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Relations Between Aortic Stiffness and Left Ventricular Structure and Function in Older Participants in the Age, Gene/Environment Susceptibility—Reykjavik Study

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Abstract

Background—Left ventricular (LV) contraction displaces the aortic annulus and produces a force that stretches the ascending aorta. We hypothesized that aortic stiffening increases this previously ignored component of LV load and may contribute to hypertrophy. Conversely, aortic stretch-related work represents stored energy that may facilitate early diastolic filling.

Methods and Results—We performed magnetic resonance imaging of the aorta and LV in 347 participants (72 to 91 years old, 189 women) in the Age, Gene/Environment Susceptibility-Reykjavik Study to examine relations of aortic stretch with LV structure and function. Aortic stiffness was evaluated as the product of Young's modulus and wall thickness. Force was computed from Young's modulus and longitudinal aortic strain; work was the integrated product of force and annulus displacement during systole. LV mass and dynamic volume were measured using the area-length method. Filling was assessed from time-resolved LV volume curves. In multivariable models that adjusted for age, sex, height, weight, end-diastolic LV volume, augmentation index, end-systolic pressure, and cardiovascular disease risk factors, higher aortic stiffness was associated with increased LV mass ($B=3.0\pm 0.8\%$ per SD, $P<0.001$; sex interaction, $P=0.8$). Greater stretch-related aortic work was associated with enhanced early filling in men ($B=4.0\pm 0.8$ mL/SD, $P<0.001$), but not in women ($B=-0.4\pm 0.7$ mL/SD, $P=0.6$).

Conclusions—Higher aortic stiffness was associated with higher LV mass, independently of pressure. Higher stretch-related work was associated with greater early diastolic filling in men

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Disclosures

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only. Impaired diastolic recovery of energy stored by systolic proximal aortic stretch may contribute to increased susceptibility to diastolic dysfunction in women.

Keywords

aorta; left ventricle; pressure; aortic stiffness; epidemiology

Left ventricular (LV) hypertrophy is a risk factor for cardiovascular disease, including heart failure.¹ LV structure and function are affected by standard cardiovascular disease risk factors including blood pressure. Evaluation of the interaction between the proximal aorta, which is a major determinant of the pulsatile component of blood pressure, and the LV may facilitate elucidation of the pathophysiology of hypertension and cardiovascular disease, and may provide insight into higher susceptibility to diastolic dysfunction in older women.^{2;3}

LV systolic long-axis shortening causes aortic annulus displacement towards the apex of the heart.⁴⁻⁶ Previously, we showed that in light of modest relative movement of the aorta at the level of the brachiocephalic artery,^{6;7} axial displacement of the aortic annulus results in longitudinal stretch of the proximal aorta.⁸ Aortic stretch represents both a previously unrecognized load on the LV and a source of stored elastic energy that may facilitate LV recoil and early diastolic filling. In order to evaluate relations between longitudinal aortic stretch and the LV, we assessed mechanical stiffness of the proximal aorta as the product of Young's modulus and aortic wall thickness. We also calculated aortic work as the integral of the product of aortic annulus displacement and the force that produced the observed longitudinal aortic stretch.

In this paper we investigate the following hypotheses: 1) aortic stretch imposes a previously unidentified load on the LV that increases with aortic stiffness and may contribute to LV hypertrophy independently of pressure and 2) aortic work performed during stretch of the elastic elements in the proximal ascending aorta represents stored energy that may enhance early diastolic LV filling as the aorta recoils.

Methods

Participants

Participant selection criteria and design of the Age, Gene/Environment Susceptibility – Reykjavik Study (AGES-Reykjavik) have been presented in detail.⁹ During a second AGES-Reykjavik exam conducted from 2008 to 2011, a subset of participants was recruited to participate in a comprehensive magnetic resonance imaging (MRI) study of aortic structure and function.¹⁰ Participants with known MRI contraindications (292 of 3316 participants, 8.8%) or who had previously refused to participate in MRI imaging studies because of claustrophobia or other reasons (279, 8.4%) were excluded prior to recruitment of our initial sample of 633 participants. The study was approved by the National Bioethics Committee in Iceland and the National Institute on Aging Intramural Institutional Review Board. All participants gave their informed written consent.

Tonometry Data Acquisition

Participants were studied supine after 10 minutes of rest. Auscultatory blood pressure was obtained with a semiautomated computer-controlled device (NIHem, Cardiovascular Engineering, Inc, Norwood, MA). Arterial tonometry and simultaneous electrocardiography (ECG) were obtained from brachial and carotid arteries with a custom transducer (Cardiovascular Engineering, Inc, Norwood, MA).

MRI Acquisition

MRI was performed in supine participants using an 8-channel torso coil in a 1.5 Tesla MRI scanner (Signa Excite, General Electric Medical Systems, Waukesha, WI). Two orthogonal multiphase FIESTA localizers of the proximal aorta were taken: a cardiac 3-chamber scan was obtained using the coronal plane localizer, and an oblique coronal scan was obtained using the cardiac 3-chamber localizer. Using the cardiac 3-chamber and oblique coronal scans as localizers, cross-sectional scans of the proximal ascending aorta were obtained approximately 10 mm distal to the sinotubular junction after a 10 ms trigger delay. Two long-axis multiphase FIESTA scans were taken of the heart; a 4-chamber scan was prescribed from the sagittal and cardiac 3-chamber localizers and a 2-chamber scan was prescribed from the cardiac 3-chamber localizer and 4-chamber scan. Detailed imaging parameters are provided in the data supplement. All acquisitions were obtained during one breath-hold, and multi-phase scans were obtained using ECG triggering.

Tonometry Data Analysis

All data was transferred to the core laboratory (Cardiovascular Engineering, Inc., Norwood, MA) for analysis by trained analyzers blinded to participant characteristics. Tonometry waveforms were signal-averaged with the ECG used as a fiducial point. Blood pressures were over-read in the core laboratory. Systolic and diastolic cuff pressures were used to calibrate the peak and trough of the signal-averaged brachial pressure waveform. Diastolic and integrated mean brachial pressures were used to calibrate carotid pressure tracings.¹¹ End-systolic pressure was taken from the carotid waveform at the time of the dicrotic notch. Augmentation index was calculated as previously described.¹⁰

MRI Data Analysis

All cases were analyzed using ImageJ version 1.44p (32-bit, National Institutes of Health, Bethesda, MD) with custom macros and plugins. Oblique coronal scans were used to measure aortic annulus displacement. The proximal aortic contour was located by using ImageJ default thresholding, and a centerline was created from the midpoints of the aortic contours.⁸ Centerlines were obtained for 30 evenly spaced phases of the cardiac cycle, each representing 1/30th of the RR interval. The aortic annulus was manually located on every third phase in the oblique coronal stack and interpolated across the two intervening phases; aortic annulus displacement was measured along the aortic centerline.

Cross-sectional FIESTA scans were used to acquire circumferential area waveforms of the ascending aorta by applying an ImageJ default threshold for auto-detection of the lumen at each phase. Double inversion recovery images were used to measure the diastolic aortic wall cross-sectional area as previously described.¹⁰ The 2-chamber and 4-chamber scans were

used to trace the diastolic epicardium of the LV and to acquire contours of the endocardium throughout the cardiac cycle using an ImageJ threshold approach.

Calculations

Aortic stiffness was assessed as the product (Eh) of incremental Young's modulus (E) and proximal ascending aortic wall thickness (h). Eh was used instead of E in order to account for overall mechanical stiffness of the aorta. Incremental Young's modulus of the ascending aorta was calculated from measured circumferential strain and calculated stress due to pressure in a constant longitudinal state. The following simplified stress equation¹² was used:

$$S_{\theta} = \left(\frac{P_i R_i^2 + P_i R_o^2}{R_o^2 - R_i^2} \right)$$

to measure circumferential stress at the inner wall of a thick-walled cylinder under pressure with the assumption extravascular pressure was zero. P_i represents intravascular pressure. R_i is the inner radius calculated from aortic lumen area, and R_o is the outer radius calculated from the sum of aortic lumen and wall areas. Wall thickness (h) represents the diastolic difference between the inner and outer aorta radius. Radial strain measurements were adjusted for longitudinal aortic strain to calculate circumferential stress in a longitudinally static state.⁸

Young's modulus was assumed to be identical in circumferential and longitudinal directions. Longitudinal aortic stress was calculated as the product of Young's modulus and ascending aortic longitudinal strain. Aortic force was calculated as the product of longitudinal stress and ascending aortic cross-sectional wall area, which was also corrected for longitudinal strain by dividing the wall area by longitudinal aortic strain at each point in time. Aortic work was calculated as the integral of aortic force and aortic annulus displacement during systole.

LV volumes and mass were computed using the area-length method as previously described.¹⁰ Early and late filling volumes were calculated from dynamic LV volume waveforms. Early filling volume was defined as the difference between the volume at LV diastasis and end-systolic volume. Late filling volume was defined as the difference between end-diastolic volume and the volume at diastasis.

As previously described and validated, measured aortic lumen and wall areas and ventricular volumes were highly reproducible when analyzed by different observers using different software.¹⁰

Statistical Analyses

Anthropometric and risk factor data were tabulated for included and excluded participants and separately by sex for included participants. Aortic and LV characteristics were tabulated by sex. In order to normalize their distributions, skewed variables were transformed by using

the square root, natural logarithm, or square as noted. Sex-differences were assessed by using an independent-samples t-test on transformed variables.

We used multivariable linear regression to examine relations between proximal aortic stiffness and annulus displacement and to examine relations between aortic properties and LV structure and function. To evaluate the hypothesis that proximal aortic stiffness imposes a load on the LV that contributes to hypertrophy and a shift to late diastolic (active) LV filling, we examined models with LV mass or late filling as dependent variables and aortic Eh as an exposure. To evaluate the hypothesis that early diastolic (passive) LV filling is facilitated by recovery of work stored as longitudinal strain of elastic elements in the proximal aorta, we examined a model with early diastolic filling as the dependent variable and aortic work as an exposure variable. Model coefficients were expressed per SD difference in the independent variable.

To account for potential confounding by traditional anthropometrics or cardiovascular disease risk factors, age, height, weight, heart rate, fasting glucose, total cholesterol, HDL cholesterol, triglycerides, diabetes, current smoking, cardiovascular disease, treated hypertension, and statin use were included as standard covariates in all statistical models. Variables with skewed distributions (heart rate, height, fasting glucose, HDL cholesterol, triglycerides) were transformed by using the natural logarithm to normalize distributions. To account for effects of chamber dimension on LV mass and filling volumes, we adjusted for end-diastolic volume. A primary goal of the analyses was to determine whether proximal aortic measures have relations with LV structure and function that are separate from potential effects of stiffness on wave reflection or blood pressure. To account for possible effects of premature wave reflection, augmentation index was included as a covariate. To account for potential effects of LV pressure load, end-systolic pressure was included in models. Relations between independent variables and dependent variables were assessed by examining scatterplots of appropriately transformed variables. Regression models were evaluated for effects of nonlinearity and heteroskedasticity by examining histograms and QQ plots of residuals and plots of residuals versus predicted values.

All dependent and independent continuous variables were assessed for normality and transformed as needed. We screened for nonlinear associations by examining scatterplots of dependent and independent variables. In addition, we examined plots of residuals versus predicted variables to screen for effects of nonlinearity or heteroskedasticity of independent or dependent variables and found a uniform distribution of residuals across the range of predicted values. We examined variance inflation factors for reported exposure variables and found that all were <1.4. Finally, to screen for influential values and ensure that we had not violated assumptions of normality, we examined the distribution of residuals by using histograms and QQ plots, which demonstrated that residuals were normally distributed.

We evaluated effect modification by sex or end-systolic pressure by adding two-way interactions to the model one at a time. Models with a significant sex-interaction were analyzed separately for men and women; otherwise sex was included as a covariate and the interaction term was removed. Interactions between end-systolic pressure and independent

variables of interest were similarly evaluated and removed from the model if the interaction term was not significant.

To illustrate relations between aortic and LV measures, we evaluated LV measures in groups defined by sex-specific median values of end-systolic pressure and either aortic Eh (for LV mass and late filling) or aortic work (early filling). Groups were compared by using ANOVA models that adjusted for covariates included in linear regression models. Adjusted mean values were reverse transformed as needed and plotted along with 95% confidence intervals. Results are presented as mean \pm SD unless stated otherwise. A two-tailed P-value <0.05 was considered significant.

Results

Among the original sample of 633 volunteers, 2 could not lie supine, 4 became fatigued or ill prior to the study, 6 were canceled for logistical reasons, 6 could not fit in the MRI gantry, 6 were claustrophobic, and 7 withdrew from the study leaving 602 participants who had any image data acquired. Of these cases, 81 had unusable hemodynamic information, 66 had unusable oblique coronal images of the aorta, 60 had unusable cross-sectional images of the proximal aorta, 6 had unusable aortic wall images, 25 had unusable 2-chamber or 4-chamber cardiac images, 13 had atrial fibrillation, and 4 had valve replacement or known dilation of the proximal aorta, leaving 347 cases with complete information required for the present analysis. No additional participants were excluded because of missing values for any covariates used in the present analyses. Excluded cases had a higher heart rate, slightly higher diastolic blood pressure, and a higher prevalence of treated hypertension and cardiovascular disease (Supplemental Table). Characteristics of the included study participants are presented by sex in Table 1.

Aortic and LV variables are presented in Table 2. Women had greater peak aortic annulus displacement. In a multivariable model, higher Eh was associated with lower annulus displacement (-0.3 ± 0.1 mm/SD, $P=0.002$) with no evidence of a sex interaction ($P=0.3$). As expected, men had larger LV volumes and LV mass. Ejection fraction was higher in women, while early filling fraction and aortic Eh were not significantly different between sexes. Aortic force and aortic work were higher in women.

Table 3 presents multivariable linear regression models of LV mass and late filling volume. Greater LV mass was associated with higher Eh and higher end-systolic pressure, while greater late filling volume was only associated with higher Eh. There was no evidence of an interaction between sex and Eh for LV mass ($P=0.8$) or late filling volume ($P=1.0$). Comparable relations were observed when LV mass was indexed to body surface area, and when models were adjusted only for sex, age, height, weight, heart rate, and end-diastolic LV volume (data not shown). Mean values for LV mass and late filling volume in groups defined by sex-specific median values of aortic Eh and end-systolic pressure are presented in Figure 1.

A multivariable linear regression model of early filling volume demonstrated an interaction between sex and aortic work ($P<0.001$); models were therefore estimated separately for men

and women (Table 4). Higher stored aortic work was associated with higher early filling volume in men but not in women. Results were comparable when models were adjusted only for age, height, weight, heart rate, and end-diastolic LV volume (data not shown). Figure 2 presents early filling volumes separately by sex for groups based on sex-specific median values of aortic work and end-systolic pressure.

Discussion

This study examined relations between aortic stiffness, longitudinal aortic stretch, and LV structure and function. Higher aortic stiffness, as assessed by the product of Young's modulus and wall thickness in the proximal aorta (Eh), was associated with higher LV mass and higher late filling volume in women and men in models that adjusted for end-systolic pressure, augmentation index, and standard cardiovascular disease risk factors, suggesting that coupling of the LV to a stiff proximal aorta may impose a pressure-independent load on the LV that has not been considered previously. Greater aortic work was positively related to early filling volume in men, suggesting that aortic stretch during systole stores elastic energy that may be recovered as enhanced early diastolic filling. In women, however, aortic work was not associated with early filling volume, which suggests that in older women, energy stored by systolic stretch of the ascending aorta is not recovered as enhanced early diastolic filling. Failure to recover stored aortic work during early diastole may enhance the susceptibility of older women to develop heart failure with preserved LV function.

Several prior studies have examined relations between aortic stiffness and LV mass. Some studies reported a positive relation between aortic stiffness and LV mass that persisted after adjusting for pressure,^{13–15} while others attributed the relation to effects of aortic stiffness on blood pressure.¹⁶ In our study, end-systolic pressure and aortic stiffness assessed as Eh had additive positive relations with LV mass in men and women. The association between LV mass and Eh was consistent when carotid peak-systolic or pulse pressure, brachial peak-systolic or pulse pressure, or mean arterial pressure were used in place of end-systolic pressure (data not shown). Additionally, we adjusted for augmentation index in our models. Thus, the residual relation between aortic stiffness and LV mass was separate from potential effects of aortic stiffness on blood pressure, pressure amplification, and wave reflection. Studies that found relations between LV mass and aortic stiffness that were independent of blood pressure attributed the relation to possible concurrent exposure to risk factors such as obesity or treated hypertension, or possible volume overload.^{13–15} In our study, the pressure-independent relation between aortic stiffness and LV mass persisted after adjustment for various risk factors, including prevalent cardiovascular disease and treated hypertension.

Early LV filling is the result of a pressure gradient from the left atrium to the LV. This pressure gradient is enhanced by early diastolic suction due to rapid expansion of LV volume. Factors that are thought to enhance early diastolic filling include elastic recoil of the LV wall after systolic myocardial compression and twist,^{17–19} erectile effect of coronary perfusion,²⁰ and recoil of the left atrium after being stretched during systole.²¹ In light of negligible movement of the apex when the LV contracts,^{22;23} long axis shortening pulls the aortic annulus towards the apex, producing longitudinal stretch in the proximal aorta. The resulting stretch-related work represents stored elastic energy in the walls of the aorta.

Ideally, when the LV stops contracting, aortic stretch-related work is recovered as elastic recoil, which pulls upward on the base of the heart, increasing LV volume and enhancing early diastolic filling.

We observed a strong positive relation between stretch-related aortic work and early LV filling in men that was independent of end-systolic pressure. However, we did not observe any relation between aortic work and early filling in women. Prior studies have noted that women have greater global longitudinal LV strain than men,²⁴ which is consistent with our observation of greater aortic annulus displacement in women (Table 2). Although older women tend to have preserved systolic function, they are more susceptible to impaired diastolic function.^{2,3} Our results suggest that work stored as longitudinal aortic stretch from systolic LV contraction represents an important contributor to early diastolic LV filling and that sex difference in diastolic recovery of that work may contribute to diastolic dysfunction and increased risk for heart failure with preserved ejection fraction in older women.^{2,3}

Limitations

Our study has limitations that need to be acknowledged. All participants were over 70 years of age and from white European descent. Thus, additional studies should be performed in other age groups and ethnicities in order to establish the generalizability of our results. In particular, our results may not be generalizable to adults younger than 50 years of age, when a prominent, nonlinear transition in age relations of key hemodynamic variables is known to occur.²⁵ For logistical reasons, tonometry was performed immediately before MRI acquisition. In future studies, intermittent blood pressure measurement during the course of the MRI acquisition would be a useful addition in order to confirm our assumption of a stable blood pressure during aortic imaging. To minimize the confounding effects of time delay between measurements, participants were placed in the body coil on a detachable MRI gurney for blood pressure and tonometry measurements and then immediately transferred into the MRI machine with no further change in posture.

Several types of acquisitions were needed for this study, rendering the final sample size sensitive to acquisition issues. For example, oblique coronal images were initially acquired as localizers without the intention of quantitative analysis and therefore were not repeated at the time of acquisition if there were minor deficiencies that did not interfere with image localization; in some cases these deficiencies did, however, obviate quantitative analysis.

Pressure at the outer wall of the aorta was assumed to be zero, but is known to be slightly negative, which may have caused an underestimation of circumferential stress and Young's modulus. The proximal aorta was assumed to be isotropic with identical circumferential and longitudinal Young's moduli.^{8,26} Additionally, because of elongation of the aortic arch in older cohorts,²⁷ it is possible that systolic movement of the aortic annulus could be caused, in part, by release of a compressive strain rather than imposition of positive stretch in the ascending aorta. Presence of diastolic compression would result in overestimation of aortic force and work because of the presence of a negative force at the onset of systole, when force was assumed to be zero. Compression of the aorta seems unlikely, however, based on positive residual longitudinal strain in excised aortas in older people.²⁸

In order to limit acquisition time, LV volumes and mass were derived from two long-axis views rather than multiple short-axis sections; the latter approach may have provided more precise estimates of volume and mass. Future studies should include additional measures such as LV strain measurements from speckle-tracking echocardiography or dynamic 3-dimensional aortic and LV imaging analysis to extend the results presented in this study. The strength of our study is the large, community-based sample of well characterized participants with central pressure measurements, sophisticated imaging, and detailed risk factor data.

Conclusions

During systole, LV contraction produces a highly variable stretching force in the proximal aorta that is proportional to proximal aortic stiffness and represents a previously ignored, potentially deleterious load on the LV. In contrast, the product of aortic force and stretch represents work stored in the elastic elements of the proximal aorta during systole that is recovered as proportional elastic recoil during diastole. Therefore, while aortic stretch represents a load on the heart, it also provides a mechanism to facilitate early diastolic filling. We found that stiffer aortas were associated with higher LV mass in men and women whereas greater stretch-related energy storage in the proximal aorta during systole was associated with greater early diastolic filling only in men. The observation that aortic stiffness is associated with LV hypertrophy in men and women whereas work stored in the aortic root is associated with greater early diastolic filling only in men may provide insights into the greater susceptibility of older women to develop heart failure with preserved ejection fraction. Further study is required to elucidate mechanisms that may contribute to blunted recovery during diastole of energy stored in the aortic root during systole.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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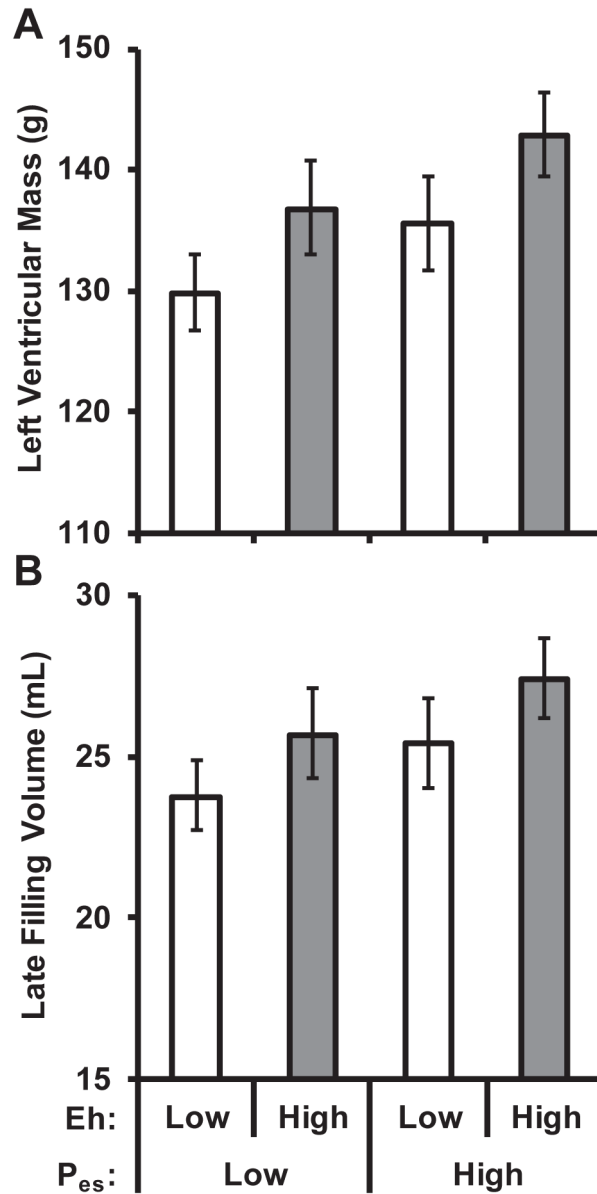


Figure 1. Relations of left ventricular mass and late filling volume with aortic stiffness and end-systolic pressure

Left ventricular mass (A) and late filling volume (B) summarized according to groups defined by sex-specific median aortic stiffness (Eh) and end-systolic pressure (P_{es}). Aortic stiffness was evaluated as the product of Young's modulus and aortic wall thickness and had a positive relation with both mass ($P=0.001$) and late filling volume ($P=0.010$). Aortic pressure was also positively related with mass ($P=0.008$) and late filling volume ($P=0.033$). Results were consistent when left ventricular mass was indexed to body surface area. There were 106 participants with low stiffness and low pressure, 68 participants had low stiffness and high pressure, 69 participants had high stiffness and low pressure, and 104 participants had high stiffness and high pressure. Left ventricular mass and late filling volume were log-transformed prior to analysis and reverse transformed for presentation. Values represent the

geometric mean and 95% confidence intervals. Values were adjusted for sex, age, height, weight, heart rate, fasting glucose, total cholesterol, HDL cholesterol, triglycerides, left-ventricular end-diastolic volume, augmentation index, diabetes, current smoking, cardiovascular disease, treated hypertension, and statin use.

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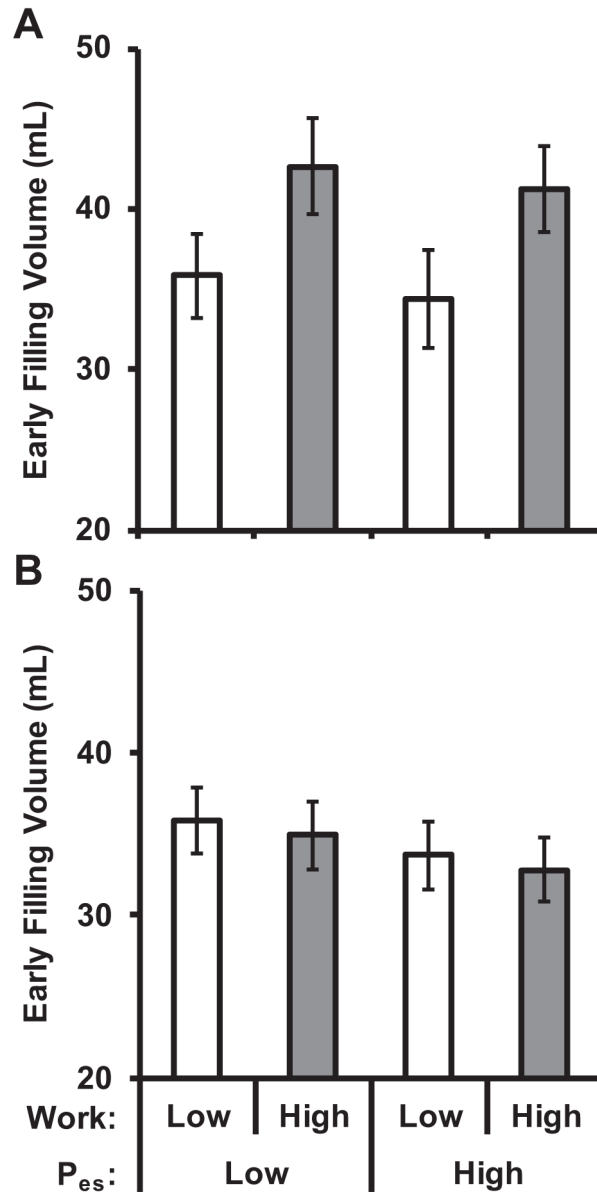


Figure 2. Relations of early filling volume with aortic work and end-systolic pressure

Early diastolic filling volume summarized according to groups defined by median values of aortic work and end-systolic pressure (P_{es}) in men (A) and women (B). In men, greater early diastolic filling was associated with higher aortic work ($P<0.001$), but was not related to end-systolic pressure ($P=0.4$). In women, early filling volume was unrelated to aortic work ($P=0.5$) and end-systolic pressure ($P=0.1$). There were 45 men with low aortic work and low pressure, 34 with low aortic work and high pressure, 35 with high aortic work and low pressure, and 44 with high aortic work and high pressure. There were 55 women with low aortic work and low pressure, 40 with low aortic work and high pressure, 40 with high aortic work and low pressure, and 54 with high aortic work and high pressure. Values represent the mean and 95% confidence intervals. Values were adjusted for age, height, weight, heart rate, fasting glucose, total cholesterol, HDL cholesterol, triglycerides, left ventricular end-

diastolic volume, augmentation index, diabetes, current smoking, cardiovascular disease, treated hypertension, and statin use.

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Table 1

Participant Characteristics

Variables	Men	Women
Sample size	158	189
Age range, years	73 to 88	72 to 91
Height, cm	177 ± 6	162 ± 6
Weight, kg	83 ± 12	72 ± 12
Body surface area, m ²	2.0 ± 0.2	1.8 ± 0.1
Body mass index, kg/m ²	27 ± 4	27 ± 4
Heart rate, min ⁻¹	61 ± 9	65 ± 9
Brachial pressures, mm Hg		
Systolic	138 ± 20	144 ± 17
Diastolic	65 ± 9	64 ± 9
Mean	92 ± 12	95 ± 11
Pulse pressure	74 ± 18	80 ± 18
Carotid pressures, mm Hg		
Peak	137 ± 24	146 ± 23
End-systolic	103 ± 16	107 ± 14
Augmentation index	6 ± 11	10 ± 15
Fasting glucose, mmol/L	5.7 ± 1.0	5.5 ± 0.8
Total cholesterol, mmol/L	4.9 ± 1.0	5.7 ± 1.1
HDL cholesterol, mmol/L	1.4 ± 0.4	1.8 ± 0.4
Triglycerides, mmol/L	1.1 ± 0.5	1.2 ± 0.5
Medical history, n (%)		
Diabetes	18 (11)	18 (10)
Treated hypertension	101 (64)	142 (75)
Statin use	71 (45)	66 (35)
Cardiovascular disease	51 (32)	21 (11)
Current smoker	15 (10)	9 (5)

HDL, high density lipoprotein

Table 2

Aortic and Left Ventricular Characteristics

Variable	Men	Women	P
Aortic annulus displacement, mm	6.9 (5.4, 8.1)	7.8 (6.3, 9.0)	<0.001
Volume, mL			
End-diastolic*	110 (95, 126)	90 (79, 103)	<0.001
End-systolic*	42 (33, 53)	30 (24, 38)	<0.001
Early filling	38 (30, 47)	34 (28, 43)	0.002
Late filling*	28 (23, 33)	23 (19, 29)	<0.001
Ejection fraction, % [†]	62 (57, 66)	66 (61, 71)	<0.001
Early filling fraction, %	58 (49, 66)	61 (53, 67)	0.5
Left ventricular mass, g*	161 (146, 177)	117 (106, 133)	<0.001
Eh, kdynes/cm*	3,194 (2,544; 4,252)	3,058 (2,471; 4,085)	0.5
Aortic force, kdynes [†]	2,123 (1,508; 2,777)	2,495 (1,860; 3,184)	<0.001
Aortic work, mJ [‡]	79 (47, 116)	106 (75, 154)	<0.001

Values are presented as median (25th, 75th percentiles) due to skewed distributions for several variables. Values were compared by using an independent-samples t-test on normally-distributed, transformed values with sex as the grouping variable.

* log transform;

[†] square root transform;

[‡] square transform. Eh, Young's modulus x aorta wall thickness product.

Table 3**Multivariable Model of Left Ventricular Mass and Late Filling Volume**

Independent Variable	LV Mass			Late Filling Volume		
	B ± SE	P	R²	B ± SE	P	R²
Aortic stiffness	3.0 ± 0.8	<0.001	0.022	3.9 ± 1.6	0.012	0.018
End-systolic pressure	2.0 ± 0.9	0.021	0.005	2.4 ± 1.6	0.1	0.004

LV mass and late filling volume were log transformed prior to analysis. B values are for the final model with all variables entered. B values were multiplied by 100 to represent % difference in the dependent variable per SD difference in the independent variable. R² represents the change in model R² after each variable entered in the order shown. LV mass final model R²=0.699; late filling volume final model R²=0.468). The model adjusted for sex, age, height, weight, heart rate, fasting glucose, total cholesterol, HDL cholesterol, triglycerides, left ventricular end-diastolic volume, augmentation index, diabetes, current smoking, cardiovascular disease, treated hypertension, and statin use. LV, left ventricular.

Table 4**Multivariable Model of Early Filling Volume**

Independent Variable	Men			Women		
	B ± SE	P	R ²	B ± SE	P	R ²
Aortic work	4.0 ± 0.8	<0.001	0.066	-0.4 ± 0.7	0.6	0.002
End-systolic pressure	-1.0 ± 0.8	0.2	0.005	-1.1 ± 0.7	0.1	0.006

B values are for the final model with all variables entered and represent mL difference in early filling volume per SD difference in the independent variable. R² represents the change in model R² after each variable entered in the order shown. For men, final model R²=0.592; for women, final model R²=0.628. The model adjusted for age, height, weight, heart rate, fasting glucose, total cholesterol, HDL cholesterol, triglycerides, left ventricular end-diastolic volume, augmentation index, diabetes, current smoking, cardiovascular disease, treated hypertension, and statin use.