

**Supplemental Table 1. Extra Data**

	<b>Total N = 626</b>	<b>RELAH n = 444</b>	<b>EILAH n = 182</b>	<b>P-value</b>
Total comorbidities		4 (3-5)	3 (2-4)	<0.001
Composite coronary artery disease	217 (35%)	150 (33.8%)	67 (38%)	0.47
# of HF hospitalizations in the past 12 months	1.0 (0.0,1.0)	1.0 (0.0,1.0)	1.0 (0.0,1.0)	0.80
Thiazides only	27 (4.3%)	21 (4.7%)	6 (3.3%)	0.42
Loop diuretic agents and thiazides	36 (5.8%)	27 (6.1%)	9 (4.9%)	0.58
Sacubitril-valsartan	0 (0.0%)	0 (0.0%)	0 (0.0%)	
SGLT2 inhibitors	16 (2.6%)	14 (3.2%)	2 (1.1%)	0.14
Digoxin	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Oral anticoagulants	309 (49.4%)	236 (53.2%)	73 (40.1%)	0.003
Anti-platelet therapy other than aspirin	71 (11.3%)	45 (10.1%)	26 (14.3%)	0.14

Total morbidities calculated as composite number of the following: any history of HTN, AF (or atrial flutter), CKD, COPD, obesity, DM, composite CAD (as defined below), and anemia.

Composite coronary artery disease includes a history of ischemic heart disease, PCI, CABG, prior MI, and clinically significant unvascularized CAD.

**Supplemental Table 2. Complete Echocardiographic Data**

	<b>Total N = 626</b>	<b>RELAH n = 444</b>	<b>EILAH n = 182</b>	<b>P-value</b>
Heart rate at time of echocardiography (beats/min)	66.0 (60.0-74.0)	66.0 (59.0-75.0)	66.0 (60.0-73.0)	0.67
Septal wall thickness (cm)	1.0 (0.9-1.1)	1.0 (0.9-1.1)	1.0 (0.9-1.1)	0.39
Posterior wall thickness (cm)	0.9 (0.8-1.0)	0.9 (0.9-1.0)	0.9 (0.8-1.0)	0.017
LV end-diastolic dimension (cm)	4.8 (4.4-5.2)	4.9 (4.5-5.3)	4.7 (4.3-5.0)	0.002
LV end-systolic dimension (cm)	3.5 (3.1-4.0)	3.5 (3.2-4.0)	3.4 (3.0-3.8)	0.015
LV mass (g)	162.0 (133.0-201.0)	164.0 (136.0-213.0)	153.0 (127.0-186.0)	0.002
LV mass indexed to BSA (g/m <sup>2</sup> )	80.8 (65.3-98.4)	82.7 (67.2-101.6)	77.4 (63.6-93.0)	0.005
LV mass indexed to height <sup>2.7</sup> (g/m <sup>2.7</sup> )	40.8 (33.5-49.3)	41.7 (34.3-51.0)	38.7 (31.9-46.2)	0.002
Relative wall thickness	0.4 (0.3-0.4)	0.4 (0.3-0.4)	0.4 (0.3-0.4)	0.77
LV end-diastolic volume (mL)	217.8 (171.1-287.4)	223.4 (170.3-298.2)	211.2 (173.4-264.2)	0.096
LV end-systolic volume (mL)	101.6 (75.9-137.8)	102.1 (77.0-145.8)	97.5 (75.6-125.0)	0.089
LV end-diastolic volume index (mL/m <sup>2</sup> )	108.0 (90.0-135.0)	109.5 (91.0-138.0)	106.0 (89.0-128.0)	0.15
LV end-systolic volume index (mL/m <sup>2</sup> )	51.0 (40.0-66.0)	51.0 (40.0-68.0)	51.0 (39.0-59.0)	0.12
LV ejection fraction—core lab (%)	54.3 (50.0-57.3)	54.0 (50.0-57.1)	54.7 (51.1-57.5)	0.29
Mitral E velocity (cm/s)	86.0 (69.0-108.0)	91.0 (72.0-114.0)	76.0 (62.0-93.0)	<0.001
Mitral A velocity (cm/s)	75.0 (55.0-94.0)	72.5 (53.0-93.0)	80.0 (60.0-95.0)	0.020
E/A ratio	1.1 (0.8-1.6)	1.2 (0.8-1.8)	0.9 (0.7-1.3)	<0.001
Septal s' velocity (cm/s)	6.0 (5.0-8.0)	6.0 (5.0-7.0)	7.0 (6.0-8.0)	0.019
Lateral s' velocity (cm/s)	7.0 (6.0-9.0)	7.0 (6.0-8.0)	8.0 (6.0-9.0)	0.007
Septal e' velocity (cm/s)	6.0 (5.0-7.0)	6.0 (5.0-7.0)	6.0 (5.0-7.0)	0.28
Lateral e' velocity (cm/s)	8.0 (6.0-10.0)	8.0 (6.0-10.0)	8.0 (6.0-10.0)	0.48
Septal a' velocity (cm/s)	7.0 (6.0-9.0)	7.0 (5.0-9.0)	8.0 (7.0-10.0)	<0.001
Lateral a' velocity (cm/s)	8.0 (6.0-10.0)	8.0 (5.0-10.0)	9.0 (7.0-11.0)	<0.001
Septal E/e' ratio	14.0 (10.7-19.3)	15.3 (11.3-20.5)	12.9 (9.8-15.8)	<0.001
Lateral E/e' ratio	10.5 (7.8-14.8)	11.2 (8.2-15.9)	9.5 (7.1-12.3)	<0.001
Average E/e' ratio	12.5 (9.6-17.1)	13.2 (10.0-17.8)	10.8 (8.8-14.0)	<0.001
LA maximal volume (mL)	64.1 (50.2-83.6)	67.2 (52.0-87.5)	57.1 (45.2-75.3)	<0.001
LA minimal volume (mL)	41.5 (29.9-56.4)	45.1 (31.4-62.0)	34.4 (26.4-46.2)	<0.001
LA maximal volume indexed to BSA (mL/m <sup>2</sup> )	31.6 (24.9-40.6)	33.0 (26.0-41.3)	28.4 (23.1-36.5)	<0.001
LA minimal volume indexed to BSA (mL/m <sup>2</sup> )	20.3 (14.5-28.1)	21.8 (15.7-30.4)	17.0 (13.1-22.7)	<0.001

LA maximal volume indexed to height <sup>2.7</sup> (mL/m <sup>2.7</sup> )	16.0 (12.4-20.5)	16.6 (13.0-21.2)	14.0 (11.9-18.4)	<0.001
LA minimal volume indexed to height <sup>2.7</sup> (mL/m <sup>2.7</sup> )	10.2 (7.2-14.3)	10.8 (7.7-15.4)	8.7 (6.6-11.7)	<0.001
Ratio of LA to RA volume	1.3 (1.0-1.6)	1.2 (1.0-1.5)	1.3 (1.1-1.6)	0.068
LA emptying fraction (%)	35.3 (25.4-43.8)	32.8 (22.5-42.9)	39.6 (31.4-46.1)	<0.001
RV end-diastolic dimension (cm)	3.7 (3.4-4.1)	3.8 (3.4-4.2)	3.7 (3.3-4.0)	0.094
RV end-systolic dimension (cm)	2.9 (2.6-3.3)	2.9 (2.6-3.3)	2.9 (2.5-3.2)	0.22
RV end-diastolic volume (mL)	43.0 (33.0-56.8)	44.0 (33.0-57.0)	41.6 (32.4-54.5)	0.18
RV end-systolic volume (mL)	21.8 (16.0-29.0)	22.0 (16.0-30.0)	20.0 (15.4-28.0)	0.15
RV ejection fraction (%)	50.0 (45.6-54.1)	50.0 (45.2-54.2)	50.0 (46.4-54.0)	0.35
RV wall thickness (cm)	0.4 (0.4-0.5)	0.4 (0.4-0.5)	0.4 (0.3-0.5)	0.051
RV s' velocity (cm/s)	11.0 (10.0-14.0)	11.0 (10.0-14.0)	11.0 (10.0-14.0)	0.77
RV e' velocity (cm/s)	9.0 (7.0-12.0)	10.0 (8.0-12.0)	9.0 (7.0-11.0)	0.091
RV a' velocity (cm/s)	12.0 (9.0-15.0)	11.0 (8.0-14.0)	12.0 (10.0-15.0)	0.091
TAPSE (cm)	2.0 (1.8-2.3)	2.0 (1.7-2.3)	2.0 (1.8-2.3)	0.17
RA volume (mL)	51.1 (38.6-68.4)	54.2 (42.4-73.5)	43.0 (34.1-58.4)	<0.001
RA volume indexed to BSA (mL/m <sup>2</sup> )	25.2 (19.0-33.1)	26.8 (20.4-35.6)	22.4 (17.3-28.6)	<0.001
RA volume indexed to height <sup>2.7</sup> (mL/m <sup>2.7</sup> )	12.9 (9.7-16.4)	13.9 (10.2-17.4)	11.2 (8.8-13.6)	<0.001
Peak TR velocity (cm/s)	261.0 (236.0-292.0)	265.5 (240.0-300.0)	250.0 (227.0-275.0)	<0.001
Estimated PA systolic pressure (mm Hg)	31.0 (26.0-39.0)	33.0 (27.0-40.0)	28.0 (24.0-33.0)	<0.001
Estimated RA pressure (mm Hg)	3.0 (3.0-3.0)	3.0 (3.0-3.0)	3.0 (3.0-3.0)	0.15
Stroke volume on echocardiography (mL)	66.1 (55.4-81.6)	65.9 (53.8-79.8)	68.4 (56.0-83.1)	0.23
Stroke volume index on echocardiography (mL/m <sup>2</sup> )	32.9 (26.9-39.9)	32.4 (26.4-39.4)	33.4 (28.1-40.8)	0.036
Cardiac output on echocardiography (L/min)	4.4 (3.7-5.4)	4.4 (3.6-5.4)	4.4 (3.8-5.4)	0.41
Cardiac index on echocardiography (L/min/m <sup>2</sup> )	2.2 (1.8-2.6)	2.2 (1.8-2.6)	2.3 (1.9-2.7)	0.084
Degree of mitral regurgitation				0.22
None	38 (7.2%)	23 (6.2%)	15 (9.6%)	
Trace	217 (41.0%)	145 (38.9%)	72 (46.2%)	
Mild	163 (30.8%)	119 (31.9%)	44 (28.2%)	
Mild-to-moderate	63 (11.9%)	46 (12.3%)	17 (10.9%)	
Moderate	38 (7.2%)	31 (8.3%)	7 (4.5%)	
Moderate-to-severe	7 (1.3%)	6 (1.6%)	1 (0.6%)	
Severe	3 (0.6%)	3 (0.8%)	0 (0.0%)	
Degree of tricuspid regurgitation				0.14

None	15 (2.8%)	11 (3.0%)	4 (2.5%)	
Trace	181 (34.3%)	118 (32.1%)	63 (39.6%)	
Mild	201 (38.1%)	138 (37.5%)	63 (39.6%)	
Mild-to-moderate	60 (11.4%)	44 (12.0%)	16 (10.1%)	
Moderate	60 (11.4%)	49 (13.3%)	11 (6.9%)	
Moderate-to-severe	6 (1.1%)	6 (1.6%)	0 (0.0%)	
Severe	4 (0.8%)	2 (0.5%)	2 (1.3%)	
Degree of aortic regurgitation				0.94
None	313 (55.7%)	216 (54.7%)	97 (58.1%)	
Trace	115 (20.5%)	81 (20.5%)	34 (20.4%)	
Mild	95 (16.9%)	70 (17.7%)	25 (15.0%)	
Mild-to-moderate	18 (3.2%)	13 (3.3%)	5 (3.0%)	
Moderate	20 (3.6%)	14 (3.5%)	6 (3.6%)	
Moderate-to-severe	1 (0.2%)	1 (0.3%)	0 (0.0%)	
Degree of pulmonic regurgitation				0.75
None	59 (14.4%)	44 (15.6%)	15 (11.7%)	
Trace	216 (52.7%)	145 (51.4%)	71 (55.5%)	
Mild	122 (29.8%)	83 (29.4%)	39 (30.5%)	
Mild-to-moderate	12 (2.9%)	9 (3.2%)	3 (2.3%)	
Moderate	1 (0.2%)	1 (0.4%)	0 (0.0%)	
LV global longitudinal strain (%)	17.7 (15.4-20.2)	17.3 (15.0-19.9)	18.9 (16.8-20.8)	<0.001
RV free wall strain (%)	22.4 (17.9-26.1)	22.0 (17.6-25.6)	23.1 (18.5-26.8)	0.067
LA reservoir strain (%)	20.3 (14.2-26.9)	18.1 (13.0-25.3)	24.5 (17.0-28.9)	<0.001
RA reservoir strain (%)	24.0 (17.8-31.3)	22.2 (17.1-29.1)	27.1 (22.2-33.1)	<0.001
Ratio of LA to RA strain	0.8 (0.6-1.1)	0.8 (0.6-1.1)	0.9 (0.6-1.1)	0.46

Data are presented as median (IQR) for continuous measures, and n (%) for categorical measures

**Supplemental Table 3. Baseline Clinical Factors Independently Associated With EILAH on Multivariable Logistic Regression**

<b>Model</b>	<b>Variable</b>	<b>Odds ratio</b>	<b>95% CI</b>	<b>P-value</b>
<b>1</b>  <b>(n = 548)</b>	Atrial fibrillation	0.47	0.30-0.74	<b>0.001</b>
	Loop diuretic	0.53	0.33-0.88	<b>0.014</b>
	Systolic blood pressure (per 10 mm Hg increase)	0.92	0.85-0.99	<b>0.029</b>
	6MWT distance (per 30-m increase)	1.09	1.03-1.17	<b>0.004</b>
	Natriuretic peptide level (per 1-SD increase)	0.42	0.24-0.71	<b>0.001</b>
<b>2</b>  <b>(n = 451)</b>	Atrial fibrillation	0.50	0.30-0.82	<b>0.007</b>
	Systolic blood pressure (per 10 mm Hg increase)	0.81	0.84-1.00	<b>0.044</b>
	6MWT distance (per 30-m increase)	1.09	1.01-1.17	<b>0.018</b>
	Natriuretic peptide level (per 1-SD increase)	0.41	0.22-0.76	<b>0.004</b>
	LV end-diastolic dimension (per 1 cm increase)	0.49	0.30-0.80	<b>0.005</b>

**Model 1 covariates:** age, sex, atrial fibrillation, pacemaker, loop diuretic, beta-blocker, mineralocorticoid receptor antagonist, systolic blood pressure, 6MWT distance, natriuretic peptide level, and total bilirubin.

**Model 2 covariates:** all Model 1 covariates + LV end-diastolic dimension, LV mass, and E/e' ratio.

**Supplemental Table 4. Complete Invasive Resting and Exercise Hemodynamic Data**

	<b>Total</b> <b>N = 626</b>	<b>RELAH</b> <b>n = 444</b>	<b>EILAH</b> <b>n = 182</b>	<b>P-value</b>
Aortic systolic pressure at rest (mm Hg)	144.0 (129.0-159.0)	146.0 (132.0-160.0)	137.0 (125.0-153.0)	<0.001
Aortic diastolic pressure at rest (mm Hg)	75.0 (67.0-83.0)	74.0 (67.0-83.0)	75.0 (68.0-81.0)	0.44
Aortic mean pressure at rest (mm Hg)	98.0 (89.7-106.3)	99.5 (90.7-107.2)	95.0 (88.3-105.0)	0.008
Aortic pulse pressure at rest (mm Hg)	68.0 (54.0-81.0)	69.0 (56.0-82.0)	64.0 (51.0-76.0)	0.001
Heart rate at rest (beats/min)	70.0 (63.0-80.0)	70.0 (62.0-80.0)	70.0 (63.0-79.0)	0.82
Right atrial pressure at rest (mm Hg)	9.0 (7.0-12.0)	10.0 (8.0-13.0)	6.0 (5.0-8.0)	<0.001
PA systolic pressure at rest (mm Hg)	40.0 (34.0-49.0)	44.0 (38.0-53.0)	32.0 (28.0-35.0)	<0.001
PA diastolic pressure at rest (mm Hg)	19.0 (15.0-23.0)	21.0 (18.0-25.0)	14.5 (12.0-16.0)	<0.001
Mean PA pressure at rest (mm Hg)	26.3 (21.3-32.0)	29.0 (24.7-33.7)	20.3 (17.7-22.7)	<0.001
PA pulse pressure at rest (mm Hg)	21.0 (17.0-27.0)	23.0 (18.0-30.0)	18.0 (14.0-21.0)	<0.001
PCWP at rest (mm Hg)	18.0 (14.0-23.0)	21.0 (17.0-25.0)	12.0 (10.0-13.0)	<0.001
PCWP V wave at rest (mm Hg)	23.0 (17.0-30.0)	27.0 (22.0-34.0)	15.0 (12.0-17.0)	<0.001
PCWP-right atrial pressure gradient at rest (mm Hg)	8.0 (5.0-12.0)	11.0 (7.0-14.0)	5.0 (3.0-6.0)	<0.001
Transpulmonary gradient at rest (mm Hg)	8.0 (6.0-11.0)	8.0 (5.7-10.7)	9.0 (6.7-11.0)	0.016
Diastolic pulmonary gradient at rest (mm Hg)	1.0 (-1.0-4.0)	0.0 (-2.0-3.0)	3.0 (1.0-5.0)	<0.001
TAPSE/PA systolic pressure ratio at rest (mm/mm Hg)	0.5 (0.4-0.6)	0.4 (0.3-0.6)	0.6 (0.5-0.8)	<0.001
Stroke volume at rest (mL)	74.6 (62.6-89.3)	75.0 (62.5-89.2)	73.8 (64.0-89.7)	0.91
Stroke volume index at rest (mL/m <sup>2</sup> )	36.8 (31.7-43.4)	36.6 (31.4-43.4)	37.3 (33.3-43.9)	0.15
Cardiac output at rest (L/min)	5.2 (4.4-6.2)	5.2 (4.4-6.3)	5.2 (4.4-6.2)	0.99
Cardiac index at rest (L/min/m <sup>2</sup> )	2.6 (2.2-3.0)	2.5 (2.2-3.0)	2.6 (2.2-3.1)	0.26
Systemic vascular resistance at rest (WU)	17.0 (13.7-20.9)	16.8 (13.6-20.9)	17.2 (14.0-20.7)	0.72
SVR index at rest (WU × m <sup>2</sup> )	34.2 (28.4-41.2)	34.5 (28.1-41.1)	33.8 (28.8-41.4)	0.74
Effective arterial elastance at rest (mm Hg/mL)	1.7 (1.4-2.1)	1.7 (1.4-2.2)	1.6 (1.4-2.0)	0.11
Pulse pressure/stroke volume ratio at rest (mm Hg/mL)	0.9 (0.7-1.1)	0.9 (0.7-1.1)	0.8 (0.6-1.1)	0.015
Total pulmonary resistance at rest (WU)	4.9 (3.8-6.4)	5.5 (4.4-6.8)	3.7 (3.2-4.5)	<0.001
Pulmonary vascular resistance at rest (WU)	1.5 (1.1-2.1)	1.4 (1.0-2.1)	1.7 (1.2-2.1)	0.062
PVR indexed to BSA at rest (WU × m <sup>2</sup> )	3.1 (2.2-4.2)	2.9 (2.1-4.2)	3.3 (2.5-4.3)	0.10
PVR indexed to height at rest (WU × m)	2.5 (1.8-3.5)	2.4 (1.7-3.5)	2.8 (2.0-3.5)	0.053

PA pulse pressure/stroke volume ratio at rest (mm Hg/mL)	0.3 (0.2-0.4)	0.3 (0.2-0.4)	0.2 (0.2-0.3)	<0.001
RV effective arterial elastance at rest (mm Hg/mL)	0.5 (0.4-0.7)	0.6 (0.5-0.8)	0.4 (0.4-0.5)	<0.001
PVR/SVR ratio at rest	0.1 (0.1-0.1)	0.1 (0.1-0.1)	0.1 (0.1-0.1)	0.068
Right atrial pressure, legs up (mm Hg)	11.0 (8.0-15.0)	12.0 (10.0-16.0)	8.5 (6.5-11.0)	<0.001
PA systolic pressure, legs up (mm Hg)	47.0 (40.0-57.0)	52.0 (43.0-62.0)	39.0 (34.0-45.0)	<0.001
PA diastolic pressure, legs up (mm Hg)	23.0 (19.0-28.0)	25.0 (21.0-29.0)	18.0 (15.0-20.0)	<0.001
Mean PA pressure, legs up (mm Hg)	31.3 (26.0-37.3)	34.0 (29.3-39.7)	25.3 (21.7-28.3)	<0.001
PA pulse pressure, legs up (mm Hg)	24.0 (19.0-32.0)	26.0 (20.0-34.0)	21.0 (18.0-26.0)	<0.001
PCWP, legs up (mm Hg)	22.0 (18.0-27.0)	25.0 (21.0-30.0)	17.0 (14.0-19.5)	<0.001
PCWP V wave, legs up (mm Hg)	29.0 (23.0-37.0)	33.0 (26.5-41.0)	22.0 (18.0-27.0)	<0.001
PCWP-right atrial pressure gradient, legs up (mm Hg)	11.0 (8.0-15.0)	12.0 (9.0-17.0)	8.0 (5.0-10.0)	<0.001
Transpulmonary gradient, legs up (mm Hg)	8.7 (5.7-11.3)	8.7 (6.3-11.7)	8.0 (5.3-10.7)	0.040
Diastolic pulmonary gradient, legs up (mm Hg)	0.0 (-3.0-3.0)	0.0 (-3.0-3.0)	1.0 (-2.0-4.0)	0.003
Right atrial pressure at 20 W exercise (mm Hg)	17.0 (13.0-21.0)	18.0 (15.0-22.0)	14.0 (11.0-17.0)	<0.001
PA systolic pressure at 20 W exercise (mm Hg)	64.0 (54.0-75.0)	69.5 (58.0-79.0)	55.0 (48.0-63.0)	<0.001
PA diastolic pressure at 20 W exercise (mm Hg)	30.0 (27.0-37.0)	32.0 (29.0-39.0)	27.0 (23.0-30.0)	<0.001
Mean PA pressure at 20 W exercise (mm Hg)	42.0 (36.0-48.7)	45.3 (38.7-51.3)	36.0 (32.0-41.0)	<0.001
PA pulse pressure at 20 W exercise (mm Hg)	32.0 (25.0-41.5)	35.0 (28.0-44.0)	28.0 (21.0-35.0)	<0.001
PCWP at 20 W exercise (mm Hg)	32.0 (27.0-38.0)	34.0 (29.0-40.0)	27.0 (24.0-31.0)	<0.001
PCWP V wave at 20 W exercise (mm Hg)	45.0 (36.5-55.0)	48.0 (39.0-57.0)	38.0 (31.0-46.0)	<0.001
PCWP-right atrial pressure gradient at 20 W exercise (mm Hg)	15.0 (11.0-19.0)	16.0 (12.0-21.0)	13.0 (10.0-17.0)	<0.001
Transpulmonary gradient at 20 W exercise (mm Hg)	9.7 (6.8-13.7)	10.0 (7.0-14.7)	9.0 (6.7-11.7)	0.018
Diastolic pulmonary gradient at 20 W exercise (mm Hg)	-1.0 (-4.0-2.0)	-2.0 (-5.0-2.0)	0.0 (-3.0-2.0)	0.004
Peak exercise capacity (W)	40.0 (20.0-60.0)	40.0 (20.0-60.0)	40.0 (40.0-60.0)	<0.001
Total duration of exercise (min)	7.0 (5.0-10.5)	7.0 (5.0-10.0)	9.0 (6.0-11.0)	<0.001
Aortic systolic pressure at peak exercise (mm Hg)	160.0 (141.0-181.5)	161.0 (142.0-182.0)	158.0 (140.0-181.0)	0.52
Aortic diastolic pressure at peak exercise (mm Hg)	85.0 (73.0-96.0)	85.0 (72.0-97.0)	85.0 (73.0-94.0)	0.56
Aortic mean pressure at peak exercise (mm Hg)	110.7 (98.0-122.7)	111.0 (98.7-124.0)	109.3 (96.7-120.7)	0.46
Aortic pulse pressure at peak exercise (mm Hg)	74.0 (59.0-90.0)	74.0 (59.0-91.0)	75.0 (59.0-89.0)	0.90
Peak heart rate (beats/min)	100.0 (86.0-113.0)	98.0 (85.0-112.0)	104.0 (92.0-114.0)	0.004
Right atrial pressure at peak exercise (mm Hg)	18.0 (14.0-22.0)	19.0 (16.0-24.0)	15.0 (12.0-18.0)	<0.001

PA systolic pressure at peak exercise (mm Hg)	69.0 (60.0-80.0)	72.0 (62.0-81.0)	62.0 (56.0-69.0)	<0.001
PA diastolic pressure at peak exercise (mm Hg)	34.0 (29.0-40.0)	35.0 (30.0-40.0)	30.0 (27.0-35.0)	<0.001
Mean PA pressure at peak exercise (mm Hg)	45.3 (39.7-52.0)	47.5 (41.7-54.0)	41.0 (36.7-46.3)	<0.001
PA pulse pressure at peak exercise (mm Hg)	35.0 (28.0-43.0)	37.0 (29.5-46.0)	32.0 (26.0-38.0)	<0.001
PCWP at peak exercise (mm Hg)	34.0 (29.0-40.0)	36.0 (32.0-42.0)	30.0 (27.0-35.0)	<0.001
PCWP V wave at peak exercise (mm Hg)	47.0 (38.0-56.0)	49.0 (41.0-59.0)	41.0 (34.5-50.0)	<0.001
PCWP-right atrial pressure gradient at peak exercise (mm Hg)	16.0 (12.0-21.0)	17.0 (13.0-21.0)	15.5 (11.0-19.0)	0.005
Transpulmonary gradient at peak exercise (mm Hg)	10.7 (7.0-15.3)	11.0 (7.3-15.7)	10.0 (6.7-14.3)	0.16
Diastolic pulmonary gradient at peak exercise (mm Hg)	-1.0 (-4.0-3.0)	-1.0 (-5.0-3.0)	0.0 (-3.0-3.0)	0.097
Stroke volume at peak exercise (mL)	52.8 (43.5-65.3)	53.5 (44.4-67.6)	51.6 (41.1-62.4)	0.083
Stroke volume index at peak exercise (mL/m <sup>2</sup> )	26.6 (22.0-31.5)	26.6 (22.1-31.7)	26.3 (21.5-30.7)	0.38
Cardiac output at peak exercise (L/min)	8.0 (6.4-10.1)	7.9 (6.1-9.7)	8.8 (7.0-11.1)	<0.001
Cardiac index at peak exercise (L/min/m <sup>2</sup> )	3.9 (3.2-4.8)	3.8 (3.1-4.6)	4.4 (3.6-5.2)	<0.001
Systemic vascular resistance at peak exercise (WU)	11.5 (9.0-15.0)	12.0 (9.1-15.4)	10.7 (8.2-14.6)	0.010
SVR index at peak exercise (WU × m <sup>2</sup> )	23.8 (18.3-30.1)	24.3 (19.3-31.2)	21.7 (17.0-27.3)	0.001
Effective arterial elastance at peak exercise (mm Hg/mL)	2.7 (2.1-3.5)	2.6 (2.0-3.4)	2.8 (2.2-3.5)	0.34
Pulse pressure/stroke volume ratio at peak exercise (mm Hg/mL)	1.4 (1.0-1.8)	1.3 (1.0-1.8)	1.4 (1.0-1.9)	0.35
Total pulmonary resistance at peak exercise (WU)	5.6 (4.4-7.3)	6.1 (4.7-7.9)	4.7 (3.8-6.1)	<0.001
Pulmonary vascular resistance at peak exercise (WU)	1.3 (0.8-2.0)	1.4 (0.9-2.1)	1.1 (0.8-1.7)	0.001
PVR indexed to BSA at peak exercise (WU × m <sup>2</sup> )	4.2 (2.7-6.0)	4.3 (2.7-6.2)	3.9 (2.7-5.5)	0.100
PVR indexed to height at peak exercise (WU × m)	2.2 (1.4-3.3)	2.4 (1.5-3.5)	2.0 (1.2-2.8)	0.001
PA pulse pressure/stroke volume ratio at peak exercise (mm Hg/mL)	0.6 (0.5-0.9)	0.7 (0.5-0.9)	0.6 (0.5-0.8)	0.014
RV effective arterial elastance at peak exercise (mm Hg/mL)	1.3 (1.0-1.6)	1.3 (1.0-1.7)	1.2 (1.0-1.5)	0.005
PVR/SVR ratio at peak exercise	0.1 (0.1-0.2)	0.1 (0.1-0.2)	0.1 (0.1-0.2)	0.34
Workload-corrected PCWP (mm Hg/W/kg)	76.6 (51.8-123.9)	86.0 (58.6-145.7)	57.8 (40.6-90.0)	<0.001
PCWP/CO slope (mm Hg/L/min)	5.9 (3.6-10.5)	6.2 (3.6-11.0)	5.4 (3.6-9.7)	0.31
Delta PCWP, rest to peak exercise (mm Hg)	16.0 (12.0-21.0)	15.0 (10.0-20.0)	19.0 (15.0-23.5)	<0.001
Delta CO, rest to peak exercise (L/min)	2.7 (1.6-4.2)	2.4 (1.5-3.9)	3.5 (2.2-4.8)	<0.001

Data are presented as median (IQR).



**Supplemental Table 5. Effects of Atrial Shunt on Echocardiographic Variables, Baseline to 12 Months**

<b>Change in Cardiac Structure at 12 months</b>	<b>Shunt</b>	<b>Sham</b>	<b>P-value</b>
<b><i>EILAH</i></b>			
<b>Right atrial volume index, mL/m<sup>2</sup></b>	+8.8 (+4.7, +13.0)	+1.6 (-1.5, +4.6)	<b>0.006</b>
<b>RV diastolic volume index, mL/m<sup>2</sup></b>	+7.4 (+2.3, +12.5)	+1.6 (-1.7, +5.0)	<b>0.07</b>
TAPSE, cm	+0.10 (+0.01, +0.20)	+0.08 (-0.02, +0.18)	0.74
Tricuspid regurgitation severity (0-4)	+0.10 (-0.05, +0.25)	-0.07 (-0.17, +0.04)	0.08
Tricuspid regurgitation velocity (cm/s)	-6.7 (-20.3, +6.9)	0.7 (-8.0, +9.5)	0.36
LA volume index, mL/m <sup>2</sup>	+1.5 (-3.3, +6.4)	+0.6 (-3.0, +4.1)	0.74
LV end diastolic volume index, mL/m <sup>2</sup>	-2.2 (-6.2, +1.9)	-2.7 (-7.5, +2.2)	0.87
LV ejection fraction, %	-0.2 (-1.3, +0.9)	+0.8 (-0.3, +1.8)	0.19
E/e' ratio	-0.9 (-1.9, +0.2)	+0.1 (-0.7, +0.9)	0.14
<b><i>RELAH</i></b>			
<b>Right atrial volume index, mL/m<sup>2</sup></b>	+9.5 (+6.5, +12.5)	-0.6 (-3.2, +1.9)	<b>&lt;0.0001</b>
<b>RV diastolic volume index, mL/m<sup>2</sup></b>	+8.9 (+5.2, +12.6)	-0.9 (-3.9, +2.1)	<b>0.0001</b>
TAPSE, cm	0.01 (-0.05, +0.07)	-0.01 (-0.07, +0.04)	0.58
<b>Tricuspid regurgitation severity (0-4)</b>	+0.18 (+0.07, +0.29)	-0.00 (-0.08, +0.08)	<b>0.009</b>
Tricuspid regurgitation velocity (cm/s)	+4.3 (-3.9, +12.4)	-0.8 (-8.6, +7.0)	0.37
LA volume index, mL/m <sup>2</sup>	-1.0 (-3.3, +1.3)	-0.7 (-3.0, +1.5)	0.86
LV end diastolic volume index, mL/m <sup>2</sup>	-7.4 (-10.2, -4.6)	-4.7 (-8.0, -1.3)	0.21
<b>LV ejection fraction, %</b>	<b>-0.7 (-1.7, +0.2)</b>	<b>+0.6 (-0.2, +1.4)</b>	<b>0.04</b>
<b>E/e' ratio</b>	<b>-1.0 (-1.9, -0.2)</b>	<b>+0.2 (-0.7, +1.2)</b>	<b>0.05</b>

Values represent mean change (95% CI).

TAPSE (tricuspid annular plane systolic excursion); LA (left atrial); LV (left ventricular).

**Supplemental Table 6A. Stratified Safety Outcomes in Patients With EILAH**

	<b>Total N = 180</b>	<b>Sham procedure n = 88</b>	<b>Atrial shunt device n = 92</b>	<b>P- value</b>
Cardiovascular mortality within 365 days	1 (0.6%)	1 (1.1%)	0 (0.0%)	0.31
Non-fatal ischemic stroke within 365 days	0 (0.0%)	0 (0.0%)	0 (0.0%)	
New onset or worsening of kidney dysfunction within 365 days	8 (4.5%)	4 (4.6%)	4 (4.4%)	0.96
Any MACE within 365 days	3 (1.7%)	1 (1.1%)	2 (2.2%)	0.58
Cardiac death within 365 days	1 (0.6%)	1 (1.1%)	0 (0.0%)	0.31
Cardiac tamponade within 365 days	1 (0.6%)	0 (0.0%)	1 (1.1%)	0.32
Emergency cardiac surgery within 365 days	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Thrombo-embolic complications within 365 days	0 (0.0%)	0 (0.0%)	0 (0.0%)	
TIA within 365 days	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Systemic embolic events within 365 days	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Newly acquired persistent or permanent atrial fibrillation or atrial flutter	1 (0.6%)	0 (0.0%)	1 (1.1%)	0.32
≥30% Increase in RV size within 365 days	49 (27.7%)	17 (19.5%)	32 (35.6%)	0.017
≥30% Decrease in TAPSE within 365 days	7 (4.0%)	5 (5.7%)	2 (2.2%)	0.23
≥30% Increase in RV size/decrease in TAPSE within 365 days	55 (31.1%)	22 (25.3%)	33 (36.7%)	0.10

Data are presented as n (%).

**Supplemental Table 6B. Safety Outcomes in Patients With RELAH**

	<b>Total</b> <b>N = 441</b>	<b>Sham</b> <b>procedure</b> <b>n = 224</b>	<b>Atrial shunt</b> <b>device</b> <b>n = 217</b>	<b>P-</b> <b>value</b>
Cardiovascular mortality within 365 days	3 (0.7%)	1 (0.5%)	2 (0.9%)	0.55
Non-fatal ischemic stroke within 365 days	1 (0.2%)	0 (0.0%)	1 (0.5%)	0.31
New onset or worsening of kidney dysfunction within 365 days	39 (8.9%)	21 (9.5%)	18 (8.3%)	0.66
Any MACE within 365 days	9 (2.1%)	1 (0.5%)	8 (3.7%)	0.017
Cardiac death within 365 days	3 (0.7%)	1 (0.5%)	2 (0.9%)	0.55
Cardiac tamponade within 365 days	1 (0.2%)	0 (0.0%)	1 (0.5%)	0.31
Emergency cardiac surgery within 365 days	1 (0.2%)	0 (0.0%)	1 (0.5%)	0.31
Thrombo-embolic complications within 365 days	0 (0.0%)	0 (0.0%)	0 (0.0%)	
TIA within 365 days	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Systemic embolic events within 365 days	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Newly acquired persistent or permanent atrial fibrillation or atrial flutter	5 (1.1%)	2 (0.9%)	3 (1.4%)	0.64
≥30% Increase in RV size within 365 days	103 (23.5%)	46 (20.8%)	57 (26.3%)	0.18
≥30% Decrease in TAPSE within 365 days	12 (2.7%)	10 (4.5%)	2 (0.9%)	0.021
≥30% Increase in RV size/decrease in TAPSE within 365 days	113 (25.8%)	54 (24.4%)	59 (27.2%)	0.51

Data are presented as n (%).

**Supplemental Figure 1.** Changes in New York Heart Association functional class with atrial shunt therapy or sham treatment in the groups with resting PCWP < 15 mm Hg (exercise-induced LA hypertension; EILAH) and those with resting PCWP  $\geq$  15 mm Hg (resting LA hypertension; RELAH). There was significant improvement in New York Heart Association functional class in the group with EILAH after atrial shunt therapy, but not in the group with RELAH.

Supplemental Figure 1

