascular deterioration occurs in the presence of dyslipidemia, (2) hypertension,(3) and the metabolic syndrome.(4) Left ventricular structure is also influenced by age with remodeling seen even in normotensive individuals.(5) However, in the presence of cardiovascular (CV) risk factors such as hypertension, remodeling and increased left ventricular mass (LVM) result,(6) thus raising

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the risk for myocardial infarction and stroke.(7) Increased carotid stiffness in adults is associated with greater LVM(8) with studies demonstrating that many carotid parameters relate to LVM independently of blood pressure (BP).(9,10) Whether similar associations exist between arterial stiffness and LVM in adolescents and young adults or if they are independent of BP is not known. Therefore, we sought to determine the associations between LVM and arterial function in children and adolescents.

Methods

The study population consisted of 670 adolescents and young adults who participated in a study comparing CV parameters among adolescents and young adults who were lean, obese or obese with type 2 diabetes mellitus (age 10–24 years, 62% non-Caucasian, 35% male, 29% with type 2 diabetes mellitus). Pregnant females were excluded from the study. Investigational review board approval was obtained and written informed consent was obtained from subjects ≥ 18 years or the guardian for subjects < 18 years. Written assent was obtained for subjects < 18 years.

After an overnight fast, questionnaire, anthropometric, BP, laboratory, arterial stiffness and echo data were collected. Two measures of height using a calibrated stadiometer (Veeder-Rood, Elizabethtown, NC) and two measures of weight using a Health-O-Meter electronic scale were averaged. Body mass index (BMI) was calculated as kilograms per meter squared. The mean of 3 resting measures of BP with mercury sphygmomanometry collected after 5 minutes of rest according to the Fourth Report on BP in Children was used.(11) Careful attention was paid to arm measurements to ensure correct BP cuff size selection.

Fasting plasma glucose was measured using a Hitachi model 704 glucose analyzer (Roche Hitachi, Indianapolis, IN) with intra-assay and inter-assay coefficients of variation of 1.2% and 1.6% respectively.(12) Plasma insulin was measured by radioimmunoassay using an anti-insulin serum raised in guinea pigs, 125I labeled insulin (Linco, St. Louis, MO) and a double antibody method to separate bound from free tracer with a sensitivity of 2 pmol and intra- and interassay coefficients of variation of 5% and 8%.(13) Fasting plasma lipid profiles were performed with NHLBI-CDC standardized methods and Low Density Lipoprotein Cholesterol (LDL-C) concentration calculated using the Friedewald equation. C-reactive protein (CRP) was measured using a high sensitivity enzyme-linked immunoabsorbent assay. Glycated hemoglobin A1c was measured in red blood cells using high pressure liquid chromatography.

Arterial Stiffness Measurements

Vascular function testing was conducted after 5 minutes of rest in the supine position. Three measures of brachial artery distensibility (BrachD), systolic (SBP), diastolic (DBP), mean arterial blood pressures (MAP), pulse pressure (PP) and heart rate (HR) were obtained with a DynaPulse Pathway instrument (Pulse Metric, Inc., San Diego, CA), as previously described.(14) This device derives brachial artery pressure curves from arterial pressure signals obtained from a standard cuff sphygmomanometer. The pressure wave is analyzed using a physical model of the CV system validated against invasive cardiac catheterization data assuming a straight tube brachial artery and T-tube aortic system.(14) Brachial artery compliance is derived from waveform parameters and then brachial artery distensibility (BrachD) is calculated as compliance normalized to baseline brachial artery diameter (estimated from a regression equation developed from ultrasound adjusting for sex and body size). This variable is equivalent to other measures of distensibility such as those measured using ultrasound in that it represents the relative change in volume per unit of pressure, or $(\Delta V/V)/\Delta P$. Therefore, it is expressed with the units of $\% \Delta/\text{mm Hg}$.(15) Repeat measures in

our laboratory show excellent reproducibility with coefficients of variability less than 9%. (16)

Pulse Wave Velocity (PWV) was measured with a SphygmoCor SCOR-PVx System (Atcor Medical, Sydney, Australia). The average of 3 measures of PWV was used in analyses. ECG leads are applied and then the distance from the carotid to the sternal notch to the distal artery of interest (femoral, radial, dorsalis pedis) is entered into the software. A pressure tonometer the size of a pencil is placed on the proximal artery (carotid) then distal artery to obtain arterial waveforms gated to the R-wave on the ECG tracing. PWV is the difference in the carotid-to-distal path length divided by the difference in R-wave-to-waveform foot times (m/sec). Repeat measures in our laboratory show excellent reproducibility with coefficients of variability less than 7%. (16)

Three measures of augmentation index (AIx) were collected with the SphygmoCor device. The pressure sensor is applied to the radial artery to collect radial artery pressure waves which are calibrated to a non-invasive blood pressure (measured with the PulseMetric device). A generalized transfer function validated against invasive catheterization data is used to calculate central (aortic) SBP, DBP, MAP and PP and reconstruct the central aortic pressure curve. This transfer function has not been validated against invasive measures in children and adolescents. However, our preliminary analyses on 12 healthy pediatric patients (age 3 to 18 years) undergoing catheterization for atrial septal defect closure (measurements done after successful device placement) resulted in a transfer function with the same peak at the fourth harmonic as demonstrate by O'Rourke and others, (17) suggesting the validity of this technique in children of different sizes and heart rates (unpublished data). AIx adjusted to a HR of 75 beats per minute is calculated from the calculated ascending aorta pressure curve. AIx, is the pressure difference between the primary (main outgoing wave) and the reflected wave of the central arterial waveform, expressed as a percentage of the central pulse pressure. (18) Reproducibility studies in our laboratory demonstrated intraclass correlation coefficients between 0.7 and 0.9 for all variables. (16)

Carotid Ultrasonography

Carotid ultrasound studies were performed by a single registered vascular technologist using high-resolution B-mode ultrasonography (GE Vivid7, Milwaukee, Wisconsin) with a high resolution linear array vascular transducer (7.5 MHz). An optimal 2-D image of the common carotid artery was obtained where both the near and far wall intima-media complex were well visualized. The M-mode cursor was then placed 1 cm proximal to beginning of the carotid bulb. (9) Multiple digital image loops were digitally transmitted using the Camtronic Medical System for off-line reading. The maximal and minimal lumen diameters were read from the M-mode tracing for calculations of carotid stiffness. Calculations included arterial compliance (AC), (19) beta stiffness index (β), (19) circumferential arterial strain (CAS), (20) Peterson's elastic modulus (PEM), (10) and Young's elastic modulus (YEM). (19) Due to pulse wave amplification along the arterial tree resulting in overestimation of brachial SBP, (21) central BPs were used in the calculations of carotid stiffness. The central BPs were obtained, on average, no more than 30 minutes prior to the carotid ultrasound.

Echocardiography Technique

Echocardiography was performed with a GE or Philips Sonos 5500 (Andover, Massachusetts) system. Absence of structural heart disease was confirmed and then with the patient in the left decubitus position, para-sternal long, short axis and apical 4 chamber views were recorded with 3 cardiac cycles averaged for each variable. Left ventricular end-diastolic dimension (LVED), end-systolic dimension (LVES), end-diastolic septal thickness (IVSd) and end-diastolic and end-systolic posterior wall thicknesses (LVPWd, LVPWs)

were measured off-line by either of two sonographers using a Cardiology Analysis System (Digisonics, Houston, Texas). $LVM(g) = (0.8)(1.04) \times [(LVED + LVPWd + IVSd)^3 - LVED^3] + 0.6$. (22) $LVM \text{ index } (LVM)/(23) = LVM/ht^{2.7}$. Relative wall thickness (RWT) at end-diastole = $[(LVPWd + IVSd)/LVED]$.

Statistical Analysis

Analyses were performed with Statistical Analyses Software (SAS, version 9.1.3).(24) Variance stabilizing measures to transform non-normal values were performed as needed. The 95th percentile for each arterial stiffness measure for lean, non-diabetic subjects was determined. Subjects were selected as lean controls for this study if their BMI was <85th% according to CDC tables.(25) For each arterial stiffness measurement greater than or equal to the 95th percentile ($\leq 5^{\text{th}}$ percentile for AC and BrachD), one stiffness point was assigned. Global stiffness index (GSI) was calculated as the sum of the stiffness points for each of the 5 measures of carotid stiffness and the 3 non-ultrasound measures of arterial stiffness. Subjects were stratified as “flexible” (F = 597) for GSI lower than the 95th percentile for the entire cohort as compared with “stiff” (S = 73). Average values were obtained by group. Chi square analyses were performed to determine differences by stiffness classification. Chi square analyses were performed for categorical variables. Bivariate correlations were calculated between GSI, covariates and LVM index or RWT and significant covariates were used in general linear models constructed to elucidate independent determinants of LVM index & RWT. GSI was treated as a continuous variable. The full model contained demographic (age, race/ethnicity, sex, presence of T2DM), anthropometric (BMI z-score), hemodynamic (SBP z-score, DBP z-score, HR), and laboratory (LDL-C, High Density Lipoprotein-Cholesterol = HDL-C, triglycerides, fasting glucose, fasting insulin, HbA1c, CRP). Significance of each covariate in the initial model was assessed and non-significant terms were removed by backward elimination until all remaining covariates or their interaction (effect modifier) terms were significant. Robustness of the models was assessed with use of the maximum R-square technique and calculation of Mallow Cp. Each model had the most ideal Cp with no further increase in R^2 with addition of other variables.

Results

Subjects in the S group were 1.8 years older, more obese and had a more adverse lipid and metabolic profile with higher levels of inflammation (Table I). They also had higher peripheral and central (aortic) BP and HR (Table II). Both LVM index and RWT were greater in subjects with higher GSI (Table II, $p \leq 0.05$). AIX, PWV, β , PWM and YEM were higher and BrachD lower in the stiff group consistent with increased arterial stiffness.

CAS was lower in the S group suggesting lower strain. However, the carotid diameter in systole did not differ between groups, and the diastolic diameter was greater in S group. As previously shown,(26) BMI in our data was an independent determinant of diastolic diameter of the carotid (data not shown), this greater diameter may relate to higher circulating blood volume due to obesity. A greater diastolic diameter leads to a number in the numerator and a larger value in the denominator resulting in a lower CAS ($CAS = \text{systolic lumen} - \text{diastolic lumen} / \text{diastolic lumen}$).(20) Therefore, CAS may not be a robust indication of carotid artery stiffness when comparing groups that differ in adiposity.

Cardiac geometry was evaluated by Chi square analysis. When all four geometric categories were compared between the F and S groups there were no differences, possibly due to the low prevalence of abnormalities (89.5% of the participants had normal LVM index and RWT). However, the prevalence of normal anatomy in the F group was 90.3 versus 83.3% in the S group (chi square $p = 0.07$). There was no difference in the prevalence of concentric

remodeling or hypertrophy, but a trend for greater eccentric hypertrophy in the S group ($S = 9.7\%$ vs $F = 4.8$, $p = 0.08$).

Multivariate models demonstrated that GSI was an independent determinate of LVM index and RWT, even after adjusting for CV risk factors, despite the observation that CAS was lower in subjects with higher GSI (Table III). Regression of LVM index (Figure) or RWT (data not shown) on GSI demonstrated a slope that significantly differed from zero ($p \leq 0.0001$). Other important determinants of LVM index were age, sex, BMI z-score, SBP z-score, HR, HbA1c, and sex-by-HR interaction ($R^2 = 0.52$, $p \leq 0.05$ for model and all parameters). For RWT, in addition to GSI, BMI z-score and triglycerides were significant ($R^2 = 0.11$, $p \leq 0.05$ for model and all parameters). Investigation of the sex-by-HR interaction revealed that increased HR was associated with increasing LVM index only in males.

Additional analyses were performed with subjects stratified into non-diabetic and diabetic groups. There were still significant differences in LVM index and RWT between non-diabetic subjects with S or F vessels ($p \leq 0.005$) but no difference was found in diabetics. Multivariate models for LVM with diabetics excluded yielded similar results (log transformed LVM index = $7.52 + \text{Arterial stiffness score} \times 0.03 + \text{BMI z-score} \times 0.14 - \text{HR} \times 0.81 - \text{female} \times 1.50 + \text{HR} \times \text{Sex interaction} \times 0.34 + \text{SBP z-score} \times 0.052 - \text{HbA1c} \times 0.48$, $r^2 = 0.52$, all parameter estimate $p \leq 0.02$). Arterial stiffness score dropped out of the model for RWT with diabetics excluded. Because this stratification reduced the sample size considerably, data on the original cohort including diabetics is presented.

Finally, analyses were repeated using fewer vascular variables to calculate global stiffness index (GSI). For all reduced models, only Young's elastic pressure modulus (YEM) was used for carotid stiffness because it was the most strongly correlated with LVM index. The second model used only YEM and omitted AIx which may also be influenced by endothelial function in addition to representing arterial stiffness. The third reduced model used only variables that did not require an ultrasound machine for measurement (AIx, BrachD, PWV). The final reduced model included only YEM and PWV(27) because these variables can be collected when an ultrasound machine is not available. For all the simplified models, GSI was an independent determinant of LVM index but less of the variance was explained. No new CV risk factors entered the models with the most persistent risk factors across models being GSI, sex, HR and sex by HR interaction, BMI z-score, and SBP z-score. Because the measures of stiffness included in the original calculation of GSI express slightly different aspects of the behavior of the arterial wall,(17) we elected to present the full data on the original GSI calculation.

Discussion

Our data demonstrate that higher LVM and RWT in adolescents and young adults are associated with increased arterial stiffness independently of traditional CV risk factors such as age, sex, obesity, BP, lipids and metabolic control. There is also a trend for a higher prevalence of eccentric hypertrophy in the adolescents and young adults with stiffer arteries which may be driven by the greater level of adiposity in the stiff artery group.

Abnormal LVM and geometry are well-established risk factors for CV events.(7,28) Hypertensive adults have a higher prevalence of left ventricular hypertrophy (LVH)(7) but increased arterial stiffness is also a risk factor for development of LVH independent of BP levels.(29) Even in healthy adults, a positive relationship is found between arterial stiffness measured by PWV and LVM(30) that remains after adjustment for traditional CV risk factors.(31) Alterations in wave reflections combined with increased central stiffness may

also contribute to LVH. Studies in hypertensive adults(32,33) found a significant correlation between AIx and LVM. The relationship was independent of BP in males although the relationship was not seen in older subjects (> 65 years of age); AIx tends to plateau around age 60 regardless of continued changes in CV risk factors.(32)

The importance of arterial stiffness in the evolution of LVH is evident in intervention studies in hypertensive adults. In the REASON study, 212 subjects were randomized to either an angiotensin converting enzyme (ACE) inhibitor or a beta-blocker.(34) The subjects on the ACE inhibitor had greater reduction in LVM than those on a beta-blocker (-13.6 ± 4.3 g, $P = .027$), with the difference retaining significance after adjustment for final BP level.(34) Improvement in arterial stiffness explained the difference because only ACE inhibition, but not beta-blockade, improved wave reflection (AIx) in this study cohort.(35) Improvement in other measures of arterial stiffness with treatment of hypertension has also been linked to lower LVM. ACE inhibition in combination with calcium channel blockade improved brachial artery distensibility, resulting in reduced LVM in subjects with mild-to-moderate hypertension.(36) Similarly, improvement in PWV with anti-hypertensive therapy has been linked to regression of LVH.(37) These data demonstrate the clinical utility of arterial stiffness measures in optimizing blood pressure treatment to effect the greatest regression of LVM in hypertensive patients.

A link between arterial stiffness and LVM has been identified in other adult diseases. Obese subjects with obstructive sleep apnea were found to have higher LVM and aortic stiffness than subjects with normal sleep studies. Aortic stiffness was an independent determinant of LVM even after adjustment for the respiratory disturbance index.(38) Similar to data from hypertensive subjects, treatment of obesity with bariatric surgery resulted in parallel improvement in aortic stiffness and LVM.(39) Diabetic adults tend to have faster carotid-femoral transit time (similar to PWV) and higher AIx (significant in men), indicating increased stiffness. These changes are associated with higher LVM as compared with controls (176 vs 147 gm, $p < 0.001$ females, 199 vs 188 gm, $p < 0.096$ males).(40) In subjects with chronic kidney disease (CKD), there was a linear rise in LVM across tertiles of PWV and this increase in arterial stiffness remained an independent predictor of LVM after adjustment for renal impairment.(41) Other investigators found AIx was an independent predictor of LVM in both sexes after adjustment for CV risk factors such as blood pressure.(42) Prospectively, a higher AIx at baseline predicted greater decline in creatinine clearance after 1-year of follow-up.(43) In patients with CKD, treatment with medications affecting the renal-angiotensin-aldosterone system (angiotensin receptor blockers) resulted in a decrease in LVM that was associated with a concomitant reduction in PWV and AIx,(44) providing more supportive evidence to the concept that regression of LVH may be best accomplished through reduction of arterial stiffness.

Few data are available examining the relationship between arterial stiffness and LVM in adolescents and young adults. Patients with bicuspid aortic valve (age 16 to 39 years of age) were found to have higher PWV, reduced aortic root distensibility and significantly increased LVM compared with controls.(45) Coarctation of the aorta (CoA) may share a genetic and developmental etiology with bicuspid aortic valve disease and has been similarly related to intrinsic arterial stiffness abnormalities. De Devitiis studied patients after repair of CoA at an average age of 19.8 years.(46) Both LVM and PWV were elevated in patients as compared with controls.(46) This finding was replicated in a younger cohort (average age 12 years), with elevations in PWV significantly correlated with higher LVM index (84 vs 73 g/m², $p < 0.01$).(47) Altered wave reflections may also play a role in development of LVH. When measured with MRI, teenaged subjects with CoA who had augmented systolic wave reflection (similar to increased AIx) had higher LVM than patients without this finding.(48) Children with renal failure also demonstrate cardiac and vascular

abnormalities. A linear increase in carotid thickness, stiffness and LVM was found comparing healthy children (average age 14 years) with those with stable CKD and to youth with severe CKD on dialysis.(49) Type of dialysis may also be important as one study found a trend for higher LVM in pediatric patients on hemodialysis as compared with peritoneal dialyses with a significantly reduced aortic distensibility in the hemodialysis group.(50) Therefore, processes that produce significant increases in arterial stiffness, even at a young age, can increase risk for development of LVH. Our study extends these observations by demonstrating a relationship between arterial stiffness and LVM in adolescents and young adults with less severe pediatric diseases including obesity, and obesity-related CV risk factors.

Our cross-sectional study cannot determine if increased arterial stiffness preceded the development of higher LVM or if these abnormalities in CV structure and function developed simultaneously. There may also have been other non-measured confounders (activity pattern and fitness level, for example) which affected the arterial-cardiac relationship. However, our findings are similar to the limited studies performed in youth and parallel results obtained in adults with CV risk factors. Additionally, due to the original study design (examining CV outcomes in diabetics compared with non-diabetic adolescents and young adults) our cohort contains a large proportion of subjects with T2DM. Because there was no difference in LVM among diabetics only, it is possible that the adverse effects of diabetes, either through elevation in traditional CV risk factors or directly on the heart, may have a greater effect on LVM than arterial stiffness. Larger studies are needed to elucidate these relationships. Finally, equipment and expertise in collecting ultrasound measures of carotid stiffness and non-ultrasound measures of arterial stiffness may not be readily available to many pediatric care providers thus limiting the applicability of the GSI calculation to the clinical setting.

In conclusion, adolescents and young adults with a stiffer arterial tree demonstrate a more adverse CV risk profile and higher LVM. The increase in cardiac mass, however, is related to greater arterial stiffness independent of traditional risk factors (demographics, BP, anthropometrics, lipids, inflammation). Because both LVH(7) and increased arterial stiffness(51) are significant predictors of CV mortality, addition of arterial stiffness measurements to echocardiography may assist in risk stratification in adolescents and young adults with elevated CV risk factor levels.

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Abbreviations List

ACE	Angiotensin converting enzyme inhibitors
AIx	Augmentation Index normalized to a heart rate of 75 beats per minute
BMI	Body Mass Index
BP	Blood Pressure
BrachD	Brachial artery Distensibility
CAS	Circumferential Arterial Strain

CKD	Chronic Kidney Disease
CoA	Coarctation of the Aorta
CRP	C-Reactive Protein
CV	Cardiovascular
DBP	Diastolic Blood Pressure
F	Flexible group
GSI	Global Stiffness Index
HbA1c	glycated Hemoglobin A1c
HDL-C	High Density Lipoprotein Cholesterol
HR	Heart Rate
IVSd	Intraventricular Septal thickness in diastole
LDL-C	Low Density Lipoprotein Cholesterol
LVED	Left Ventricular End Diastolic dimension
LVES	Left Ventricular End Systolic dimension
LVH	Left Ventricular Hypertrophy
LVM	Left Ventricular Mass
LVPWd	Left Ventricular Posterior Wall thickness in diastole
LVPWs	Left Ventricular Posterior Wall thickness in systole
MAP	Mean Arterial Pressure
PEM	Peterson's Elastic Modulus
PP	Pulse Pressure
PWV	Pulse Wave Velocity
RWT	Relative Wall Thickness
S	Stiff group
SBP	Systolic Blood Pressure
YEM	Young's Elastic Modulus

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Figure.

Left ventricular mass index regressed on global stiffness index (mean with 95% confidence limit). $R^2 = 0.52$; p for slope differs from zero ≤ 0.0001 .

Table 1
Demographic, Anthropometric, Laboratory and Physical Activity Values Overall and by Stiffness Group (Means $\pm$ SD)

Variable*	All N = 670		Flexible n = 558		Stiff n = 73	
	Mean	SD	Mean	SD	Mean	SD
Age [†]	18.1	3.4	17.9	3.3	19.7	3.2
Sex (% Male)	34.6		35.5		27.4	
Race (% Caucasian)	37.8		40.0		30.0	
Ht	166.8	10.6	166.7	10.7	167.6	9.8
Wt [‡]	88.4	30.5	85.8	29.9	110.2	27.0
BMI [‡]	31.6	10.0	30.7	9.9	39.0	8.1
Waist [‡]	101.1	24.0	98.8	23.5	120.1	19.1
Waist/ht [‡]	0.61	0.14	0.59	0.14	0.72	0.11
TChol [‡]	171.7	36.8	169.8	35.4	187.2	43.8
LDL [‡]	101.6	32.0	99.6	30.1	117.0	41.3
HDL [‡]	50.0	12.9	50.5	13.1	46.3	10.7
TG [‡]	100.2	69.2	97.2	68.3	124.5	71.8
Glucose [‡]	109.0	52.7	106.9	49.4	126.4	72.5
Insulin [‡]	18.3	14.7	17.8	14.9	22.7	12.0
HbA1c [‡]	6.21	2.09	6.12	2.02	6.90	2.51
CRP [‡]	4.13	6.43	3.87	6.29	6.23	7.15

* Age (years), Ht = Height (cm), Wt = Weight (kg), BMI = Body Mass Index (kg/m²), Waist = Waist Circumference (mm), Waist/ht = Waist/height ratio, TChol = Total Cholesterol (mg/dl), LDL = LDL-Cholesterol (mg/dl), HDL = HDL-Cholesterol (mg/dl), TG = Triglycerides (mg/dl), Glucose = Fasting Glucose (mg/dl), Insulin = Fasting Insulin (microUnits/ml), HbA1c = glycated hemoglobin A1c (%), CRP = C-Reactive Protein (mg/L), P $\leq$ 0.05 for

[†] Stiff>Flexible,

[‡] Flexible>Stiff.

Table 2

CV parameters by Arterial Stiffness Group (Means $\pm$ SD)

Variable*	All N = 670		Flexible n = 597		Stiff n = 73	
	Mean	SD	Mean	SD	Mean	SD
SBP [†]	115.2	12.5	114.1	12.0	124.1	13.1
DBP [†]	64.2	12.8	63.3	12.3	71.7	14.8
MAP [†]	82.9	9.3	82.0	8.7	90.4	10.6
PP	50.7	12.8	50.4	12.8	52.4	13.0
Central SBP [†]	103.4	11.0	102.3	10.4	113.4	10.5
Central DBP [†]	70.5	8.5	69.8	7.9	75.9	10.7
Central MAP [†]	85.6	9.0	84.7	8.4	92.9	10.3
Central PP [†]	32.9	7.1	32.3	6.9	37.5	7.4
HR [†]	66.1	10.9	65.5	10.8	70.7	10.7
LVMI [†]	34.4	10.1	33.8	9.9	40.4	10.7
RWT [†]	0.30	0.06	0.30	0.07	0.34	0.06
AIx [†]	2.69	11.58	1.95	11.08	8.98	13.71
BrachD [‡]	5.99	1.33	6.14	1.31	4.83	0.73
PWV [†]	6.07	1.13	5.91	1.01	7.32	1.24
AC [‡]	0.26	0.07	0.27	0.07	0.20	0.07
β [†]	2.24	0.65	2.16	0.54	2.93	0.98
CAS [‡]	0.18	0.05	0.19	0.04	0.15	0.05
PEM [†]	194	67	192	65	211	78

Variable*	All N = 670		Flexible n = 597		Stiff n = 73	
	Mean	SD	Mean	SD	Mean	SD
YEM [†]	269	124	254	112	394	148

* SBP = systolic blood pressure (mmHg), DBP = diastolic blood pressure (mmHg), MAP = mean arterial pressure (MAP), PP = pulse pressure (mmHg), HR = heart rate (beats/minute), LVMI = left ventricular mass index (g/m^2), RWT = relative wall thickness, AIx = augmentation index at a HR of 75 (%), BrachD = brachial artery distensibility (%change/mmHg), PWV = carotid-femoral pulse wave velocity, AC = arterial compliance (mm/mmHg), β = Beta Stiffness index (unitless), PEM = Peterson's elastic modulus (mmHg/mm²), YEM = Young's elastic modulus (mmHg/mm), $P < 0.001$ for

[†] Stiff>Flexible,

[‡] Flexible>Stiff..

Table 3

Independent Determinants of LVMI and RWT.

Variable		LVMI	RWT
Intercept		6.01	−1.05
Global Stiffness Index	Level 1	−0.12	−0.37
	Level 2	−0.062	−0.32
	Level 3	−0.040	−0.33
	Level 4	−0.065	−0.30
	Level 5	−0.036	−0.32
	Level 6	−0.078	−0.24
	Level 7 (worst)	Reference = 0	Reference = 0
Age		0.0056	
Female		−1.02	
BMI z-score		0.15	0.029
SBP z-score		0.038	
Heart Rate		−0.59	
Heart Rate * Sex		0.23	
interaction			
Triglycerides		−0.10	0.032
HbA1c		−0.10	
<i>R</i>²		0.52	0.11

* All model and parameter $p \leq 0.05$.