Sex Differences in the Associations of Hemodynamic Load With Left Ventricular Hypertrophy and Concentric Remodeling

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BACKGROUND
Left ventricular hypertrophy (LVH) and concentric remodeling are associated with adverse cardiovascular outcomes. We hypothesized that measures of arterial load are associated with LVH and concentric remodeling, and that associations differ by sex.

METHODS
We studied 600 non-Hispanic whites (59% women) belonging to hypertensive sibships. By integrating arterial tonometry with echocardiography, we obtained the following hemodynamic measures: aortic characteristic impedance (Z_c), proximal aortic compliance (PAC), systemic vascular resistance, augmentation index, and carotid–femoral pulse wave velocity (cfPWV). LVH and concentric remodeling were assessed by left ventricular mass indexed to body surface area (LVMI) and relative wall thickness (RWT), respectively. LVMI was log-transformed to reduce skewness. Hemodynamic measures were indexed to body size. Sex-specific multivariable linear regression analyses adjusting for confounders were performed to assess the associations of measures of arterial load with log LVMI and RWT.

RESULTS
None of the hemodynamic measures were associated with LVMI in either sex, or with RWT in men. However, in women, measures of aortic stiffness and early, pulsatile hemodynamic load were independently associated with increased RWT: $\beta \pm SE = 0.008 \pm 0.004$ for Z_c; 0.003 ± 0.001 for cfPWV, and -0.009 ± 0.003 for PAC ($P \leq 0.05$ for each). Female sex was a significant effect modifier of the associations of Z_c, cfPWV, and PAC with RWT ($P \leq 0.03$ for each of the interaction terms).

CONCLUSIONS
Greater Z_c and cfP WV and lower PAC are independently associated with increased RWT in women but not in men. Our findings suggest that aortic stiffness and greater early, pulsatile hemodynamic load affect left ventricular concentric remodeling in a sex-specific manner.

Keywords: arterial stiffness; blood pressure; hypertension; left ventricular hypertrophy; left ventricular mass index; left ventricular remodeling; relative wall thickness; sex differences.

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Left ventricular (LV) hypertrophy (LVH) and remodeling represent adaptive mechanisms to pressure or volume overload. According to the Laplace's Law, wall tension varies directly with pressure and inversely with wall thickness. Thus, in conditions where LV systolic pressure is increased, LV mass increases and walls thicken to maintain a normal wall tension/wall stress.[1] Despite being adaptive mechanisms, LVH and concentric remodeling are associated with adverse cardiovascular events.[2,3] In addition, concentric remodeling, even in the absence of LVH, is also associated with higher risk of cardiovascular events compared to normal LV geometry,[4] independently of LV mass.[5] Thus, identifying individuals with concentric LV geometries (measured by high relative wall thickness (RWT)) is also relevant for risk stratification.

The response of the LV to pressure overload may differ by sex,[6,7] suggesting greater sensitivity to pressure overload in women. For instance, in isolated systolic hypertension, women are more likely to develop concentric LVH.[7] Moreover, subjects with concentric hypertrophy have a much higher risk of developing heart failure than those with other LV geometric patterns,[8] and concentric LV geometry has been postulated as one of the potential mechanisms for the higher prevalence of heart failure with preserved ejection fraction (HFpEF) in women.[9] Thus, identifying the mechanisms promoting LV remodeling in women may help us understand the female predominance of this syndrome while highlighting potential targets for early detection and treatment.

In older, predominantly hypertensive adults, we have previously shown that ventricular–arterial interactions differ by sex.[10] What remains unknown is whether there are sex differences in how the LV geometry adapts in response to

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arterial load, and what components of arterial load (steady vs. pulsatile; early vs. late) may promote LVH and concentric remodeling in men and women. To this end, we performed a comprehensive noninvasive hemodynamic evaluation in a community-based cohort enriched for hypertension, with the goal of determining which measures of hemodynamic load are associated with higher LV mass index (LVMI) and RWT in men and women.

METHODS

Study participants and assessment of baseline characteristics

The study was approved by the Mayo Clinic's Institutional Review Board and participants gave informed consent. We studied non-Hispanic whites from the Genetic Epidemiology Network of Arteriopathy study[11] who belonged to hypertensive sibships. Hypertension was defined based on a prior diagnosis of hypertension and/or current treatment with antihypertensives. Between October 2009 and December 2011, 635 participants completed the study protocol and had complete data on LVMI and RWT. We excluded 2 participants with history of aortic valve replacement, 3 with more than mild aortic stenosis, 14 with atrial fibrillation, and 16 with technically inadequate data, leaving 600 participants for final analyses.

On the day of the study, participants met with the study coordinator and completed a comprehensive questionnaire. A blood specimen was collected, serum creatinine and glucose were measured by standard enzymatic methods, and glomerular filtration rate was estimated.[12] Diabetes was considered present if a subject was being treated with insulin or oral agents or had a fasting glucose level ≥ 126 mg/dl. Smoking was defined as having smoked more than 100 cigarettes in the past. Weight (in kilograms) was measured by an electronic scale, height (in meters) by a stadiometer, and body surface area (BSA) as calculated using the Gehan Method.[13]

Noninvasive hemodynamic assessment

A comprehensive noninvasive hemodynamic evaluation was performed at the Mayo Clinic's Echocardiography Laboratory as previously described.[10] Participants withheld vasoactive medications, alcohol and caffeine for at least 12 hours prior to the study. Brachial blood pressure was obtained by using a computer-controlled sphygmomanometer 3 times, 2 minutes apart. Applanation tonometry of the brachial, radial, femoral, and carotid arteries was performed while participants were lying supine, with simultaneous electrocardiogram. The average systolic and diastolic blood pressures were used to calibrate the peak and trough of the brachial pressure waveform, respectively. Diastolic and integrated mean brachial pressures were used to calibrate carotid, radial, and femoral pressure tracings. Next, a limited 2-dimensional echocardiogram was performed to estimate aortic flow.[14] A parasternal long axis view was taken to measure the left ventricular outflow tract, followed by an apical 5-chamber view to obtain pulsed Doppler of the left ventricular outflow tract (20 seconds). This was followed by repeat carotid tonometry; carotid pressure was used as a surrogate of aortic pressure. Doppler audio was digitized online throughout these acquisitions.

Analysis of pressure data was performed in conjunction with flow data as previously described,[10,15,16] using a custom software program capable of analyses of the pressure and flow data obtained (NIHem, Cardiovascular Engineering, Norwood, MA).[10] With this technique we estimated several measures of arterial stiffness and hemodynamic load.[10] To assess *aortic stiffness*, we used the carotid–femoral pulse wave velocity (cfPWV), the gold-standard measure of aortic stiffness.[17] cfPWV was calculated as aortic transit distance (estimated by the subtraction method)[17] divided by the time delay between the foot of the carotid and femoral waveforms. We also estimated proximal aortic compliance (PAC), calculated from the Bramwell–Hill equation: $co2 = V\Delta P/\rho\Delta V$, where V is aortic volume, P is aortic pressure, and ρ is blood density. For *arterial load* estimation, we calculated systemic vascular resistance (SVR) to represent the *steady* component of load. During pressure/flow analyses, SVR is calculated as the impedance at zero frequency (Z_0). We chose the aortic characteristic impedance (Z_c) as a measure of *pulsatile* load. Z_c is the pulsatile analogue of a resistance term and represents the ratio of pulsatile pressure to pulsatile flow in early systole, prior to return of the reflected pressure wave. Lastly, to determine potential effects of *wave reflections* on LVH and remodeling, we used the augmentation index (AIx). AIx represents the contributions of wave reflections to the central pulse pressure and was calculated as augmented pressure divided by central pulse pressure.[10,18] Some physiological indices may be related to body size, which is expected to differ between men and women. Thus, we scaled SVR and PAC to BSA (SVR × BSA; PAC/BSA), Z_c and AIx to height (Z_c × height; AIx × height). These linear indexations were chosen because their absolute allometric exponents have been shown not to differ from the unity.[19]

Assessment of LV structure

A 2-dimensional transthoracic echocardiography was performed to assess LV structure. LV septal and posterior wall thickness, end-systolic and diastolic diameters were measured, and LV ejection fraction was calculated according to guidelines.[14] LV end-diastolic volume was estimated based on the Teichholz formula.[20] LV mass was derived from the simplified cubed equation formula and indexed to body surface area (LVMI) to normalize heart size to body size, according to guidelines.[14] RWT was calculated as the sum of LV septal and posterior wall thickness at end diastole divided by LV internal dimension at end diastole.[14]

Statistical methods

Continuous variables were described as mean ± SD; categorical variables were described as percentages of the total. To assess differences between men and women, we employed a *t*-test for continuous variables and a chi-square test for categorical variables.

To reduce skewness, LVMI was log-transformed. Sex-specific associations of cfPWV and indexed Z_c, PAC, SVR, and AIx with log LVMI and RWT were assessed with multivariable linear regression analyses. Generalized estimating equations were used to account for familial relatedness among participants. Covariates that may influence hemodynamic load or LV structure were included: age, mean arterial pressure, heart rate, estimated glomerular filtration rate, history of hypertension, diabetes, and smoking and use of diuretics, beta-blockers, calcium channel blockers, and inhibitors of the renin–angiotensin–aldosterone system. To determine whether sex modified the associations of measures of hemodynamic load with LVMI and RWT, we included interaction terms for sex and each load measure in the models. To reduce the possibility of type I errors, we applied the procedure described by Benjamini and Hochberg,[21] using a threshold of $P = 0.05$ for significance in the main effect analyses and $P = 0.10$ for the interaction term analyses. Statistical analyses were performed with SPSS version 22 (IBM Corp., Armonk, NY).

RESULTS

Participant characteristics are summarized in Table 1. LVMI was higher in men than women, but RWT was similar between sexes. Z_c and AIx (absolute and indexed values) were higher in women, consistent with greater pulsatile arterial load and wave reflections in women. Results of univariate linear regression are depicted in Figures 1 (LVMI) and 2 (RWT). Arterial hemodynamic measures accounted for a small percentage of the variability in LVMI and RWT. Higher Z_c, cfPWV, and lower PAC were associated with higher LVMI and RWT in women, but not in men. In addition, higher SVR was also significantly associated with higher RWT in women only.

Independent predictors of higher LVMI and RWT are depicted in Table 2. Sex-specific associations of hemodynamic measures with LVMI and RWT are outlined in Table 3. None of the hemodynamic measures was independently associated with LVMI in men or women. However, greater cfPWV and lower PAC were independently associated with higher RWT in women, but not in men. The association of Z_c with RWT in women was of borderline significance after applying the Benjamini–Hochberg procedure ($P = 0.05$). Neither SVR nor AIx was associated with RWT in men or women. When we used the global reflection coefficient (i.e., reflected-to-forward pressure wave amplitude ratio) instead of AIx as a measure of wave reflection, inferences remained unchanged (analyses not shown). There were significant interactions of cfPWV ($P = 0.02$), indexed PAC ($P = 0.02$), and Z_c ($P = 0.03$) with female sex in the prediction of RWT, confirming that sex modifies the associations of aortic stiffness and pulsatile arterial load with LV concentric remodeling. The interactions of indexed SVR ($P = 0.46$) and AIx ($P = 0.67$) with sex were not significant. Of note, although men had a higher prevalence of smoking and diabetes, and were more likely to be taking antihypertensives than women, in interaction analyses, history of smoking, diabetes, and antihypertensive use did not modify the associations of arterial stiffness and pulsatile load with RWT and LVMI in men or women (analyses not shown).

DISCUSSION

In a large community-based cohort enriched for hypertension, we assessed sex differences in the associations of measures of hemodynamic load with LV structure and geometry. In women but not men, greater aortic stiffness and early, pulsatile hemodynamic load were associated with concentric LV geometry (higher RWT). To the best of our knowledge, this is the first report demonstrating sex differences in how hemodynamic load may affect LV geometry. Our findings are relevant for understanding the differential impact of arterial stiffness and hemodynamic load on LV remodeling in men and women and highlight potential pathophysiologic mechanisms linking hemodynamic load to HFpEF and adverse cardiovascular events in women.

Sex differences in aortic stiffness and hemodynamic load

We have previously shown that proximal aortic stiffness and pulsatile hemodynamic load are higher in hypertensive women than men.[10] It has been proposed that potential sex differences in arterial hemodynamics may be driven by differences in body size. However, in the present study, we confirmed that sex differences persisted despite indexation of the hemodynamic variables to body size according to recommendations.[19] Our findings add to a growing body of evidence supporting different age-related changes in conduit artery function between men and women,[10,22–25] which can potentially explain the female predominance of cardiovascular diseases such as HFpEF and isolated systolic hypertension.[26]

Sex differences in the associations of aortic stiffness and hemodynamic load with LV concentric remodeling

The LV and systemic arteries are closely coupled in order to allow ample transfer of blood forward while minimizing energetic expenditure.[27] As such, the stiffness (elastance) achieved by the contracting LV is closely matched to the arterial elastance. In situations where arterial elastance is increased (for instance, aortic stiffness), the LV must increase its systolic elastance in order to match the changes in arterial elastance and maintain optimal delivery of blood forward. This can be accomplished through increases in contractility, development of concentric remodeling, and increases in passive myocardial stiffness.[27] Thus, LV concentric remodeling is thought to be an adaptive response to chronic increases in arterial load. Since we[10] and others[28] have shown that elderly women have greater pulsatile arterial load than men, findings from our study suggest that greater age-related increases in aortic stiffness and pulsatile arterial load in women may serve a stimulus to promote concentric remodeling over time; while in men, the development of concentric remodeling appears to be independent of arterial load.

Previous studies have evaluated the prognostic effects of LV hypertrophy and remodeling, consistently showing an

Table 1. Participant characteristics

Variable	Men (n = 249)	Women (n = 351)	*P* value
Age, years	67.1 ± 9.2	65.3 ± 9.5	0.02
Height, m	1.77 ± 0.07	1.63 ± 0.06	<0.0001
Weight, kg	97.3 ± 17.8	80.1 ± 17.2	<0.0001
BMI, kg/m^2	31 ± 5	30 ± 6	0.03
BSA, m^2	2.2 ± 0.2	1.9 ± 0.2	<0.0001
Brachial SBP, mm Hg	138 ± 17	139 ± 18	0.39
Brachial DBP, mm Hg	71 ± 9	69 ± 8	0.02
MAP, mm Hg	93 ± 11	92 ± 11	0.48
Brachial PP, mm Hg	67 ± 16	70 ± 18	0.33
Heart rate, BPM	60 ± 9	62 ± 10	0.99
History of hypertension, n (%)	217 (87%)	266 (76%)	0.02
History of diabetes, n (%)	73 (29%)	52 (15%)	<0.0001
History of smoking, n (%)	147 (59%)	121 (34%)	<0.0001
Postmenopause status, n (%)	—	324 (92%)	—
Diuretic use, n (%)	124 (50%)	187 (53%)	0.21
Beta-blocker use, n (%)	128 (51%)	132 (38%)	0.004
ACEi/ARB use, n (%)	144 (58%)	140 (40%)	<0.0001
Calcium channel blocker use, n (%)	53 (21%)	65 (19%)	0.47
Other antihypertensive use, n (%)	17 (7%)	2 (0.6%)	<0.0001
Serum creatinine, g/dl	1.0 ± 0.3	0.8 ± 0.2	<0.0001
eGFR, l/min/1.73 m^2	76.4 ± 19.7	74.8 ± 17.3	0.32
Echocardiographic variables			
LV ejection fraction, %	61 ± 7	65 ± 6	<0.0001
LVMI, g/m^2	99.0 ± 24.1	86.6 ± 18.0	<0.0001
RWT	0.46 ± 0.07	0.45 ± 0.07	0.18
Indexed LV end-diastolic volume, ml/m	57 ± 23	45 ± 15	<0.0001
Ascending aorta diameter, mm	35.5 ± 3.7	32.4 ± 3.6	<0.0001
Arterial load variables			
cfPWV, m/sec	11.7 ± 3.4	10.6 ± 3.3	0.0002
SVR, dyne × sec/cm^5	1605.3 ± 387.8	1828.4 ± 447.1	<0.0001
SVR × BSA	3508.5 ± 811.5	3475.6 ± 814.4	0.63
Z_c, dyne × sec/cm^5	176.2 ± 64.7	216.4 ± 75.9	<0.0001
Z_c × height	311.4 ± 112.3	352.5 ± 122.0	<0.0001
PAC, 10^{-6} cm^4/dyne	6.05 ± 2.9	5.5 ± 3.1	0.03
PAC/BSA	2.76 ± 1.33	2.88 ± 1.61	0.37
AIx, %	14.0 ± 11.9	21.0 ± 12.0	<0.0001
AIx × height	21.1 ± 22.0	27.0 ± 20.7	0.0002

Continuous variables are presented as mean ± SD.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; AIx, augmentation index; ARB; angiotensin receptor blocker; BMI; body mass index; BPM, beats per minute; BSA, body surface area; cfPWV, carotid–femoral pulse wave velocity; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; LV, left ventricle; LVMI, left ventricular mass index; MAP, mean arterial pressure; PAC, proximal aortic compliance; PP, pulse pressure; RWT, relative wall thickness; SBP, systolic blood pressure; SVR, systemic vascular resistance; Z_c, characteristic impedance of the aorta.

association of concentric LV geometries with the greatest risk of adverse events[2,3,8] and highlighting the need to better understand the pathophysiology of LV remodeling. In this context, it appears that women's hearts are more sensitive to pressure overload than men's.[6] Supportive of this concept is the finding that women with isolated systolic hypertension,

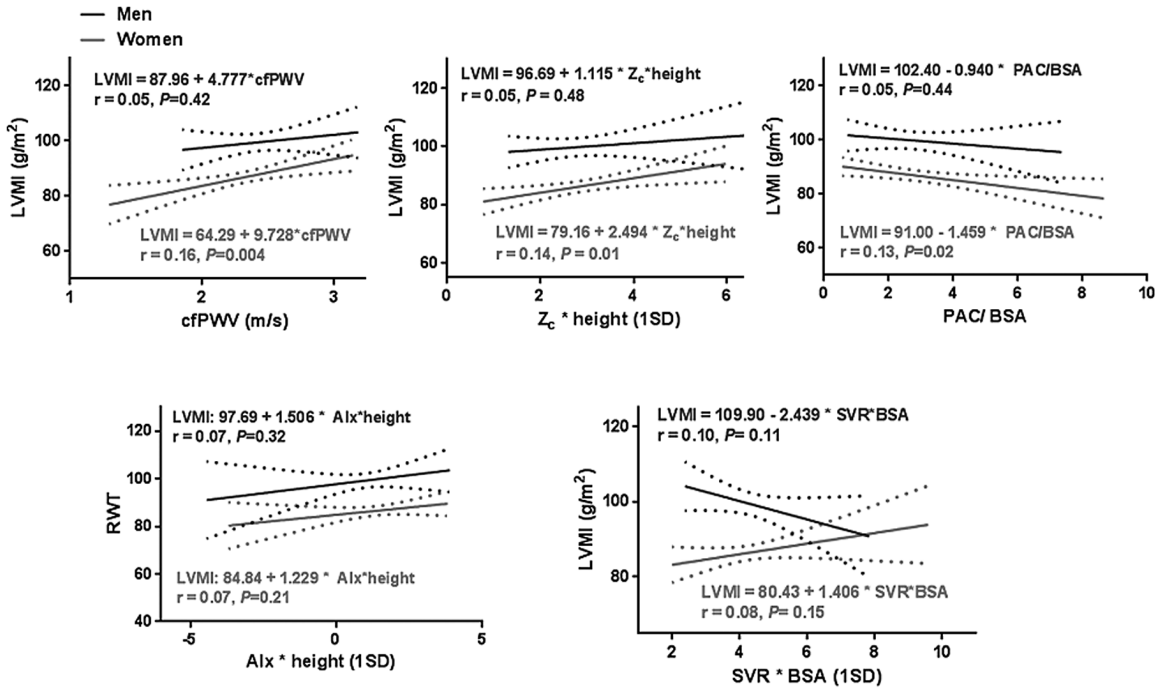

Figure 1. Sex-specific associations of measures of aortic stiffness and hemodynamic load with LVMI. In unadjusted analyses, measures of aortic stiffness and early, pulsatile arterial load (Z_c, cfPWV, and PAC) were associated with higher LVMI in women but not in men. Abbreviations: AIx, augmentation index; BSA, body surface area; cfPWV, carotid–femoral pulse wave velocity; LVMI, left ventricular mass index; PAC, proximal aortic compliance; RWT, relative wall thickness; SVR, systemic vascular resistance; Z_c, characteristic impedance of the aorta.

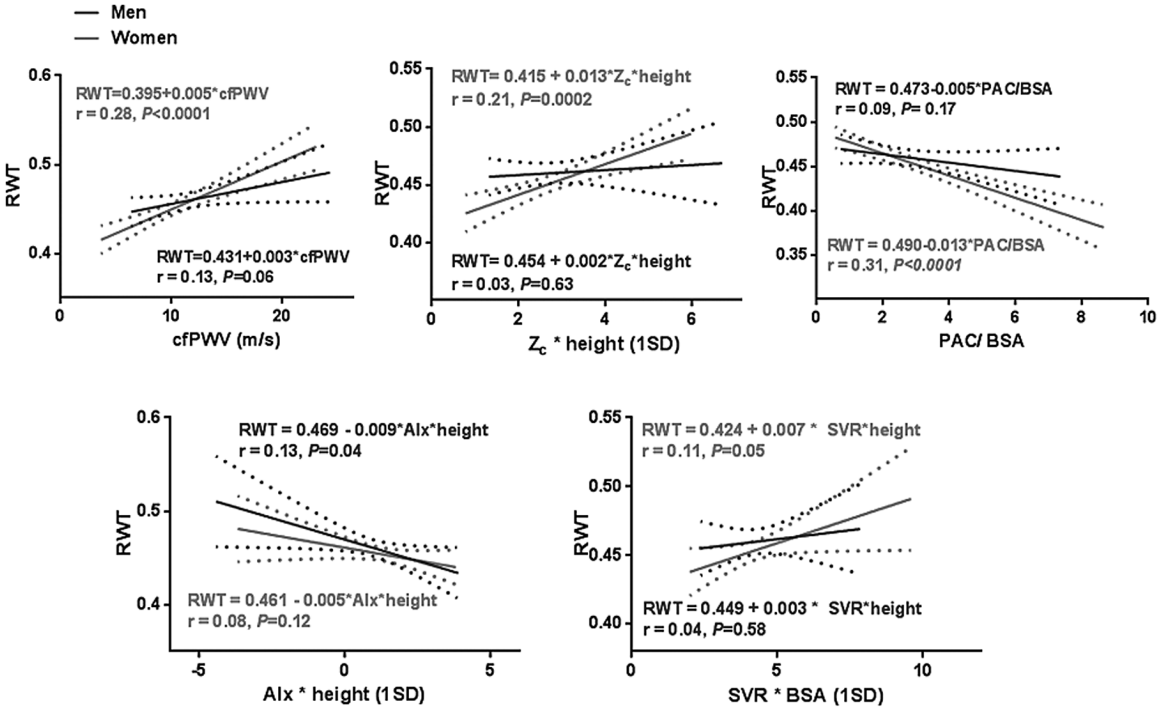

Figure 2. Sex-specific associations of measures of aortic stiffness and hemodynamic load with RWT. In unadjusted analyses, all measures of aortic stiffness and load were associated with higher RWT in women, but not in men. Abbreviations: AIx, augmentation index; BSA, body surface area; cfPWV, carotid–femoral pulse wave velocity; PAC, proximal aortic compliance; RWT, relative wall thickness; SVR, systemic vascular resistance; Z_c, characteristic impedance of the aorta.

a condition characterized by aortic stiffness, have higher RWT than men.[7] Such sex differences in LV remodeling in response to pressure overload are important when viewed in the context of HFpEF. HFpEF is more common in women,[29] having hypertension and elevated RWT as common features.[30] While the precise mechanisms leading to the greater prevalence of HFpEF in women remain unclear, greater LV concentric remodeling and impaired ventricular–arterial coupling in women are thought to contribute to the pathophysiology of the syndrome.[9]

We[10] and others[31] have shown that greater proximal aortic stiffness and pulsatile load are associated with impaired diastolic function[10,31] and ventricular–arterial coupling[10] in women, but not in men; findings that support the hypothesis that greater arterial stiffness in women may predispose to deleterious alterations in cardiovascular function and efficiency that may ultimately lead to heart failure despite a normal LV ejection fraction. The present study extends these observations by showing that greater aortic stiffness and pulsatile load are also independently associated with alterations in LV structure (concentric remodeling) in women only. Thus, the combination of findings points to aortic stiffness and the resulting increase in pulsatile load as potential common denominators that link hypertension, diastolic dysfunction, ventricular–arterial mismatch, and LV concentric remodeling in women, all of which are key features of patients with HFpEF. Since clinical trials to ameliorate the symptoms of HFpEF have been uniformly negative, identification of physiologic parameters that potentially predispose to HFpEF, such as arterial stiffness and measures of pulsatile hemodynamic load, will be essential in the development and testing of preventative strategies for this disease, particularly in women.

Zamani et al.[28] recently evaluated associations of arterial load with LV mass and geometry in subjects from the Multi-Ethnic Study of Atherosclerosis (MESA). In this study, a measure of pulsatile load (total arterial compliance) was associated with greater LV mass and RWT in men and women. These findings contrast with the results from our study; however, important differences between the 2 studies were present: subjects from our study were older (66.0 vs. 61.3 years) and more likely to be hypertensive (77% vs. 42%) and white (100% vs. 38%). Since age and the presence of hypertension are the strongest determinants of arterial stiffness, it is possible that the sex-specific effects of arterial stiffness and load on LV structure and geometry differ in the presence of hypertension. It is also possible that the impact of hemodynamic load on LV geometry may also differ based on race.

In addition, AIx, a measure of arterial wave reflections and late hemodynamic load, and SVR, a measure of steady load, were not associated with LVMI or RWT in men or women. These findings suggest that it may be the intrinsic elastic properties of the aorta and the resulting increase in early, pulsatile hemodynamic load that predominantly contribute to opposition of flow from the LV and may ultimately promote concentric remodeling of the LV myocardium in older women. These findings are in contrast with reports by Chirinos et al.[32] and Borlaug et al.,[33] who found that late systolic loading was associated with impaired LV diastolic function. However, these studies did not assess the impact of arterial load on LV geometry and included younger individuals, in whom wave reflections are known to have a greater contribution to central pulsatile hemodynamics than in the

Table 2. Independent predictors of LVMI and RWT

Variable	β	SE	*P* value
log LVMI model			
Age, years	0.002	0.001	0.03
History of smoking	0.044	0.017	0.009
History of diabetes	0.079	0.026	0.003
Heart rate, BPM	–0.005	0.001	<0.001
Calcium channel blocker use	0.046	0.022	0.04
RAASi use	0.04	0.02	0.05
RWT model			
Age, years	0.001	0.0003	<0.0001
History of hypertension	0.028	0.009	0.001
History of diabetes	0.024	0.009	0.006
History of smoking	0.013	0.005	0.02
Heart rate, BPM	0.001	0.0003	0.007

Abbreviations: LVMI, left ventricular mass index; RAASi, renin–angiotensin–aldosterone system inhibitor; RWT, relative wall thickness.

Table 3. Sex-specific associations of hemodynamic load with LVMI and RWT

	Log LVMI models				RWT models			
	Men		Women		Men		Women	
Variable	β ± SE	*P* value	β ± SE	*P* value	β ± SE	*P* value	β ± SE	*P* value
PAC/BSA	0.010 ± 0.012	0.39	0.006 ± 0.008	0.42	0.002 ± 0.004	0.71	–0.009 ± 0.003	0.001
cfPWV (1 m/sec)	0.001 ± 0.005	0.84	0.002 ± 0.005	0.61	0.001 ± 0.002	0.79	0.003 ± 0.001	0.02
Z_c × height (1-SD increase)	–0.026 ± 0.014	0.06	0.003 ± 0.01	0.80	–0.004 ± 0.005	0.46	0.008 ± 0.004	0.05
SVR × height (1-SD increase)	–0.036 ± 0.016	0.03	–0.009 ± 0.02	0.57	0.005 ± 0.005	0.33	0.006 ± 0.004	0.11
AIx (1-SD increase)	0.005 ± 0.023	0.39	0.008 ± 0.013	0.51	–0.005 ± 0.005	0.36	–0.002 ± 0.004	0.60

Abbreviations: AIx, augmentation index; BSA, body surface area; cfPWV, carotid–femoral pulse wave velocity; LVMI, left ventricular mass index; PAC, proximal aortic compliance; RWT, relative wall thickness; SVR, systemic vascular resistance; Z_c, characteristic impedance of the aorta.

elderly.[18] On the other hand, in the aforementioned MESA study, the amplitude of the reflected pressure wave (representing late load) was *inversely* associated with LV mass in older men and women and with RWT in women. Thus, it is possible that the individual effects of aortic compliance, arterial wave reflections, and loading sequence to LV structure and function may differ with aging.

Strengths of our study include the comprehensive hemodynamic evaluation and the community-based nature of our cohort. Limitations include the lack of ethnic diversity in our study cohort. In addition, almost all of the female participants from our study were postmenopausal, and it is possible that these associations may be different in younger subjects. Lastly, the cross-sectional nature of our study only provides a snapshot of complex and longstanding physiological processes that promote LV remodeling in humans. Thus, our study does not allow us to infer the causality or temporality of the associations found or to address other potential mediators of the associations of arterial load with ventricular remodeling in men and women.

In conclusion, in a community-based cohort enriched for hypertension, measures of aortic stiffness and pulsatile hemodynamic load were independently associated with higher LV RWT in postmenopausal women but not in men, corroborating the notion that women's hearts may be more sensitive to changes in aortic stiffness and highlighting the potential role of greater pulsatile hemodynamic load in the development of concentric LV geometries in women. Since concentric LV remodeling/hypertrophy is a major risk factor for mortality and cardiovascular events, and is commonly present in patients with HFpEF, our findings motivate further prospective studies aimed at assessing the role of arterial stiffness and pulsatile arterial load as precursors of LV concentric hypertrophy and as a potential therapeutic target aimed at preventing LV remodeling and its clinical consequences, particularly in women.

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DISCLOSURE

The authors declared no conflict of interest.

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