SUPPLEMENTAL MATERIAL

Supplementary Methods

Transthoracic Echocardiography

Quantification of end-systolic and end-diastolic LV volumes were performed using TomTec Image Arena (TomTec Imaging Systems, Unterschleissheim, Germany) using Simpson's method of discs, to derive LVEF (21). Diastolic function was assessed using pulse wave Doppler of mitral inflow velocities and tissue mitral annular velocities obtained from the apical 4-chamber view (22) Mitral inflow parameters, including early mitral inflow velocity (E-wave) and atrial mitral inflow velocity (a-wave), were quantified. The early diastolic annular velocity (e') was quantified via pulsed wave tissue Doppler of the septal and lateral mitral annuli and average values derived.

Echocardiographic Strain Analysis

The LV endocardial border was manually traced at the end-systolic frame of one cardiac cycle from the apical views. In individual segments with poor tracking, the borders were manually readjusted. Peak longitudinal strain was computed automatically and averaged across all segments

Vascular Hemodynamics

For quality control of tonometry tracings, all Doppler waveforms from each case were visually by a cardiologist experienced in pressure-flow analyses (JAC). This included the primary signals (tonometry and Doppler recordings), the signal averaged waveforms of pressure and flow,

alignment of pressure and flow waveforms. and physiologic consistency of the data, followed by pressure-flow modeling.

Supplementary Table 1. Mean change in vascular function from visit 1 to visit 2, stratified according to the addition of cardiac medications reported at visit 2

Vascular Function Parameter	Baseline Median (IQR)	No Change in Meds Mean Change	95% CI	Change in Meds Mean Change	95% CI	Interaction p value
Blood Pressure						
Peripheral SBP (mmHg)	130.5 (116.8, 141.0)	9.7	(-0.4, 19.8)	9.3	(-2.3, 20.9)	0.962
Peripheral DBP (mmHg)	74.5 (65.8, 81.2)	8.7	(5.3, 12.0)	5.3	(0.6, 10.0)	0.261
Central SBP (mmHg)	115.7 (104.4, 128.5)	11.5	(3.0, 20.0)	11.0	(0.8, 21.2)	0.950
Peripheral PP (mmHg)	56.5 (45.0, 67.0)	1.0	(-8.6, 10.7)	4.0	(-6.1, 14.1)	0.679
Peripheral MAP (mmHg)	91.5 (84.8,100.0)	9.0	(4.5, 13.6)	6.7	(0.6, 12.7)	0.545
Arterial Stiffness						
Carotid-Femoral PWV (m/s)	9.5 (7.7, 11.0)	0.8	(0.3, 1.3)	0.6	(0.2, 1.1)	0.664
Resistive Load						
Total peripheral resistance (dyn.sec.cm^-5)	1369.8 (1101.9, 1938.6)	732.8	(320.3, 1145.4)	521.0	(129.0, 913.0)	0.469
Ea (mmHg/ml)	1.3 (1.0, 1.7)	0.6	(0.3, 1.0)	0.5	(0.1, 0.9)	0.658
Pulsatile Load						

Aortic characteristic impedance (Zc) (dyn·sec·cm^{-5})	138.9 (94.3, 171.8)	26.3	(-11.6, 64.3)	-1.4	(-101.7, 98.9)	0.616
Total arterial compliance (TAC)(mL/mmHg)	1.2 (0.8, 1.6)	-0.3	(-0.5, -0.1)	-0.4	(-0.6, -0.1)	0.741
Augmentation Pressure (mmHg)	3.0 (-2.0, 8.0)	5.3	(1.4, 9.1)	2.3	(-1.8, 6.3)	0.741
Augmentation index (AI) (%)	9.0 (-7.0, 17.5)	9.0	(3.1, 15.0)	4.4	(-2.6, 11.5)	0.337
Reflected wave transit time (msec)	26.2 (14.2, 43.3)	-12.6	(-23.6, -1.6)	-8.5	(-25.5, 8.4)	0.694
Reflection magnitude	0.4 (0.3, 0.4)	0.0	(0.0, 0.1)	0.0	(0.0, 0.2)	0.928
Forward wave amplitude (mmHg)	42.2 (33.8, 50.0)	2.6	(-1.9, 7.1)	0.4	(-13.1, 14.0)	0.769
Backward wave amplitude (mmHg)	15.9 (11.4, 19.8)	2.0	(0.2, 3.9)	1.5	(-3.3, 6.4)	0.860

Change defined as the addition of a new anti-hypertensive medication by visit 2. Participants in the "No Change in Meds" subgroup did not have the addition of any anti-hypertensive medications. By visit 2, 16 patients initiated ACE inhibitor or angiotensin receptor blocker; 5 patients initiated a beta blocker; 14 patients initiated a calcium channel blocker; 3 patients initiated a diuretic; and 5 patients initiated an alpha blocker. Vascular function variables scaled by their standard deviations. Regression coefficients adjusted for age, gender, and categorical visit number. Abbreviations: CI, confidence interval; PWV, pulse wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure.

Supplementary Table 2. Association between change in vascular function variables from visit 1 to visit 2 and change in LVEF from visit 1 to visit 2.

Vascular Function Parameter	Adjusted Beta	95% CI	p value
Blood Pressure			
Peripheral SBP (mmHg)	-0.3	(-2.0, 1.4)	0.76
Peripheral DBP (mmHg)	-1.3	(-3.0, 0.4)	0.15
Central SBP (mmHg)	-0.8	(-2.5, 0.9)	0.35
Peripheral PP (mmHg)	0.2	(-1.5, 1.9)	0.80
Peripheral MAP (mmHg)	-0.8	(-2.5, 0.9)	0.35
Arterial Stiffness			
Carotid-Femoral PWV (m/s)	-1.0	(-2.4, 0.5)	0.21
Resistive Load			
Total peripheral resistance (dyn.sec.cm^-5)	-0.3	(-2.2, 1.6)	0.75
Ea (mmHg/ml)	-0.2	(-2.1, 1.6)	0.81
Pulsatile Load			
Aortic characteristic impedance (Zc) ($dyn \cdot sec \cdot cm^{-5}$)	0.1	(-1.7, 2.0)	0.89
Total arterial compliance (TAC)(mL/mmHg)	0.8	(-1.0, 2.7)	0.37
Augmentation Pressure (mmHg)	-0.9	(-2.8, 0.9)	0.33
Augmentation index (AI) (%)	-1.3	(-3.1, 0.4)	0.15
Reflected wave transit time (msec)	1.3	(-0.5, 3.0)	0.17
Reflection magnitude	0.0	(-1.9, 1.8)	0.96
Forward wave amplitude (mmHg)	-0.5	(-2.3, 1.4)	0.62
Backward wave amplitude (mmHg)	-0.7	(-2.5, 1.2)	0.48

Vascular function variables scaled by their standard deviations, and regression coefficients are multiplied by 100 and adjusted for age, gender, and categorical visit number. As an example, for each standard deviation increase in SBP from visit 1 to 2 there was a nonsignificant 0.3% decrease in LVEF from visit 1 to 2 (p=0.76). Abbreviations: LVEF, left ventricular ejection fraction; PWV, pulse wave velocity; CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure.

Supplementary Table 3. Association between change in vascular function variables from visit 1 to visit 2 and change in LVEF from visit 1 to visit 3.

Vascular Function Parameter	Adjusted Beta	95% CI	p value
Blood Pressure			
Peripheral SBP (mmHg)	-0.2	(-2.0,1.6)	0.83
Peripheral DBP (mmHg)	0.2	(-1.8, 2.2)	0.85
Central SBP (mmHg)	-0.5	(-2.3, 1.4)	0.62
Peripheral PP (mmHg)	-0.3	(-2.0, 1.5)	0.77
Peripheral MAP (mmHg)	-0.1	(-2.0, 1.9)	0.95
Arterial Stiffness			
Carotid-Femoral PWV (m/s)	0.3	(-2.0, 2.6)	0.80
Resistive Load			
Total peripheral resistance (dyn.sec.cm^-5)	-1.6	(-4.2, 0.9)	0.22
Ea (mmHg/ml)	-1.3	(-3.7, 1.0)	0.27
Pulsatile Load			
Aortic characteristic impedance (Zc) ($dyn \cdot sec \cdot cm^{-5}$)	-1.3	(-3.4, 0.7)	0.21
Total arterial compliance (TAC)(mL/mmHg)	2.0	(0.1, 4.0)	0.04
Augmentation Pressure (mmHg)	-1.0	(-3.7, 1.7)	0.46
Augmentation index (AI) (%)	-1.2	(-3.5, 1.0)	0.30
Reflected wave transit time (msec)	-0.4	(-2.4, 1.7)	0.74
Reflection magnitude	-0.9	(-2.9, 1.0)	0.36
Forward wave amplitude (mmHg)	-1.5	(-3.5, 0.5)	0.14
Backward wave amplitude (mmHg)	-1.8	(-3.7, 0.1)	0.08

Vascular function variables scaled by their standard deviations, and regression coefficients are multiplied by 100 and adjusted for age, gender, and categorical visit number. For example, for each standard deviation increase in SBP from visit 1 to 2 there was a nonsignificant 0.2% decrease in LVEF from visit 1 to 3 (p=0.83). Abbreviations: LVEF, left ventricular ejection fraction; PWV, pulse wave velocity; CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure.

Supplementary Table 4. Association between change in vascular function variables from visit 1 to visit 2 and change in longitudinal strain from visit 1 to visit 2.

Vascular Function Parameter	Adjusted Beta	95% CI	p value
Blood Pressure			
Peripheral SBP (mmHg)	-0.4	(-1.7, 1.0)	0.62
Peripheral DBP (mmHg)	-0.1	(-1.0, 0.8)	0.79
Central SBP (mmHg)	-0.4	(-1.6, 0.8)	0.47
Peripheral PP (mmHg)	-0.5	(-2.4, 1.4)	0.61
Peripheral MAP (mmHg)	-0.2	(-1.2, 0.8)	0.69
Arterial Stiffness			
Carotid-Femoral PWV (m/s)	0.5	(-0.2, 1.3)	0.18
Resistive Load			
Total peripheral resistance (dyn.sec.cm^-5)	0.0	(-1.0, 0.9)	0.96
Ea (mmHg/ml)	0.2	(-0.8, 1.1)	0.74
Pulsatile Load			
Aortic characteristic impedance (Zc) ($dyn \cdot sec \cdot cm^{-5}$)	0.1	(-0.7, 1.0)	0.76
Total arterial compliance (TAC)(mL/mmHg)	-0.7	(-1.5, 0.2)	0.13
Augmentation Pressure (mmHg)	-0.2	(-1.1, 0.8)	0.70
Augmentation index (AI) (%)	-0.3	(-1.3, 0.6)	0.48
Reflected wave transit time (msec)	0.2	(-0.7, 1.1)	0.73
Reflection magnitude	-0.4	(-1.3, 0.5)	0.41
Forward wave amplitude (mmHg)	0.4	(-0.6, 1.3)	0.45
Backward wave amplitude (mmHg)	0.3	(-0.8, 1.4)	0.58

Vascular function variables scaled by their standard deviations. Regression coefficients adjusted for age, gender, and categorical visit number. For example, for each standard deviation increase in SBP from visit 1 to 2, there was a nonsignificant -0.4% decrease in longitudinal strain from visit 1 to 2, for example from -15% to -15.4% (p=0.62). Abbreviations: CI, confidence interval; PWV, pulse wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure.

Supplementary Table 5. Association between change in vascular function variables from visit 1 to visit 2 and change in longitudinal strain from visit 1 to visit 3.

Vascular Function Parameter	Adjusted Beta	95% CI	p value
Blood Pressure			
Peripheral SBP (mmHg)	-0.4	(-1.9, 1.2)	0.65
Peripheral DBP (mmHg)	-0.4	(-1.4, 0.6)	0.44
Central SBP (mmHg)	-0.3	(-1.6, 1.0)	0.62
Peripheral PP (mmHg)	0.0	(-2.2, 2.2)	0.98
Peripheral MAP (mmHg)	-0.4	(-1.5, 0.7)	0.51
Arterial Stiffness			
Carotid-Femoral PWV (m/s)	-0.1	(-1.2, 0.9)	0.81
Resistive Load			
Total peripheral resistance (dyn.sec.cm^-5)	0.5	(-1.0, 2.0)	0.52
Ea (mmHg/ml)	0.5	(-0.9, 1.9)	0.49
Pulsatile Load			
Aortic characteristic impedance (Zc) ($dyn \cdot sec \cdot cm^{-5}$)	1.5	(-1.1, 4.0)	0.26
Total arterial compliance (TAC)(mL/mmHg)	-0.5	(-1.4, 0.3)	0.22
Augmentation Pressure (mmHg)	-0.5	(-1.8, 0.7)	0.40
Augmentation index (AI) (%)	-0.5	(-1.5, 0.6)	0.36
Reflected wave transit time (msec)	0.1	(-0.9, 1.0)	0.86
Reflection magnitude	-0.2	(-1.2, 0.8)	0.71
Forward wave amplitude (mmHg)	0.9	(-0.91, 2.7)	0.35
Backward wave amplitude (mmHg)	0.4	(-1.16, 2.0)	0.60

Vascular function variables scaled by their standard deviations. Regression coefficients adjusted for age, gender, and categorical visit number. For example, for each standard deviation increase in SBP from visit 1 to 2, there was a nonsignificant -0.4% decrease in longitudinal from visit 1 to 3, for example from -15% to -15.4% (p=0.65). Abbreviations: CI, confidence interval; PWV, pulse wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure.

Supplementary Table 6. Association between change in vascular function variables from visit 1 to visit 2 and change in E/e' from visit 1 to visit 2.

Vascular Function Parameter	Adjusted Beta	95% CI	p value
Blood Pressure			
Peripheral SBP (mmHg)	-0.7	(-1.4, 0.0)	0.05
Peripheral DBP (mmHg)	0.2	(-0.5, 0.9)	0.61
Central SBP (mmHg)	-0.8	(-1.4, -0.1)	0.04
Peripheral PP (mmHg)	-0.9	(-1.6, -0.2)	0.02
Peripheral MAP (mmHg)	-0.4	(-1.1, 0.3)	0.29
Arterial Stiffness			
Carotid-Femoral PWV (m/s)	0.1	(-0.6, 0.8)	0.82
Resistive Load			
Total peripheral resistance (dyn.sec.cm^-5)	-1.0	(-1.7, -0.3)	0.01
Ea (mmHg/ml)	-0.9	(-1.6, -0.2)	0.01
Pulsatile Load			
Aortic characteristic impedance (Zc) ($dyn \cdot sec \cdot cm^{-5}$)	-0.8	(-1.5, 0.0)	0.04
Total arterial compliance (TAC)(mL/mmHg)	0.2	(-0.5, 1.0)	0.54
Augmentation Pressure (mmHg)	-0.8	(-1.5, 0.0)	0.05
Augmentation index (AI) (%)	-0.8	(-1.5, -0.1)	0.04
Reflected wave transit time (msec)	0.2	(-0.5, 0.9)	0.59
Reflection magnitude	-0.6	(-1.3, 0.1)	0.12
Forward wave amplitude (mmHg)	-0.2	(-0.9, 0.6)	0.65
Backward wave amplitude (mmHg)	-0.3	(-1.1, 0.4)	0.39

Vascular function variables scaled by their standard deviations. Regression coefficients adjusted for age, gender, and categorical visit number. For example, for each standard deviation increase in SBP from visit 1 to 2, there was a 0.7 decrease in E/e' from visit 1 to 2 (p=0.05).
Abbreviations: CI, confidence interval; PWV, pulse wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure.

Supplementary Table 7. Association between change in vascular function variables from visit 1 to visit 2 and change in E/e' from visit 1 to visit 3.

Vascular Function Parameter	Adjusted Beta	95% CI	p value
Blood Pressure			
Peripheral SBP (mmHg)	-0.5	(-1.3, 0.2)	0.17
Peripheral DBP (mmHg)	0.1	(-0.7, 1.0)	0.77
Central SBP (mmHg)	-0.5	(-1.2, 0.3)	0.25
Peripheral PP (mmHg)	-0.6	(-1.2, 0.1)	0.13
Peripheral MAP (mmHg)	-0.4	(-1.2, 0.4)	0.38
Arterial Stiffness			
Carotid-Femoral PWV (m/s)	1.0	(0.1, 1.9)	0.04
Resistive Load			
Total peripheral resistance (dyn.sec.cm^-5)	-0.8	(-1.8, 0.2)	0.13
Ea (mmHg/ml)	-0.7	(-1.6, 0.2)	0.12
Pulsatile Load			
Aortic characteristic impedance (Zc) ($dyn \cdot sec \cdot cm^{-5}$)	-0.7	(-1.5, 0.0)	0.07
Total arterial compliance (TAC)(mL/mmHg)	-0.1	(-0.9, 0.7)	0.81
Augmentation Pressure (mmHg)	0.7	(-0.4, 1.8)	0.21
Augmentation index (AI) (%)	0.2	(-0.8, 1.2)	0.67
Reflected wave transit time (msec)	-0.5	(-1.3, 0.3)	0.27
Reflection magnitude	-0.3	(-1.1, 0.5)	0.50
Forward wave amplitude (mmHg)	-0.5	(-1.3, 0.3)	0.25
Backward wave amplitude (mmHg)	-0.4	(-1.2, 0.4)	0.36

Vascular function variables scaled by their standard deviations. Regression coefficients adjusted for age, gender, and categorical visit number. For example, for each standard deviation increase in SBP from visit 1 to 2, there was a nonsignificant 0.5 decrease in E/e' from visit 1 to 3 (p=0.17). Abbreviations: CI, confidence interval; PWV, pulse wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure.

Supplementary Table 8. Association between change in vascular function variables from visit 1 to visit 2 and change in Log_{10} BNP from visit 1 to visit 2.

Vascular Function Parameter	Adjusted Beta	95% CI	p value
Blood Pressure			
Peripheral SBP (mmHg)	-0.1	(-0.3, 0.1)	0.47
Peripheral DBP (mmHg)	0.1	(-0.2, 0.4)	0.52
Central SBP (mmHg)	-0.1	(-0.3, 0.2)	0.49
Peripheral PP (mmHg)	-0.1	(-0.3, 0.1)	0.34
Peripheral MAP (mmHg)	-0.0	(-0.3, 0.2)	0.80
Arterial Stiffness			
Carotid-Femoral PWV (m/s)	0.2	(0.0, 0.4)	0.06
Resistive Load			
Total peripheral resistance (dyn.sec.cm^-5)	0.0	(-0.5, 0.6)	0.86
Ea (mmHg/ml)	0.1	(-0.4, 0.6)	0.79
Pulsatile Load			
Aortic characteristic impedance (Zc) ($dyn \cdot sec \cdot cm^{-5}$)	0.3	(-0.5, 1.1)	0.51
Total arterial compliance (TAC)(mL/mmHg)	-0.0	(-0.3, 0.3)	0.98
Augmentation Pressure (mmHg)	-0.0	(-0.3, 0.2)	0.83
Augmentation index (AI) (%)	-0.1	(-0.4, 0.2)	0.47
Reflected wave transit time (msec)	0.2	(-0.0, 0.5)	0.10
Reflection magnitude	-0.1	(-0.4, 0.2)	0.43
Forward wave amplitude (mmHg)	0.2	(-0.2, 0.7)	0.33
Backward wave amplitude (mmHg)	0.1	(-0.3, 0.4)	0.77

Vascular function variables scaled by their standard deviations. Regression coefficients adjusted for age, gender, and categorical visit number. Abbreviations: CI, confidence interval; PWV, pulse wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure.

Supplementary Table 9. Association between change in vascular function variables from visit 1 to visit 2 and change in Log_{10} BNP from visit 1 to visit 3.

Vascular Function Parameter	Adjusted Beta	95% CI	p value
Blood Pressure			
Peripheral SBP (mmHg)	0.1	(-0.7, 0.9)	0.82
Peripheral DBP (mmHg)	0.2	(-0.3, 0.6)	0.49
Central SBP (mmHg)	0.1	(-0.5, 0.7)	0.73
Peripheral PP (mmHg)	-0.2	(-1.4, 1.0)	0.74
Peripheral MAP (mmHg)	0.1	(-0.4, 0.7)	0.61
Arterial Stiffness			
Carotid-Femoral PWV (m/s)	0.2	(-0.2, 0.7)	0.37
Resistive Load			
Total peripheral resistance (dyn.sec.cm^-5)	-0.4	(-1.1, 0.4)	0.33
Ea (mmHg/ml)	-0.4	(-1.1, 0.3)	0.26
Pulsatile Load			
Aortic characteristic impedance (Zc) ($dyn \cdot sec \cdot cm^{-5}$)	-0.1	(-0.5, 0.3)	0.57
Total arterial compliance (TAC)(mL/mmHg)	0.5	(-0.1, 1.1)	0.11
Augmentation Pressure (mmHg)	-0.2	(-0.8, 0.5)	0.66
Augmentation index (AI) (%)	-0.5	(-1.1, 0.2)	0.18
Reflected wave transit time (msec)	-0.2	(-0.7, 0.3)	0.47
Reflection magnitude	-0.2	(-0.7, 0.3)	0.51
Forward wave amplitude (mmHg)	-0.1	(-0.5, 0.3)	0.75
Backward wave amplitude (mmHg)	-0.1	(-0.6, 0.4)	0.72

Vascular function variables scaled by their standard deviations. Regression coefficients adjusted for age, gender, and categorical visit number. Abbreviations: CI, confidence interval; PWV, pulse wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure.