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# Resistive and Pulsatile Arterial Load as Predictors of Left Ventricular:

## Mass and Geometry: The Multiethnic Study of Atherosclerosis

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## Abstract

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Arterial load is comprised of resistive and various pulsatile components, but their relative contributions to left ventricular (LV) remodeling in the general population are unknown. We studied 4,145 participants enrolled in the Multi-Ethnic Study of Atherosclerosis, who underwent cardiac magnetic resonance imaging 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 ($P_b$). TAC and SVR were adjusted for body surface area to allow for appropriate gender comparisons. We performed allometric adjustment of LV mass for body size and gender, 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), $P_b$ (β=0.73;*P*<0.001), and $P_f$ (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 $P_f$ (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/$m^2$, *P*<0.0001), while men demonstrated a higher indexed SVR (34.0 versus 32.8 Wood Units*$m^2$, *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 (i.e. early load versus late load) is an important determinant of LV response to arterial load.

**Keywords**

left ventricular hypertrophy; left ventricular remodeling; arterial load; afterload; wave reflections; vascular resistance; arterial hemodynamics

## Introduction

In the absence of aortic valve stenosis, the arterial system presents the main opposition (i.e., 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 (left ventricular hypertrophy, LVH) 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 LVH in older studies.[1, 2] However, stroke volume is naturally related to LV mass at any given ejection fraction and relative geometry, making the 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.[3-8] However, other components of arterial load (such as TAC or

SVR) were generally not simultaneously analyzed, preventing the discrimination of independent associations between components of resistive and pulsatile load and LV remodeling. Similarly, prior studies have suggested gender-related differences in pulsatile load,[5, 9-12] although the impact of these differences on LV structure and function has not been thoroughly addressed. This is particularly important, as 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, gender comparisons regarding 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 gender differences in arterial load and their impact 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 6,814 men and women aged 45-84 years from six centers across the United States to ensure inclusion of subjects from diverse ethnic backgrounds. Subjects self-reported their ethnicity as African-American, Asian-American (predominantly Chinese), White, or Hispanic. All subjects were free of cardiovascular disease by self-report at the time of inclusion. Subjects were enrolled between 2000-2002. The study was approved by the institutional review boards of all participating centers, and subjects signed informed consent at the time of enrollment.

### Assessment of LV Mass and Relative Geometry

A total of 5,098 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 ms/3-5 ms, flip angle 20°, 6mm slice thickness, 4mm 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 semi-automated method (MASS 4.2, Medis, Leiden, the Netherlands).[20] Myocardial volume was defined as the difference between epicardial and endocardial areas 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.[22] Cardiac output was determined by multiplying the stroke volume with the heart rate at the time of the examination.

We calculated the LV wall-to-cavity volume ratio as an indicator of LV concentric vs. 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, impaired fasting glucose, or diabetic medication use. Log-Log models were created by regressing log (LV mass) on log (height), log (weight), and gender to obtain appropriate allometric coefficients for height and weight, while adjusting for the effect of gender. Predicted LV mass was determined using the following formula: 100 * LV mass(g)/ (a * height(m)$^{0.54}$ * weight(kg)$^{0.61}$) where a=6.82 in women and 8.25 in men.[20] LV mass was expressed as a percentage of the predicted value; values greater than 100 indicate larger LV mass than predicted by body size and gender, whereas, values less than 100 indicate smaller values. Additional models (Supplemental Table S1) were also created in which LV mass was indexed to body surface area, 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.[23] For radial tonometry, thirty-seconds of data was recorded using the HDI/PulseWave-CR2000 tonometry device (Hypertension Diagnostics, Eagan, Minnesota) and digitized at 200 Hz for offline processing. Custom-designed software was written in MatLab (The Mathworks, Natick, Massachusetts) 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 the central pressure waveform.[24] A physiologic 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 physiologic consistency. We excluded averaged waveforms that met any of the following criteria: (1) A non-physiologic 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) Less than 10 adequately recorded cycles available for signal averaging; (5) Inability to clearly identify key landmark points of the pressure waveform required for wave separation using an averaged physiologic flow approach. We also created models for LV mass and the LV wall-to-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 as 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 the supplement (Supplemental 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 (i.e., 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]

$$Form\quad Factor\quad (FF) = \frac{Radial\quad Mean\quad Pressure - Radial\quad Diastolic\quad Pressure}{Radial\quad Systolic\quad Pressure - Radial\quad Diastolic\quad Pressure}$$

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 + FF*(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.

Total arterial compliance was approximated as the ratio of the stroke volume to the central pulse pressure obtained using arterial tonometry. Given that arterial load is highly dependent on body size,[19] we indexed TAC and SVR for body surface area (BSA ) by dividing TAC by BSA and multiplying SVR by BSA.[19] 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.[26]

We restricted the range of observations to those individuals who had a cardiac output indexed to BSA that was between 2 and 5 liters/min/$m^2$ to minimize the impact of outlier data-points.

## Statistical Analysis

Descriptive data are presented as mean±standard deviations, medians (interquartile range), or percentages as appropriate. Regression models were created to determine the significant predictors of: (1) Percent predicted LV mass; (2) The LV wall-to-cavity volume ratio. Models were adjusted for covariates known to impact LV mass or geometry including: gender,[28] diabetes,[29] age, smoking status,[30] diagnosis of hypertension and antihypertensive medication use, ethnicity,[31, 32] renal function,[33] lipid profile, statin use,[34] and heart rate. Because the amplitude of the backward wave ($P_b$) depends strongly on the amplitude of the forward wave, all models that included $P_b$ also included $P_f$ 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 $R^2$. Further details regarding the explanatory power of the model and its components may be found in the supplement (Supplemental Table S3). Tests for interactions between gender and each metric of afterload (indexed SVR, indexed TAC, and $P_b$) were performed by adding an interaction term to the model. If the interaction term was significant ($P<0.05$), gender-stratified analyses were performed. All analyses were performed using STATA 13 (StataCorp, College Station, TX).

## Results

A total of 5,098 participants in MESA underwent baseline cardiac MRI examination of which 5004 subjects had information regarding LV mass. Four thousand six hundred and 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 and seventy-seven (6%) of these subjects had a nonphysiologic determination of cardiac output; thus, the final cohort for this analysis includes 4,145 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% vs. 40%, $P$=0.02) or used antihypertensive medications (36% vs. 33%, $P$=0.02). LV mass was significantly greater in men than women (168.5±35.9 versus 123.9±26.8 grams, $P$<0.001); however, percent 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-to-cavity volume ratio: 1.16±0.22 versus 1.06±0.19; $P$<0.001).

Indexed metrics of arterial load are presented in Table 2. Men had slightly higher indexed SVR (34.0 [95%CI 33.7-34.4] versus 32.8 [95%CI 32.5-33.1] Wood Units*$m^2$, $P$<0.0001), indicative of greater resistive load. Women, on the other hand, had greater pulsatile load, as evidenced by a lower indexed TAC (0.89 [95%CI 0.88-0.90] versus 1.04 [95%CI 1.03-1.06] mL/mmHg/$m^2$, $P$<0.0001), greater $P_f$ (32.4 [95%CI 32.0-32.7] versus 29.0 [95%CI 28.6-29.3] mmHg, $P$<0.0001), greater $P_b$ (27.2 [95%CI 26.8-27.5] versus 24.3 [95%CI 24.0-24.6] mmHg, $P$<0.0001), and a greater $P_b/P_f$ ratio (reflection magnitude [RM], a dimensionless index of wave reflections; 0.840 [95%CI 0.838-0.842] versus 0.836 [95%CI 0.834-0.838], $P$=0.005). After adjusting for $P_f$ amplitude, $P_b$ amplitude was not significantly different between men and women ($P$=0.07).

Data from regression models for percent-predicted LV mass are presented in Table 3. In the overall model ($R^2$ = 20.9%, see Supplemental Table S3 for the from each variable), SVR ($P$<0.001), TAC ($P$<0.001), $P_b$ ($P$<0.001), and $P_f$ ($P$=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 gender and metrics of pulsatile load (gender-TAC, $P$=0.01; gender-$P_b$, $P$=0.02; gender-$P_f$, $P$=0.02), though not for SVR (gender-SVR, $P$=0.87). Additional models were also created in which LV mass was indexed to body surface area, or in which log (LV mass) was modeled with adjustment for log (height) and log (weight). These models, presented in Supplemental Table S1, demonstrated consistent relationships to the allometrically-adjusted model for percent-predicted LV mass.

Models assessing metrics of arterial load as predictors of the LV wall-to-cavity volume ratio are presented in Table 4. In the overall model ($R^2$=37.6%; Supplemental 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-to-cavity volume ratio. $P_b$ was not associated with the LV wall-to-cavity volume ratio (P=0.15) though Pf demonstrated a

negative association ($P<0.004$). Formal testing demonstrated a significant interaction between metrics of pulsatile load and gender (gender-TAC, $P=0.003$; gender-$P_b$, $P=0.001$; gender-$P_f$, $P=0.002$), though not for resistive load (gender-SVR, $P=0.08$). In women only, greater forward wave magnitude was associated with lower LV wall-to-cavity volume ratios.

Analogous models for LV mass and the LV wall-to-cavity volume ratios were created using AIx instead of $P_b$ and $P_f$, as AIx does not require wave separation analysis and can be derived solely from the arterial waveform during tonometry (Supplemental Table S2). In general, these models are consistent with the results obtained using $P_b$ and $P_f$ and demonstrate that greater wave reflections (i.e. a higher AIx) are associated with increased LV mass. Conversely, greater AIx was associated with smaller LV wall-to-cavity volume ratios, likely reflecting the contribution of $P_f$ on AIx (Supplemental Table S2).

## Discussion

Our study demonstrates that components of arterial load associate differently with LV hypertrophy and concentric remodeling. SVR, TAC, $P_b$, and $P_f$ were significant independent correlates of LV mass. Late systolic load, as demonstrated by $P_b$, was associated with increased LV mass; whereas, load experienced earlier by the ventricle (i.e., $P_f$), was associated with lower LV mass. SVR and TAC were significant predictors of LV relative geometry (wall-to-cavity volume ratio), while $P_b$ 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.

### Left Ventricular 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, left ventricular 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 left ventricle occurs during this early systolic period.[35] 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.[35] Reflected waves, in contrast, more selectively impose mid-to-late systolic load on the LV.[35] In our study, SVR demonstrated a weak relationship to LV mass, as evidenced by its relatively small standardized beta coefficient, implying that LV mass is not merely determined by the key arterial properties that governs absolute wall stress throughout ejection. On the other hand, $P_b$, 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 impact on LV hypertrophy. Indeed, in our models that included both $P_b$ and $P_f$, both were associated with LV mass, but with opposite signs, implicating the loading sequence (early vs. 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.[36] Similarly, observational studies in both animals and humans have correlated compliance and wave reflections to LV hypertrophy.[3-7, 37, 38] 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.[39, 40]

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.[19] 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 $P_b$ 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. Future 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-to-cavity volume ratio, with higher SVR, or lower TAC, associated with more concentric geometry. As 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-to-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-to-cavity volume ratio may again be a manifestation of the loading sequence on the LV. Interestingly, $P_f$ was negatively associated with LV wall-to-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.

### Gender Differences in Pulsatile Load

In our study, we demonstrate that women exhibited greater pulsatile load (Table 2). Previously, Coutinho *et al*. demonstrated gender differences in pulsatile load amongst a cohort of 461 subjects.[41] 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] As metrics of pulsatile load bear important relationships to body size, careful scaling is required to discern true gender differences.[26] Our findings, which utilized allometric indexation of arterial load indices,

reinforce the presence of a difference in pulsatile load between men and women, and a greater impact of pulsatile hemodynamics and the loading sequence on the myocardium in women as compared to men.[41, 43, 44]

Our study should be interpreted in the context of its strengths and limitations. Strengths of our study include the large, multi-ethnic 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 (i.e. the arterial load).[46, 47] Our study focuses on arterial load and therefore adds to the literature by isolating the impact 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 regarding relationships with LV remodeling.[27] We approximated TAC as the ratio of stroke volume to 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, since 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 $P_b$ and $P_f$, we applied an averaged physiologic flow waveform, rather than measured time-resolved flow.[25] This may have introduced noise in our measurements of $P_b$, $P_f$, 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. Amongst the components of afterload, the main correlate of LV hypertrophy was $P_b$, supporting the role of the loading sequence in LV hypertrophy. We demonstrate that SVR and TAC influence relative geometry (i.e., 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 impacts the LV in men and women from the general population.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Novelty and Significance

1. What is new?
   - **a.** We investigated the impact of resistive and pulsatile hemodynamics on LV mass and geometry.
   - **b.** We studied a large cohort of well-characterized individuals.
   - **c.** We demonstrate that both pulsatile and resistive components of the hydraulic load are important in determining LV mass and geometry.
   - **d.** We highlight gender differences in pulsatile hemodynamics, with women demonstrating greater pulsatile load.
2. What is relevant?
   - **a.** Both resistive and pulsatile components of the arterial load are important in determining LV mass and geometry.
   - **b.** 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.
   - **c.** These findings highlight the differential impact of different components of arterial load on LV remodeling.
3. Summary:
   - **a.** Reflected wave magnitude is the most important correlate of LV mass.
   - **b.** Both pulsatile and resistive components are important determinants of relative LV geometry.
   - **c.** Women demonstrate greater pulsatile load than men.

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**Table 1**

Overall Characteristics of the MESA Cohort

| Descriptive Characteristics | Overall n= 4145 | Men n=2001 | Women n=2144 | *P*-Value |
|---|---|---|---|---|
| **Age (years), mean (SD)** | 61.3 (10.1) | 61.3 (10.1) | 61.3 (10.1) | 1.00 |
| **Height (cm), mean (SD)** | 166.4 (10.0) | 173.4 (7.7) | 160.0 (7.1) | <0.001 |
| **Weight (kg), mean (SD)** | 76.9 (16.1) | 82.4 (14.6) | 71.8 (15.7) | <0.001 |
| **Diabetes, n (%)** | 489 (12%) | 263 (13%) | 226 (11%) | 0.009 |
| **Hypertension, n (%)** | 1739 (42%) | 803 (40%) | 936 (44%) | 0.02 |
| **Current Smoker, n (%)** | 1466 (35%) | 861 (43%) | 605 (28%) | <0.001 |
| **Race** | | | | |
| **White, n (%)** | 1569 (38%) | 754 (38%) | 815 (38%) | 0.83 |
| **Black, n (%)** | 1019 (25%) | 462 (23%) | 557 (26%) | 0.03 |
| **Chinese, n (%)** | 571 (14%) | 287 (14%) | 284 (13%) | 0.31 |
| **Hispanic, n (%)** | 986 (24%) | 498 (25%) | 488 (23%) | 0.11 |
| **Urine Albumin:Creatinine Ratio (mg/g); median (25%, 75%)** | 5.18 (3.3, 10.2) | 4.7 (3.0, 9.7) | 5.59 (3.6, 10.7) | 0.06 |
| **Estimated GFR (mL/min/1.73 $m^2$), mean (SD)** | 78.5 (15.7) | 78.9 (15.6) | 78.2 (15.9) | 0.15 |
| **Total Cholesterol (mg/dL), mean (SD)** | 194.4 (35.2) | 188.6 (34.0) | 199.8 (35.5) | <0.001 |
| **LDL (mg/dL), mean (SD)** | 117.2 (31.2) | 117.2 (30.9) | 117.3 (31.5) | 0.89 |
| **HDL (mg/dL), mean (SD)** | 51.1 (14.9) | 45.1 (11.6) | 56.7 (15.4) | <0.001 |
| **Triglycerides (mg/dL), mean (SD)** | 131.9 (82.7) | 135.2 (88.6) | 128.9 (76.6) | 0.01 |
| **Statin Use, n (%)** | 595 (14.3%) | 272 (13.6%) | 323 (15%) | 0.17 |
| **Systolic Blood Pressure, mean (SD)** | 134.0 (20.5) | 133.7 (19.1) | 134.2 (21.7) | 0.38 |
| **Diastolic Blood Pressure, mean (SD)** | 77.4 (11.0) | 80.0 (10.3) | 75.0 (11.1) | <0.001 |
| **Mean Arterial Pressure, mean (SD)** | 100.8 (14.0) | 101.6 (13.0) | 100.0 (14.8) | <0.001 |
| **Antihypertensive Medication Use, n (%)** | 1428 (34%) | 653 (33%) | 775 (36%) | 0.02 |
| **LV Mass (grams), mean (SD)** | 145.5 (38.6) | 168.5 (35.9) | 123.9 (26.8) | <0.001 |
| **LV Mass indexed to BSA (g/$m^2$), mean (SD)** | 78.1 (15.6) | 85.7 (15.4) | 70.9 (12.1) | <0.001 |
| **Percent Predicted LV mass (%), mean (SD)** | 103.9 (17.9) | 103.2 (18.3) | 104.5 (17.5) | 0.02 |
| **LV Wall Volume to Cavity Volume Ratio, mean (SD)** | 1.11 (0.21) | 1.16 (0.22) | 1.06 (0.19) | <0.001 |

**Table 2**

Indexed Metrics of Hydraulic Load

| Load Metric | Overall (n=4145) | Men (n=2001) | Women (n=2144) | P-value |
|---|---|---|---|---|
| **Indexed Systemic Vascular Resistance (Wood Units*$m^2$), mean (95% CI)** | 33.4 (33.2-33.6) | 34.0 (33.7-34.4) | 32.8 (32.5-33.1) | <0.0001 |
| **Indexed Total Arterial Compliance (mL/mm Hg/$m^2$), mean (95% CI)** | 0.96 (0.96-0.97) | 1.04 (1.03-1.06) | 0.89 (0.88-0.90) | <0.0001 |
| **$P_b$ (mm Hg), mean (95% CI)** | 25.8 (25.5-26.0) | 24.3 (24.0-24.6) | 27.2 (26.8-27.5) | <0.0001 |
| **$P_f$ (mm Hg), mean (95% CI)** | 30.7 (30.5-31.0) | 29.0 (28.6-29.3) | 32.4 (32.0-32.7) | <0.0001 |
| **$P_b$, adjusted for $P_f$ (95% CI)** | 25.8 (25.7-25.8) | 25.7 (25.6-25.8) | 25.8 (25.7-25.9) | 0.07 |
| **Reflection Magnitude, mean (95% CI)** | 0.838 (0.837-0.840) | 0.836 (0.834-0.838) | 0.840 (0.838-0.842) | 0.005 |

**Table 3**

Relationship between Metrics of Afterload and Percent Predicted LV mass

| Load Metric | Overall (n=4031) | | | Men (n=1942) | | | Women (n=2089) | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Beta Coefficient** | **Standardized β** | ***P*** | **Beta Coefficient** | **Standardized β** | ***P*** | **Beta Coefficient** | **Standardized β** | ***P*** |
| **Systemic Vascular Resistance (Wood Units*m$^2$)** | 0.19 | 0.08 | <0.001 | | | | | | |
| **Indexed TAC (mL/mm Hg/m$^2$)** | 26.65 | 0.44 | <0.001 | 22.82 | 0.39 | <0.001 | 32.33 | 0.48 | <0.001 |
| **$P_b$ (mmHg)** | 1.76 | 0.73 | <0.001 | 1.91 | 0.72 | <0.001 | 1.67 | 0.72 | <0.001 |
| **$P_f$ (mmHg)** | −0.48 | −0.23 | 0.001 | −0.57 | −0.24 | 0.01 | −0.41 | −0.21 | 0.03 |

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

**Table 4**

Relationship between Metrics of Afterload and LV Wall-To-Cavity Volume Ratio

| Load Metric | Overall (n=4031) | | | Men (n=1942) | | | Women (n=2089) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Beta Coefficient | Standardized β | *P* | Beta Coefficient | Standardized β | *P* | Beta Coefficient | Standardized β | *P* |
| **Indexed Systemic Vascular Resistance (Wood Units*m$^2$)** | 0.006 | 0.22 | <0.001 | | | | | | |
| **Indexed TAC (mL/mmHg/m$^2$)** | −0.30 | −0.43 | <0.001 | −0.33 | −0.49 | <0.001 | −0.31 | −0.41 | <0.001 |
| **$P_b$ (mmHg)** | −0.003 | −0.09 | 0.15 | −0.005 | −0.15 | 0.10 | −0.001 | −0.04 | 0.63 |
| **$P_f$ (mmHg)** | −0.004 | −0.18 | 0.004 | −0.004 | −0.13 | 0.15 | −0.006 | −0.25 | 0.003 |

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