Epidemiology

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

Vanessa Bell, BS; Sigurdur Sigurdsson, MS; Jos J.M. Westenberg, PhD; John D. Gotul, MSEE; Alyssa A. Torjesen, BS; Thor Aspelund, PhD; Lenore J. Launer, MS, PhD; Tamara B. Harris, MD, MS; Vilmundur Gudnason, MD, PhD; Albert de Roos, MD; Gary F. Mitchell, MD

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 MRI of the aorta and LV in 347 participants (72–91 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 aortic 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 (β=3.0±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 (β=4.0±0.8 mL/SD; P<0.001), but not in women (β=−0.4±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 only. Impaired diastolic recovery of energy stored by systolic proximal aortic stretch may contribute to increased susceptibility to diastolic dysfunction in women.

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Key Words: aorta ▪ epidemiology ▪ heart ventricles ▪ pressure ▪ vascular stiffness

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

See Clinical Perspective

LV systolic long-axis shortening causes aortic annulus displacement toward 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.

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 article, 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 examination conducted from 2008 to 2011, a subset of participants was recruited to participate in a comprehensive 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 studies because of claustrophobia or other reasons (279, 8.4%) were excluded before 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 ECG were obtained from brachial and carotid arteries with a custom transducer (Cardiovascular Engineering, Inc.).

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 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 \(+10\) mm distal to the sinotubular junction after a 10-ms trigger delay. Two long-axis multiphase 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 acquired from the cardiac 3-chamber localizer and 4-chamber scan. Detailed imaging parameters are provided in the Data Supplement. All acquisitions were obtained during 1 breathhold, and multiphase scans were obtained using ECG triggering.

Tonometry Data Analysis
All data were transferred to the core laboratory (Cardiovascular Engineering, Inc) 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 overread 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 annular contours.\(^6\) 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 2 intervening phases; aortic annulus displacement was measured along the aortic centerline. Cross-sectional fast imaging employing steady-state acquisition 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 to account for overall mechanical stiffness of the aorta. E was calculated from measured central pressure, circumferential strain, and associated stress, assuming a constant longitudinal state. The following simplified stress equation\(^12\)

\[ S_\theta = \left( P R_s^2 + P R_o^2 / R_s^2 - R_o^2 \right) \]

was used to measure circumferential stress at the inner wall of a thick-walled cylinder under pressure with the assumption extra-vascular pressure was zero. \(P\) represents intravascular pressure. \(R_s\) 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.\(^11\) 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. 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, high-density lipoprotein cholesterol, triglycerides, diabetes mellitus, 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, high-density lipoprotein cholesterol, and 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 values 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.

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 into original units and plotted along with 95% confidence intervals. Results were presented as mean±SD unless stated otherwise. A 2-tailed P value of <0.05 was considered significant.

Results

Among the original sample of 633 volunteers, 2 could not lie supine, 4 became fatigued or ill before 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 (Table I in the Data Supplement). 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, whereas 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, whereas 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 systolic 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, whereas others attributed the relation to effects of aortic stiffness on blood pressure. 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

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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).

In addition, 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. 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 because of 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 toward 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

### Table 2. Aortic and Left Ventricular Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Men</th>
<th>Women</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic annulus displacement, mm</td>
<td>6.9 (5.4, 8.1)</td>
<td>7.8 (6.3, 9.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Volume, mL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic*</td>
<td>110 (95, 126)</td>
<td>90 (79, 103)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>End-systolic*</td>
<td>42 (33, 53)</td>
<td>30 (24, 38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Early filling</td>
<td>38 (30, 47)</td>
<td>34 (28, 43)</td>
<td>0.002</td>
</tr>
<tr>
<td>Late filling*</td>
<td>28 (23, 33)</td>
<td>23 (19, 29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ejection fraction, %†</td>
<td>62 (57, 66)</td>
<td>66 (61, 71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Early filling fraction, %</td>
<td>58 (49, 66)</td>
<td>61 (53, 67)</td>
<td>0.5</td>
</tr>
<tr>
<td>Left ventricular mass, g*</td>
<td>161 (146, 177)</td>
<td>117 (106, 133)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Eh, kdynes/cm*</td>
<td>3194 (2544, 4252)</td>
<td>3058 (2471, 4085)</td>
<td>0.5</td>
</tr>
<tr>
<td>Aortic force, kdynes‡</td>
<td>2123 (1508, 2777)</td>
<td>2495 (1860, 3184)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aortic work, mJ‡</td>
<td>79 (47, 116)</td>
<td>106 (75, 154)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are presented as median (25th, 75th percentiles) because of 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. Eh indicates the product of Young’s modulus and aortic wall thickness.

*Log transform.
†Square transform.
‡ Square-root transform.
to impaired diastolic function. 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 of heart failure with preserved ejection fraction in older women.

**Limitations**

Our study has limitations that need to be acknowledged. All participants were aged >70 years and from white European descent. Thus, additional studies should be performed in other age groups and ethnicities 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. 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 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. In some cases these deficiencies did, however, obviate quantitative analysis.

Pressure at the outer wall of the aorta was assumed to be 0, 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. Additionally, because of elongation of the aortic arch in older cohorts, it is possible that systolic movement of the aortic annulus could be caused, in part, by release of a compressive force at the onset of systole, when force was assumed to be 0. Compression of the aorta seems unlikely, however, based on positive residual longitudinal strain in excised aortas in older people.

To limit acquisition time, LV volumes and mass were derived from 2 long-axis views rather than multiple short-axis views.
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, although 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 stress-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.

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Disclosures
Dr Mitchell is the owner of Cardiovascular Engineering, Inc, a company that develops and manufactures devices to measure vascular stiffness, serves as a consultant to and receives honoraria from Novartis, Merck, and Servier, and was funded by research grants HL094898, DK082447, HL107385, and HL104184 from the National Institutes of Health, V. Bell, J. D. Gotal, and A. A. Torjesen are employees of Cardiovascular Engineering, Inc. The other authors report no conflicts.

References
2. Alagia K, Banach M, Jones LG, Datta S, Ahmed A, Aronow WS. Update on diastolic heart failure or heart failure with preserved


**CLINICAL PERSPECTIVE**

Stiffening of the proximal aorta is associated with pressure-independent, adverse effects on left ventricular (LV) structure and function that are not completely understood. During systole, longitudinal LV contraction pulls on the aortic annulus and produces longitudinal aortic stretch, which represents a novel, pressure-independent load on the LV. Conversely, the resulting energy stored in the stretched elastic elements of the aorta may also facilitate LV filling in early diastole, as aortic recoil pulls upward on the base of the heart and promotes chamber lengthening. In models that adjusted for vascular risk factors, systolic pressure, and wave reflection, we found that greater aortic stiffness was associated with reduced systolic aortic annulus displacement and higher LV mass in men and women in our older cohort, suggesting that local ascending aortic stiffness contributed directly to load on the LV. Men had a positive association between stretch-related aortic work at end systole and LV filling in early diastole. Although women produced greater stretch-related aortic work than men, there was no association between aortic work and early LV filling volume in women, suggesting that women were unable to recover stored energy stored in the aorta. The dramatic sex difference in relations between aortic stretch and early filling volume may contribute to the greater susceptibility of older women to develop heart failure with preserved ejection fraction. Further evaluation of relations between direct aortic-LV coupling, longitudinal aortic stretch, and LV structure and function has the potential to elucidate novel mechanisms that contribute to LV hypertrophy and diastolic dysfunction.
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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SUPPLEMENTAL MATERIAL

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

The oblique coronal scan of the aortic root was obtained with a 3.2 ms repetition time, 1.4 ms echo time, and 8 mm slice thickness with 30 phases per cardiac cycle. The imaging matrix was 224x224 with a reconstruction matrix of 256x256 and a 1.41 mm average pixel size.

The first cross-sectional aortic scan was taken using FIESTA sequences with a 4.3 ms repetition time, 1.9 ms echo time, and 6 mm slice thickness with 30 phases per cardiac cycle. Early in the study, images were obtained using 256x256 imaging and reconstruction matrices in all participants. The imaging matrix was later adjusted to 352x352 (reconstruction matrix 512x512) for all participants who were able to hold their breath long enough to obtain the higher resolution sequence. Average pixel size was 0.66 mm for the 512x512 images and 1.33 mm for the 256x256 images. The second cross-sectional aortic acquisition was obtained as a single 6 mm slice, using an ECG-triggered double inversion recovery fast spin echo sequence with 52 ms echo time, gated at end-diastole with one acquisition at every other heartbeat to prevent slow-flow artifacts. The imaging matrix was 256x192 with a reconstructed matrix of 512x512 and a 1.41 mm average pixel size.

The cardiac 4-chamber and 2-chamber scans were obtained using FIESTA sequences with a repetition time of 3.2 ms for the 4-chamber and 3.1 ms for the 2-chamber, echo time of 1.4 ms for the 4-chamber and 1.3 ms for the 2-chamber, and 8 mm slice thickness with 30 phases per cardiac cycle. The imaging matrix was 224x224 with a reconstructed matrix of 256x256 and a 1.41 mm average pixel size.
<table>
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<tr>
<th>Variables</th>
<th>Included</th>
<th>Excluded</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>347</td>
<td>255</td>
<td></td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>189 (55)</td>
<td>150 (59)</td>
<td>0.3</td>
</tr>
<tr>
<td>Age range, years</td>
<td>72 to 91</td>
<td>72 to 97</td>
<td>0.1</td>
</tr>
<tr>
<td>Height, cm</td>
<td>169 ± 9</td>
<td>168 ± 10</td>
<td>0.3</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>77 ± 14</td>
<td>77 ± 15</td>
<td>0.9</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.9 ± 0.2</td>
<td>1.9 ± 0.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27 ± 4</td>
<td>27 ± 4</td>
<td>0.4</td>
</tr>
<tr>
<td>Heart rate, min⁻¹</td>
<td>63 ± 9</td>
<td>65 ± 11</td>
<td>0.003</td>
</tr>
<tr>
<td>Brachial pressure, mm Hg</td>
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<td></td>
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<tr>
<td>Systolic</td>
<td>141 ± 19</td>
<td>143 ± 20</td>
<td>0.3</td>
</tr>
<tr>
<td>Diastolic</td>
<td>64 ± 9</td>
<td>66 ± 11</td>
<td>0.046</td>
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<tr>
<td>Mean</td>
<td>94 ± 11</td>
<td>96 ± 13</td>
<td>0.1</td>
</tr>
<tr>
<td>Pulse pressure</td>
<td>77 ± 18</td>
<td>77 ± 19</td>
<td>0.6</td>
</tr>
<tr>
<td>Carotid pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak</td>
<td>142 ± 24</td>
<td>143 ± 27</td>
<td>0.5</td>
</tr>
<tr>
<td>End-systolic</td>
<td>105 ± 15</td>
<td>108 ± 18</td>
<td>0.1</td>
</tr>
<tr>
<td>Augmentation index</td>
<td>8 ± 14</td>
<td>10 ± 15</td>
<td>0.1</td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>5.6 ± 0.9</td>
<td>5.6 ± 0.9</td>
<td>0.8</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.3 ± 1.1</td>
<td>5.3 ± 1.2</td>
<td>1.0</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.6 ± 0.4</td>
<td>1.6 ± 0.4</td>
<td>0.6</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.2 ± 0.5</td>
<td>1.2 ± 0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Medical history, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>36 (10)</td>
<td>24 (9)</td>
<td>0.8</td>
</tr>
<tr>
<td>Treated hypertension</td>
<td>243 (70)</td>
<td>199 (78)</td>
<td>0.032</td>
</tr>
<tr>
<td>Statin use</td>
<td>137 (40)</td>
<td>101 (40)</td>
<td>1.0</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>72 (21)</td>
<td>83 (33)</td>
<td>0.002</td>
</tr>
<tr>
<td>Current smoker</td>
<td>24 (7)</td>
<td>20 (8)</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Included verses excluded participant comparisons were performed using an independent-samples t-test for continuous variables and a cross-tab for dichotomous medical history variables. HDL, high density lipoprotein.