Resistive and Pulsatile Arterial Load as Predictors of Left Ventricular Mass and Geometry
The Multi-Ethnic Study of Atherosclerosis


See Editorial Commentary, pp 29–30

Abstract—Arterial load is composed of resistive and various pulsatile components, but their relative contributions to left ventricular (LV) remodeling in the general population are unknown. We studied 4145 participants enrolled in the Multi-Ethnic Study of Atherosclerosis, who underwent cardiac MRI and radial arterial tonometry. We computed systemic vascular resistance (SVR=mean arterial pressure/cardiac output) and indices of pulsatile load including total arterial compliance (TAC, approximated as stroke volume/central pulse pressure), forward wave amplitude (P_f), and reflected wave amplitude (P_r). TAC and SVR were adjusted for body surface area to allow for appropriate sex comparisons. We performed allometric adjustment of LV mass for body size and sex and computed standardized regression coefficients (β) for each measure of arterial load. In multivariable regression models that adjusted for multiple confounders, SVR (β=0.08; P<0.001), TAC (β=0.44; P<0.001), P_f (β=0.73; P<0.001), and P_r (β=−0.23; P=0.001) were significant independent predictors of LV mass. Conversely, TAC (β=−0.43; P<0.001), SVR (β=0.22; P<0.001), and P_r (β=−0.18; P=0.004) were independently associated with the LV wall/LV cavity volume ratio. Women demonstrated greater pulsatile load than men, as evidenced by a lower indexed TAC (0.89 versus 1.04 mL/mmHg per square meter; P<0.0001), whereas men demonstrated a higher indexed SVR (34.0 versus 32.8 Wood Units×m²; P<0.0001). In conclusion, various components of arterial load differentially associate with LV hypertrophy and concentric remodeling. Women demonstrated greater pulsatile load than men. For both LV mass and the LV wall/LV cavity volume ratio, the loading sequence (ie, early load versus late load) is an important determinant of LV response to arterial load. (Hypertension. 2015;65:85-92. DOI: 10.1161/HYPERTENSIONAHA.114.04333.) ● Online Data Supplement

Key Words: hypertrophy, left ventricular ■ vascular resistance ■ ventricular remodeling

In the absence of aortic valve stenosis, the arterial system presents the main opposition (ie, impedance) to the flow generated by the left ventricle (LV). In settings of increased afterload, the LV undergoes geometric remodeling leading to an increased LV mass (LV hypertrophy) and increased wall thickness relative to cavity size (concentric remodeling). Arterial load is complex and is determined by systemic vascular resistance (resistive load, largely determined by the microvasculature) and pulsatile load, which is influenced by phenomena related to wave travel and reflections, proximal aortic properties, and the overall reservoir function of the arterial tree (total arterial compliance [TAC]).

The relationships between the various components of arterial load and LV geometry are incompletely understood. Both increased stroke volume and systemic vascular resistance have been associated with LV hypertrophy in older studies. However, stroke volume is naturally related to LV mass at any given ejection fraction and relative geometry, making the

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A full list of participating Multi-Ethnic Study of Atherosclerosis (MESA) investigators and institutions can be found at http://www.mesa-nhlbi.org.

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interpretation of the former relationship difficult. Several studies have noted a relationship between indices of wave reflections, such as the augmentation index or reflection magnitude, and LV mass.\(^1\)\(^2\) However, other components of arterial load (such as TAC or systemic vascular resistance [SVR]) were generally not simultaneously analyzed, preventing the discrimination of independent associations between components of resistive and pulsatile load and LV remodeling. Similarly, previous studies have suggested sex-related differences in pulsatile load\(^3\)\(^-\)\(^12\) although the effect of these differences on LV structure and function has not been thoroughly addressed. This is particularly important because women are known to have a greater incidence of heart failure with preserved ejection fraction,\(^13\)\(^-\)\(^14\) a condition associated with increased pulsatile load.\(^15\)\(^-\)\(^18\) Furthermore, to the degree that women demonstrate smaller body size than men, and both arterial load\(^19\) and LV mass\(^20\) are highly dependent on body size, sex comparisons on arterial load and LV geometry require careful allometric adjustments for body size.

In this cross-sectional study, we aimed to assess 1) the relationship between various indices of arterial load and LV remodeling and (2) potential sex differences in arterial load and their effect on LV remodeling. We performed these assessments in the Multi-Ethnic Study of Atherosclerosis (MESA) cohort, which included a large, multiethnic, community-based population sample of adults.

Methods

Study Population

The design of MESA has been described elsewhere.\(^21\) MESA enrolled 6814 men and women aged 45 to 84 years from 6 centers across the United States to ensure inclusion of subjects from diverse ethnic backgrounds. Subjects self-reported their ethnicity as black, Asian-American (predominantly Chinese), white, or Hispanic. All subjects were free of cardiovascular disease by self-report at the time of enrollment. Subjects were enrolled between 2000 and 2002. The study was approved by the institutional review boards of all participating centers, and subjects signed informed consent at the time of entry. The enrollment rate was 97% of those eligible.

Assessment of LV Mass and Relative Geometry

A total of 5098 participants in MESA underwent baseline cardiac MRI examination.\(^20\) Cardiac MRI was performed with 1.5-Tesla field strength systems to determine LV mass and volume, as previously described.\(^22\) In brief, short-axis images of the entire LV were acquired with a gradient-echo cine sequence (time to repetition/time to echo, 8–10 /3–5 ms; flip angle, 20\(^\circ\); 6-mm slice thickness; 4-mm gap; flow compensation; in-plane resolution, 1.4–1.6 mm [frequency]×2.2–2.5 mm). Endocardial and epicardial borders were traced using a semiautomated method (MASS software, Medis, Leiden, the Netherlands).\(^20\) Myocardial volume was assumed to be the difference between epicardial and endocardial slices for all slices at end-diastole, multiplied by the slice thickness and the interslice gap. Myocardial mass was computed from myocardial volume assuming a myocardial density of 1.04 g/mL.\(^20\) Papillary muscles were included as part of the ventricular cavity and excluded from the determination of LV mass. This method of LV mass and volume quantification has been shown to have excellent reproducibility.\(^23\) Cardiac output was determined by multiplying the stroke volume with the heart rate at the time of the examination.

We calculated the LV wall:cavity volume ratio as an indicator of LV concentric versus eccentric geometry. Greater values demonstrate greater increases in myocardial wall as opposed to cavity volume, such as would be seen in concentric hypertrophy.

LV mass was indexed for body height and weight as previously described.\(^20\) Briefly, a sample of 1746 MESA participants was selected from the total cohort based on the absence of obesity, hypertension, antihypertensive medication use, diabetes mellitus, impaired fasting glucose, or diabetic medication use. Log-Log models were created by regressing log (LV mass) on log (height), log (weight), and sex to obtain appropriate allometric coefficients for height and weight, while adjusting for the effect of sex. Predicted LV mass was determined using the following formula: 100×LV mass (g)/(a×height [m]\(^b\)×weight [kg]\(^c\)), where a=6.82 in women and 8.25 in men.\(^20\) LV mass was expressed as a percentage of the predicted value; values >100 indicate larger LV mass than predicted by body size and sex, whereas values <100 indicate smaller values. Additional models (Table S1 in the online-only Data Supplement) were also created in which LV mass was indexed to body surface area (BSA), or in which log (LV mass) was modeled as the dependent variable with adjustment for log (height) and log (weight). As the results for these alternative methods of indexation were highly consistent with the results derived from allometric models, only the results of allometric models are discussed in the text.

Hemodynamic Measurements

Brachial blood pressure was obtained before and after the MRI scan, while the subject was on the MRI table, with the results averaged.\(^24\) For radial tonometry, 30 s of data was recorded using the HDI/PulseWave-CR2000 tonometry device (Hypertension Diagnostics, Eagan, MN) and digitized at 200 Hz for offline processing. Custom-designed software was written in MatLab (The MathWorks, Natick, MA) for analysis of waveforms and to generate an averaged waveform for each individual. A generalized transfer function was applied to radial artery pressure waveforms to arrive at a physiological flow waveform.\(^24\) A physiological flow waveform was applied to the central pressure waveform to separate the forward-traveling (\(P_f\)) and backward-traveling (reflected; \(P_b\)) waves, as previously described in detail.\(^25\) All pressure waveforms were visually inspected by an investigator (J.A.C.) for quality and physiological consistency. We excluded averaged waveforms that met any of the following criteria: (1) a nonphysiological appearance (usually from bigeminy, trigeminy, or contamination of the signal average by aberrantly recorded complexes); (2) cardiac cycle duration variation ≥10%; (3) pulse height (beat-to-beat pulse pressure) variation ≥20%; (4) <10 adequately recorded cycles available for signal averaging; (5) inability to identify key landmark points of the pressure waveform required for wave separation using an averaged physiological flow approach clearly. We also created models for LV mass and the LV wall:cavity volume ratio using augmentation index (AIX), an index of wave reflections that does not require wave separation in its derivation. Augmentation index was divided by height; such linear indexation is appropriate because the allometric exponent relating AIX to height is negative and not significantly different from the unity.\(^26\) Results from these models can be found in Table S2.

Mean arterial pressure is usually computed with a formula using diastolic and systolic blood pressure. Such approach assumes a constant relationship between mean pressure and diastolic/systolic pressures (ie, a constant form factor). However, this relationship varies according to the morphology of the waveform in the upper limb. Therefore, rather than assuming that in all subjects mean arterial pressure relates consistently to systolic and diastolic blood pressure, a subject-specific form factor was computed for each individual based on the radial tonometric waveform. The form factor was calculated as\(^27\)

\[
\text{Form factor} = \frac{\text{Radial mean pressure} - \text{radial diastolic pressure}}{\text{Radial systolic pressure} - \text{radial diastolic pressure}}
\]

Mean arterial pressure at the time of the MRI was then calculated based on systolic and diastolic blood pressure measured at the time of the MRI examination as follows: diastolic pressure+form
factor×(pulse pressure). SVR, expressed in Wood units, was calculated as the ratio of the mean arterial pressure at the time of the cardiac MRI divided by the cardiac output obtained during the MRI.

TAC was approximated as the ratio of the stroke volume:central pulse pressure obtained using arterial tonometry. Given that arterial load is highly dependent on body size, we indexed TAC and SVR for BSA by dividing TAC by BSA and multiplying SVR by BSA. Such linear indexation is justified because absolute allometric exponents relating both TAC and SVR to BSA are approximately (and not significantly different from) the unity.

We restricted the range of observations to those individuals who had a cardiac output indexed to BSA that was between 2 and 5 L/min per square meter to minimize the effect of outlier data points.

**Statistical Analysis**

Descriptive data are presented as mean±SD, medians (interquartile range), or percentages as appropriate. Regression models were created to determine the significant predictors of (1) percentage predicted LV mass; (2) the LV wall:cavity volume ratio. Models were adjusted for covariates known to affect LV mass or geometry, including sex, diabetes mellitus, age, smoking status, diagnosis of hypertension and antihypertensive medication use, ethnicity, renal function, lipid profile, statin use, and heart rate. Because the amplitude of the backward wave (P) depends strongly on the amplitude of the forward wave, all models that included P also included the amplitude. Beta coefficients and standardized β-coefficients are presented from the adjusted models, with P<0.05 considered as significant. The proportion of the variability in the dependent variable explained by the model is presented as the R2. Additional details on the explanatory power of the model and its components may be found in Table S3. Tests for interactions between sex and each metric of afterload (indexed SVR, indexed TAC, and P) were performed by adding an interaction term to the model. If the interaction term was significant (P<0.05), sex-stratified analyses were performed. All analyses were performed using STATA 13 (StataCorp, College Station, TX).

**Results**

A total of 5098 participants in MESA underwent baseline cardiac MRI examination, of which 5004 subjects had information on LV mass. Four thousand six hundred sixty-four (93%) subjects with LV mass information also had radial tonometry performed, of which 4422 (95%) allowed for successful wave separation analysis. Two hundred seventy seven (6%) of these subjects had a nonphysiological determination of cardiac output; thus, the final cohort for this analysis includes 4145 individuals (48% men and 52% women). Demographic, anthropometric, and laboratory characteristics are presented in Table 1. As expected, height and weight were significantly greater in men (P<0.001), with a slightly greater proportion of diabetics in men (13% versus 11%; P=0.009). A greater proportion of women had a diagnosis of hypertension (44%...
versus 40%; \( P=0.02 \)) or used antihypertensive medications (36% versus 33%; \( P=0.02 \)). LV mass was significantly greater in men than in women (168.5±35.9 versus 123.9±26.8 g; \( P<0.001 \)); however, percentage predicted LV mass was slightly greater in women (104.5±17.5 versus 103.2±18.3%; \( P=0.02 \)). Men displayed a more concentric geometry than women (LV wall:cavity volume ratio, 1.16±0.22 versus 1.06±0.19; \( P=0.01 \)).

Indexed metrics of arterial load are presented in Table 2. Men had slightly higher indexed SVR (34.0; 95% confidence interval [CI], 33.7–34.4 versus 32.8; 95% CI, 32.5–33.1 Wood units×m²; \( P<0.001 \)). LV mass was significantly greater in men than in women (168.5±35.9 versus 123.9±26.8%; \( P<0.001 \); however, percentage predicted LV mass was slightly greater in women (104.5±17.5 versus 103.2±18.3%; \( P=0.02 \)). Men displayed a more concentric geometry than women (LV wall:cavity volume ratio, 1.16±0.22 versus 1.06±0.19; \( P=0.01 \)).

Data from regression models for percentage predicted LV mass are presented in Table 3. In the overall model (\( R^2=20.9\% \); see Table S3 for the contributions from each variable), SVR (\( P<0.001 \)), TAC (\( P<0.001 \)), \( P_f \) (\( P<0.001 \)), and \( P_b \) (\( P=0.001 \)) were associated with LV mass. In this model, \( P_b \) was positively associated with LV mass, whereas \( P_f \) was negatively associated. Indexed SVR was positively associated with LV mass. Formal testing demonstrated significant interactions between sex and metrics of pulsatile load (sex-TAC, \( P=0.01 \); sex-\( P_f , P=0.02 \); sex-\( P_b , P=0.02 \)) although not for SVR (sex-SVR, \( P=0.87 \)). Additional models were also created in which LV mass was indexed to BSA, or in which log (LV mass) was modeled with adjustment for log (height) and log (weight). These models, presented in Table S1, demonstrated consistent relationships to the allometrically adjusted model for percentage predicted LV mass.

Models assessing metrics of arterial load as predictors of the LV wall:cavity volume ratio are presented in Table 4. In the overall model (\( R^2=37.6\% \); Table S3), indexed SVR (\( P<0.001 \)) and indexed TAC (\( P<0.001 \)) were both associated with LV geometry, with increasing SVR and lower TAC predicting a higher LV wall:cavity volume ratio. \( P_b \) was not associated with the LV wall:cavity volume ratio (\( P=0.15 \)) although \( P_f \) demonstrated a negative association (\( P<0.004 \)). Formal testing demonstrated a significant interaction between metrics of pulsatile load and sex (sex-TAC, \( P=0.003 \); sex-\( P_f , P=0.001 \); sex-\( P_b , P=0.002 \)) although not for resistive load (sex-SVR, \( P=0.08 \)). Only in women, greater forward wave magnitude was associated with lower LV wall:cavity volume ratios.
In contrast, more selectively impose mid-to-late systolic load on the LV. In our study, SVR demonstrated a weak relationship with LV mass, as evidenced by its relatively small standardized β coefficient, implying that LV mass is not merely determined by the key arterial properties that governs absolute wall stress throughout ejection. However, P_s, which selectively imposes load on the LV during mid-to-late systole, demonstrated the strongest relationship with LV mass, suggesting that mid-to-late systolic loading has the greatest effect on LV hypertrophy. Indeed, in our models that included both P_s and P_f, both were associated with LV mass, but with opposite signs, implicating the loading sequence (early versus late load, rather than absolute load per se) as a correlate of LV hypertrophy. This paradigm is highly consistent with animal experiments in which, for any given peak pressure, late systolic loading resulted in much more prominent hypertrophy than early systolic loading. Similarly, observational studies in both animals and humans have correlated compliance and wave reflections to LV hypertrophy. Furthermore, reductions in wave reflections correlated closely to the reduction in LV mass seen with antihypertensive treatment, independent of the degree of blood pressure reduction.

In our study, a weak positive association between TAC and LV mass was found, a seemingly counterintuitive finding. Compliance in the arterial tree is largely provided by large conduit vessels and is linearly proportional to vessel volume and inversely proportional to wall stiffness. This means that larger vessels accommodate larger stroke volumes with less change in pressure for a given stiffness. In models that adjusted for P_f and P_s amplitude, it is possible that TAC captured some variability in arterial size (such as eccentric arterial remodeling), which in turn may drive its positive relationship with LV mass. Of note, this relationship persisted even when indexing LV mass to body size using numerous different methods. Additional studies with detailed measurements of arterial size, geometry, and stiffness, ideally in several conduit arterial segments, may clarify this relationship.

### LV Concentric Remodeling, Resistive, and Pulsatile Load

In our study, both SVR and TAC were associated with the LV wall:cavity volume ratio, with higher SVR, or lower

#### Table 4. Relationship Between Metrics of Afterload and Left Ventricle Wall:Cavity Volume Ratio

<table>
<thead>
<tr>
<th>Load Metric</th>
<th>Overall (n=4031)</th>
<th>Men (n=1942)</th>
<th>Women (n=2089)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indexed systemic vascular resistance, Wood units×m²</td>
<td>0.006 0.22 &lt;0.001</td>
<td>… … …</td>
<td>… … …</td>
</tr>
<tr>
<td>Indexed TAC, mL/mm Hg square meter</td>
<td>−0.30 −0.43 &lt;0.001</td>
<td>−0.33 −0.49 &lt;0.001</td>
<td>−0.31 −0.41 &lt;0.001</td>
</tr>
<tr>
<td>P_s, mm Hg</td>
<td>−0.003 −0.09 0.15</td>
<td>−0.005 −0.15 0.10</td>
<td>−0.001 −0.04 0.63</td>
</tr>
<tr>
<td>P_f, mm Hg</td>
<td>−0.004 −0.18 0.004</td>
<td>−0.004 −0.13 0.15</td>
<td>−0.006 −0.25 0.003</td>
</tr>
</tbody>
</table>

Adjusted for sex, age, diabetes mellitus, diagnosis of hypertension, current smoking, ethnicity, estimated glomerular filtration rate, uric acid:creatinine ratio, cholesterol profile, statin therapy, antihypertensive therapy, and heart rate. P_s indicates reflected wave amplitude; P_f forward wave amplitude; and TAC, total arterial compliance.

#### Discussion

Our study demonstrates that components of arterial load associate differently with LV hypertrophy and concentric remodeling. SVR, TAC, P_s, and P_f were significant independent correlates of LV mass. Late systolic load, as demonstrated by P_s, was associated with increased LV mass, whereas load experienced earlier by the ventricle (ie, P_f) was associated with lower LV mass. SVR and TAC were significant predictors of LV relative geometry (wall:cavity volume ratio), whereas P_f was not. Women demonstrated greater pulsatile load than men, even after adjustment for body size. In contrast, men demonstrated greater resistive load. Our findings implicate arterial load in LV remodeling in the general population, with various components of arterial load differentially associating with LV hypertrophy and concentric remodeling.

#### LV Mass: Resistive Versus Pulsatile Load

In the absence of aortic stenosis, the arterial system imposes the load opposing LV ejection. However, the different segments and properties of the arterial tree contribute to the load differently and at different times during the cardiac cycle. At the beginning of systole, LV geometry is quasi-diastolic, with a large chamber radius and relatively thin walls, both of which contribute to greater wall stress, as predicted by Laplace’s Law. Peak wall stress experienced by the LV occurs during this early systolic period. A previous study demonstrates that peak stress is largely determined by SVR and to a lesser degree, by proximal aortic characteristic impedance, without significant contributions from TAC and reflected waves: SVR is the main determinant of the wall stress-time integral throughout ejection. Reflected waves,
TAC, associated with more concentric geometry. Because both SVR and TAC are important determinants of the total LV systolic wall stress,35 perhaps relative geometry is determined, at least in part, by the wall stress experienced by the ventricle.

Furthermore, TAC was the most significant predictor of the LV wall:cavity volume ratio. Previous study demonstrates that TAC is not a significant contributor to peak wall stress, which manifests during early systole.35 Thus, the relationship between lower TAC and increased LV wall:cavity volume ratio may again be a manifestation of the loading sequence on the LV. Interestingly, $P_f$ was negatively associated with LV wall:cavity volume ratio, suggesting that either early load is associated with more eccentric, as opposed to concentric, geometry, or that more concentric ventricles generate forward waves of lower amplitude. Importantly, the relationship with $P_f$ was driven by women, which raises the possibility that the myocardium in women may be more susceptible to changes in the loading sequence. These issues should be addressed in future research.

Sex Differences in Pulsatile Load

In our study, we demonstrate that women exhibited greater pulsatile load (Table 2). Previously, Coutinho et al41 demonstrated sex differences in pulsatile load among a cohort of 461 subjects. However, the metrics of pulsatile load measured in this study were not scaled to body size, raising the possibility that the differences in size may, at least partially, underlie the differences in pulsatile load.42 Because metrics of pulsatile load bear important relationships with body size, careful scaling is required to discern true sex differences.26 Our findings, which used allometric indexation of arterial load indices, reinforce the presence of a difference in pulsatile load between men and women and a greater effect of pulsatile hemodynamics and the loading sequence on the myocardium in women when compared with men.41,43,44

Our study should be interpreted in the context of its strengths and limitations. Strengths of our study include the large, multiethnic, well-characterized, population-based sample, the separation of arterial load into resistance and pulsatile components, and the accurate determination of LV mass and geometry using cardiac MRI. A strength of our study is that we focused on indices of arterial load (derived from pressure and flow measurements), rather than blood pressure alone. Although blood pressure is known to be associated with LV mass,34,45 the former is a composite resulting from LV pumping function and input impedance (ie, the arterial load).46,47 Our study focuses on arterial load and, therefore, adds to the literature by isolating the effect of arterial properties on the LV, without focusing on blood pressure alone.

Our study also has significant limitations. We did not account for brachial-to-radial pulse pressure amplification although this is unlikely to have systematically affected our results on relationships with LV remodeling.25 We approximated TAC as the ratio of stroke volume:central pulse pressure. This method neglects the run off of blood from the arterial system into the venous beds, and thus is confounded by SVR, because the arterial system is not a truly closed system in which changes in intra-arterial pressure relate exclusively to the injection of stroke volume during systole.19 Adjustment for SVR in the models should have mitigated this limitation. Time-resolved flow measurements were not available. As such, characteristic impedance of the aorta, an important determinant of pulsatile load, could not be determined. Similarly, to determine $P_r$ and $P_f$, we applied an averaged physiological flow waveform, rather than measured time-resolved flow.23 This may have introduced noise in our measurements of $P_r$, $P_f$, and their ratio. Despite this, important relationships between the loading sequence and LV mass were apparent in this large sample.

Perspectives

In a large cohort of well-characterized subjects, we demonstrate the relative contributions of resistive and pulsatile load on LV remodeling. Among the components of afterload, the main correlate of LV hypertrophy was $P_f$, supporting the role of the loading sequence in LV hypertrophy. We demonstrate that SVR and TAC influence relative geometry (ie, concentric remodeling) of the LV. We also confirm the presence of greater pulsatile load in women and demonstrate greater importance of the loading sequence in the response of the LV to arterial load in women. Our study highlights important aspects of the arterial system and how arterial load affects the LV in men and women from the general population.

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Disclosures

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References


**Novelty and Significance**

**What Is New?**
- We investigated the effect of resistive and pulsatile hemodynamics on left ventricular (LV) mass and geometry.
- We studied a large cohort of well-characterized individuals.
- We demonstrate that both pulsatile and resistive components of the hydraulic load are important in determining LV mass and geometry.
- We highlight sex differences in pulsatile hemodynamics, with women demonstrating greater pulsatile load.

**What Is Relevant?**
- Both resistive and pulsatile components of the arterial load are important in determining LV mass and geometry.

**Summary**
- Reflected wave magnitude is the most important correlate of LV mass. Both pulsatile and resistive components are important determinants of relative LV geometry. Women demonstrate greater pulsatile load than men.

**Reflected wave amplitude**, which increases LV load in mid-to-late systole, is the load index with the strongest association with LV mass. In contrast, total arterial compliance and systemic vascular resistance were important determinants of LV geometry.

- These findings highlight the differential effect of different components of arterial load on LV remodeling.
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Supplemental Material

Title: Resistive and Pulsatile Arterial Load as Predictors of Left Ventricular Mass and Geometry: The Multiethnic Study of Atherosclerosis

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(9) Los Angeles Biomedical Research Institute, Torrance, CA, USA.
(10) Biofluid, Tissue, and Solid Mechanics for Medical Applications, IBiTech, iMinds Medical IT, Ghent University, Ghent, Belgium.
Supplemental Table S1 – Relationship between Metrics of Afterload and LV Mass in 4031 subjects in the MESA cohort

<table>
<thead>
<tr>
<th>Load Metric</th>
<th>Model 1: Allometric Adjustment for Height and Weight*</th>
<th>Model 2: LV Mass Adjusted to BSA*</th>
<th>Model 3: Log (LV Mass) adjusted for Log (Height) and Log (Weight)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Beta</td>
<td>St. β</td>
<td>P</td>
</tr>
<tr>
<td>Indexed SVR (WU*m²)</td>
<td>0.19</td>
<td>0.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Indexed TAC (mL/mm Hg/m²)</td>
<td>26.65</td>
<td>0.44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P_b (mmHg)</td>
<td>1.76</td>
<td>0.73</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P_f (mmHg)</td>
<td>-0.48</td>
<td>-0.23</td>
<td>0.001</td>
</tr>
</tbody>
</table>

SVR = systemic vascular resistance  
St. β = standardized β coefficient  
WU = Wood Units  
*Adjusted for: gender, age, diabetes, diagnosis of hypertension, current smoking, ethnicity, estimated GFR, urine albumin:creatinine ratio, cholesterol profile, statin therapy, antihypertensive therapy, and heart rate
## Supplemental Table S2 – Relationship between LV Mass and Expressions of Arterial Hemodynamics

<table>
<thead>
<tr>
<th>Load Metric</th>
<th>LV Mass</th>
<th>LV Mass-to-Volume Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Beta</td>
<td>St. β</td>
</tr>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indexed SVR</td>
<td>0.19</td>
<td>0.08</td>
</tr>
<tr>
<td>Indexed TAC</td>
<td>26.65</td>
<td>0.44</td>
</tr>
<tr>
<td>P_b</td>
<td>1.76</td>
<td>0.73</td>
</tr>
<tr>
<td>P_f</td>
<td>-0.48</td>
<td>-0.23</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indexed SVR</td>
<td>0.03</td>
<td>0.01</td>
</tr>
<tr>
<td>Indexed TAC</td>
<td>6.53</td>
<td>0.11</td>
</tr>
<tr>
<td>Indexed Aortic Alx</td>
<td>5.09</td>
<td>0.04</td>
</tr>
</tbody>
</table>

SVR = systemic vascular resistance  
St. β = standardized β coefficient  
WU = Wood Units

*Adjusted for: gender, age, diabetes, diagnosis of hypertension, current smoking, ethnicity, estimated GFR, urine albumin:creatinine ratio, cholesterol profile, statin therapy, antihypertensive therapy, and heart rate
Supplemental Table S3. Proportion of Variability in LV Mass and the LV Wall-to-Cavity Volume Ratio Explained in the Models

<table>
<thead>
<tr>
<th>Description</th>
<th>LV Mass</th>
<th>LV Wall-to-Cavity Volume Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of variability explained by full model</td>
<td>20.9%</td>
<td>37.6%</td>
</tr>
<tr>
<td>Proportion of variability explained by individual components of the full model</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Descriptive Variables¹</td>
<td>12.7%</td>
<td>21.2%</td>
</tr>
<tr>
<td>Indexed SVR (Wood Units*m²)</td>
<td>0.6%</td>
<td>11.4%</td>
</tr>
<tr>
<td>Indexed TAC (mL/mm Hg/m²)</td>
<td>5.0%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Pb/Pt</td>
<td>2.6%</td>
<td>2.1%</td>
</tr>
</tbody>
</table>

¹ Includes gender, age, diabetes, hypertension, smoking status, ethnicity, estimated GFR, urine albumin:creatinine ratio, cholesterol profile, statin use, antihypertensive