

Physiological Characterization of Pressure-Strain Loops Indices as Non-Invasive Surrogates for Ventriculo-Arterial Coupling: A Proof-of-Concept Study

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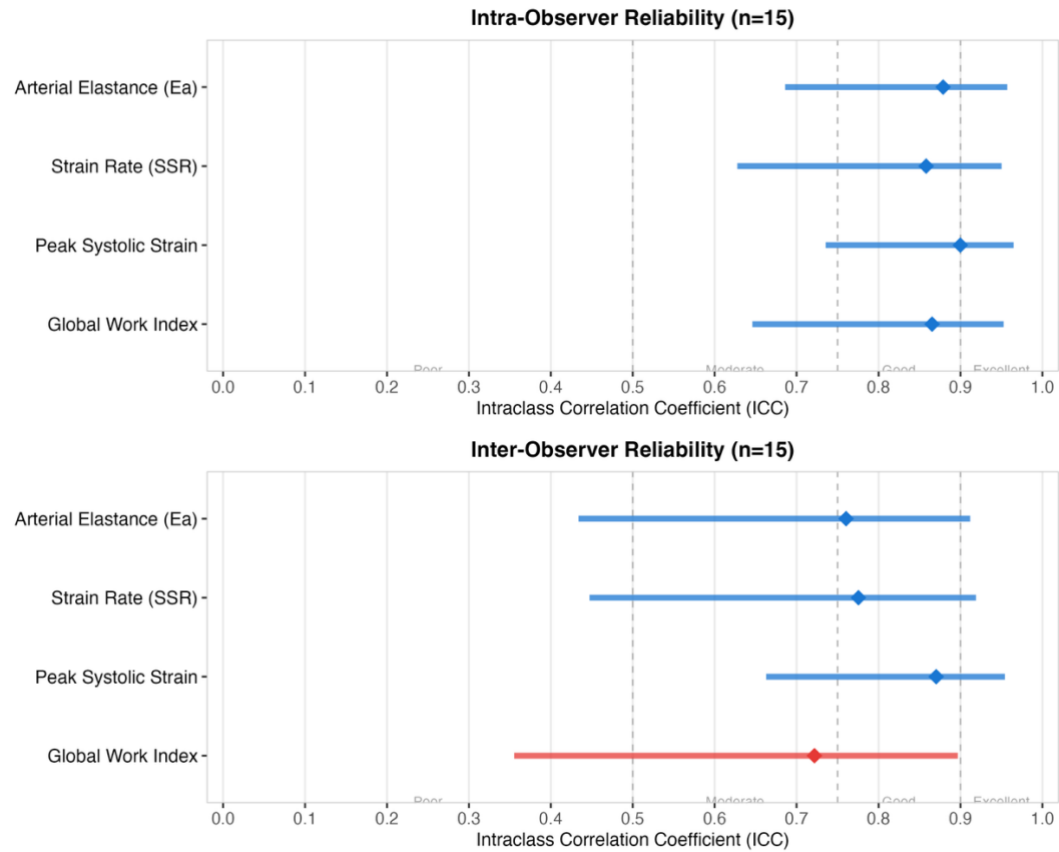
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Index of Supplementary Materials

Supplementary Figure S1 - Intra- and Interobserver Reliability of Pressure-Strain Loop Parameters	3
Supplementary Figure S2 - Intra-Observer Bland-Altman Plots for Pressure-Strain Loop Parameters	4
Supplementary Figure S3 - Inter-Observer Bland-Altman Plots for Pressure-Strain Loop Parameters	5
Supplementary Table S1 - Directional Hypotheses Based on PV Loop Physiology(1–4).....	6
Supplementary Table S2 - Baseline Characteristics by Test in Per-Protocol Population	7
Supplementary Table S3: Baseline Correlations — Five Co-Primary Endpoints	8
Supplementary Table S4 - Primary endpoints within-subject change.....	9
Supplementary Table S5 - Exercise Intervention - Echocardiographic Responses	10
Supplementary Table S6 - Handgrip Intervention - Echocardiographic Responses.....	11
Supplementary Table S7 - PLR Intervention - Echocardiographic Responses.....	12
Supplementary Table S8 - Comprehensive Sensitivity Analyses Results	13
Supplementary Table S9 - Exploratory Analysis of Secondary Endpoints	14

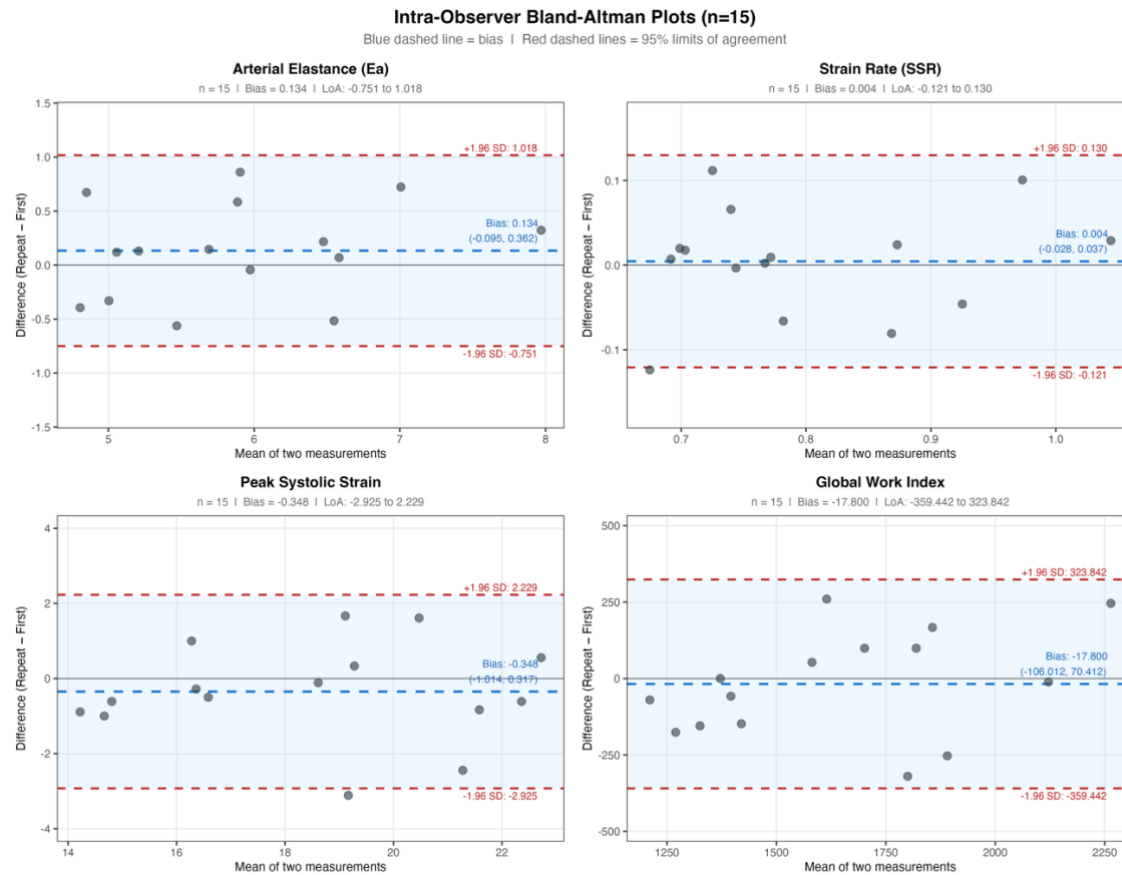
Supplementary Figure S1- Intra- and Interobserver Reliability of Pressure-Strain Loop Parameters



Intraclass correlation coefficients (ICC) with 95% confidence intervals for strain-derived parameters in 15 participants. ICC values are color-coded: poor (<0.5), moderate (0.5-0.75), good (0.75-0.90), excellent (>0.90).

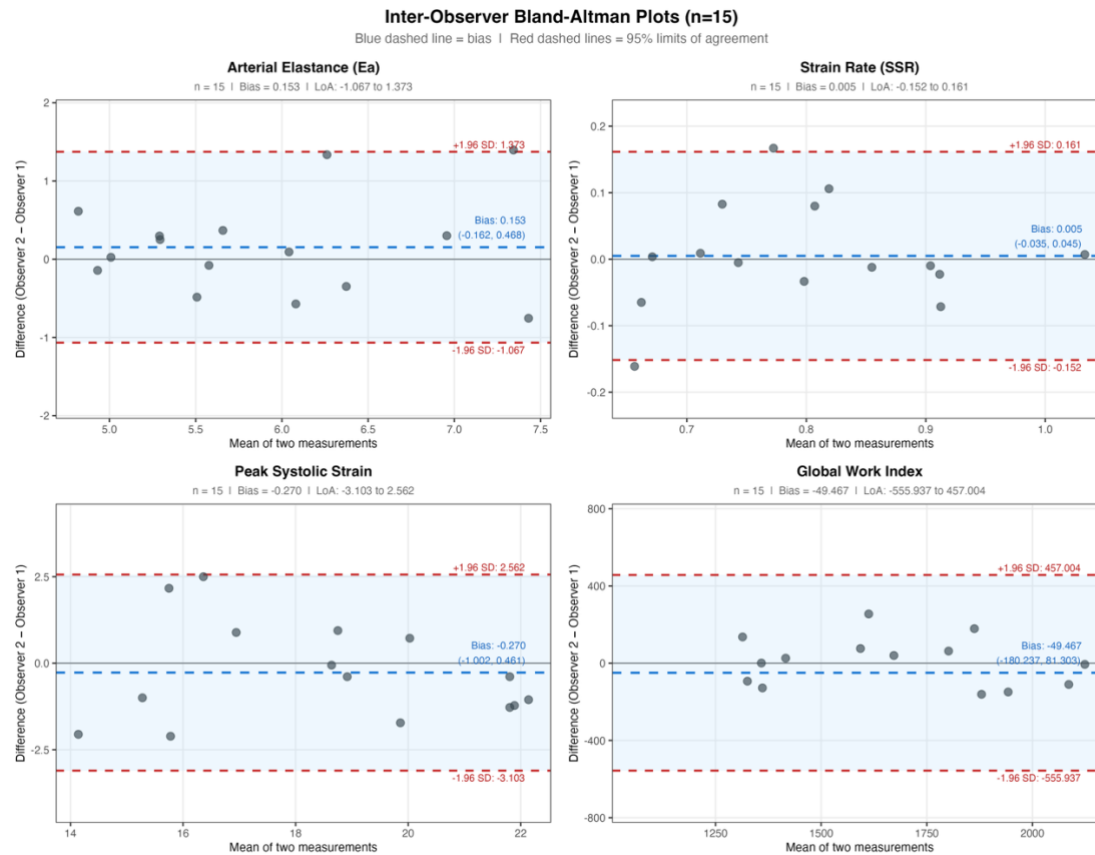
Abbreviations: SSR (systolic strain rate)

Supplementary Figure S2 - Intra-Observer Bland-Altman Plots for Pressure-Strain Loop Parameters



Bland-Altman plots showing intra-observer agreement for strain-derived parameters in 15 participants. The primary observer repeated offline pressure-strain loop analysis after 8 weeks. Each plot shows individual paired measurements (gray circles), mean bias (blue dashed line), and 95% limits of agreement (red dotted lines, mean \pm 1.96 SD). End-systolic pressure was excluded as it did not vary between measurements. Minimal systematic bias was observed across all parameters, with acceptable measurement variability. Ea = arterial elastance; SSR = systolic strain rate; GWI = global work index.

Supplementary Figure S3 - Inter-Observer Bland-Altman Plots for Pressure-Strain Loop Parameters



Bland-Altman plots showing inter-observer agreement for strain-derived parameters in 15 participants. Two independent observers performed offline pressure-strain loop analysis on the same echocardiographic images. Each plot shows individual paired measurements (gray circles), mean bias (blue dashed line), and 95% limits of agreement (red dotted lines, mean \pm 1.96 SD). End-systolic pressure was excluded as it did not vary between measurements. Minimal systematic bias was observed across all parameters, with acceptable inter-observer measurement variability. Ea = arterial elastance; SSR = systolic strain rate; GWI = global work index

Supplementary Table S1 - Directional Hypotheses Based on PV Loop Physiology(1–4)

Primary Endpoint	Dataset column	Rationale	Expected - Handgrip	Expected - PLR	Expected - Exercise
Arterial Elastance (Ea)	ESP/Peak Systolic Strain	Afterload	↑	↑	↓/↔
Strain rate	SSR_global	Contractility	↔/↓	↔/↑	↑
End-systolic pressure	ES_P_est	Afterload, contractility and preload	↑	↑	↑
Peak strain	Peak_Systolic_strain	Contractility	↓/↔	↔/↑	↑ (more negative)
Loop area	GWI	Contractility, afterload, preload	↔/↑	↑	↑

Note: Arrows indicate direction of change. For strain parameters, ↓ indicates less negative values (reduced deformation), ↑ indicates more negative values (increased deformation). PLR (passive leg raising). Due to operational constraints (absence of a second operator), volunteers maintained leg elevation on a platform with knee flexion in a table-top position.

1. Patterson T, Rivolo S, Burkhoff D, Schreuder J, Briceno N, Williams R, et al. Impact of coronary artery disease on contractile function and ventricular-arterial coupling during exercise: Simultaneous assessment of left-ventricular pressure–volume and coronary pressure and flow during cardiac catheterization. *Physiol Rep* [Internet]. 2021 May [cited 2025 Oct 31];9(10). Available from: <https://onlinelibrary.wiley.com/doi/10.14814/phy2.14768>
2. Penicka M, Bartunek J, Trakalova H, Hrabakova H, Maruskova M, Karasek J, et al. Heart Failure With Preserved Ejection Fraction in Outpatients With Unexplained Dyspnea. *J Am Coll Cardiol*. 2010 Apr;55(16):1701–10.
3. Rommel KP, Von Roeder M, Latuscynski K, Oberueck C, Blazek S, Fengler K, et al. Extracellular Volume Fraction for Characterization of Patients With Heart Failure and Preserved Ejection Fraction. *J Am Coll Cardiol*. 2016 Apr;67(15):1815–25.

Supplementary Table S2 - Baseline Characteristics by Test in Per-Protocol Population

Characteristic	Exercise — Total N = 56 ¹	Exercise — Included N = 31 ¹	P value	Maneuvers — Total N = 47 ¹	Maneuvers — Included N = 30 ¹	P value
Sex						
Female	32 (57%)	20 (65%)	0.332	27 (57%)	14 (47%)	0.093
Male	24 (43%)	11 (35%)	0.161	20 (43%)	16 (53%)	0.292
Age (years)	44 ± 9	42 ± 8	0.077	42 ± 8	43 ± 8	0.199
Brachial Systolic BP (mmHg)	119 ± 15	122 ± 15	0.197	117 ± 18	121 ± 20	0.057
Brachial Diastolic BP (mmHg)	72 ± 7	72 ± 8	0.899	68 ± 9	69 ± 9	0.169
BMI (kg/m²)	28.4 ± 4.4	29.0 ± 4.7	0.264	25.3 ± 3.3	25.1 ± 3.2	0.479
Any medication	16 (29%)	8 (26%)	0.832	12 (26%)	8 (27%)	1.000

¹n (%); Mean ± SD

Note:

This table presents baseline demographic and clinical characteristics stratified by intervention type (handgrip, passive leg raising, and exercise) for participants included in the per-protocol analysis.

Abbreviations:

Any Medication (antidepressants, Beta 2 mimetics for asthma); BMI, body mass index; BP, blood pressure; PP, per-protocol.

Supplementary Table S3: Baseline Correlations — Five Co-Primary Endpoints

Endpoint	ESP	Ea	SSR	Peak Strain	GWI
End-Systolic Pressure (ESP)	—	0.425***	0.030	0.005	0.489***
Arterial Elastance (Ea)	0.425***	—	-0.644***	-0.849***	-0.508***
Systolic Strain Rate (SSR)	0.030	-0.644***	—	0.695***	0.604***
Peak Systolic Strain	0.005	-0.849***	0.695***	—	0.781***
Global Work Index (GWI)	0.489***	-0.508***	0.604***	0.781***	—

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Spearman r at baseline ($n=61$). The Ea–Peak Systolic Strain pair ($r=-0.849$) reflects the formula relationship ($Ea = ESP/$ Peak Systolic Strain) rather than empirical redundancy. Apart from this formula-derived association, pairwise correlations are low to moderate ($|r| = 0.005-0.781$), with ESP showing negligible correlation with strain-based indices, supporting the conceptualisation of these endpoints as a complementary panel capturing distinct hemodynamic constructs.

Supplementary Table S4 - Primary endpoints within-subject change

Intervention	Endpoint	Baseline (mean ± SD)	Post-maneuver (mean ± SD)	Change from baseline [95% CI]	Effect size [95% CI]	Adjusted P
Exercise	Global Work Index	1412.97 ± 287.40	1807.48 ± 381.54	394.52 (253.53, 535.50)	1.026 (0.584, 1.458)	<0.001**
	Peak Systolic Strain	14.93 ± 2.01	17.27 ± 3.12	2.34 (1.37, 3.30)	0.884 (0.462, 1.295)	<0.001**
	End-Systolic Pressure	109.05 ± 13.05	132.39 ± 19.74	23.34 (16.53, 30.15)	1.257 (0.767, 1.748)	<0.001**
	Systolic Strain Rate	0.72 ± 0.12	0.98 ± 0.21	0.26 (0.18, 0.33)	1.292 (0.807, 1.766)	<0.001**
	Arterial Elastance	7.49 ± 1.30	7.80 ± 1.66	0.31 (-0.24, 0.87)	0.207 (-0.151, 0.561)	0.259
Handgrip	Global Work Index	1683.77 ± 275.87	1763.17 ± 265.92	79.40 (-3.93, 162.73)	0.356 (-0.016, 0.722)	0.183
	Peak Systolic Strain	18.75 ± 2.67	18.19 ± 2.22	-0.57 (-1.23, 0.09)	-0.322 (-0.687, 0.047)	0.183
	End-Systolic Pressure	106.14 ± 8.32	115.17 ± 11.59	9.03 (6.00, 12.06)	1.112 (0.649, 1.563)	<0.001**
	Systolic Strain Rate	0.82 ± 0.10	0.80 ± 0.12	-0.02 (-0.06, 0.02)	-0.196 (-0.573, 0.181)	0.183
	Arterial Elastance	5.89 ± 0.98	6.70 ± 1.26	0.81 (0.43, 1.19)	0.791 (0.375, 1.197)	<0.001**
PLR	Global Work Index	1683.77 ± 275.87	1767.90 ± 213.09	84.13 (-11.91, 180.17)	0.327 (-0.043, 0.692)	0.186
	Peak Systolic Strain	18.75 ± 2.67	17.76 ± 2.06	-0.99 (-1.79, -0.20)	-0.465 (-0.838, -0.084)	0.066
	End-Systolic Pressure	106.14 ± 8.32	114.75 ± 8.31	8.61 (5.95, 11.27)	1.207 (0.728, 1.674)	<0.001**
	Systolic Strain Rate	0.82 ± 0.10	0.79 ± 0.08	-0.02 (-0.06, 0.02)	-0.228 (-0.589, 0.136)	0.222
	Arterial Elastance	5.89 ± 0.98	6.62 ± 0.99	0.73 (0.37, 1.08)	0.766 (0.353, 1.170)	0.001**

95% confidence intervals are unadjusted. Standardized effect size (Cohen's *d*z or rank-biserial *r*). Statistical significance was determined using Holm-Bonferroni adjusted p-values to control the family-wise error rate across the five co-primary endpoints within each intervention. **Effect size:** Cohen's $|dz| < 0.2$ (negligible), 0.2-0.5 (small), 0.5-0.8 (medium), >0.8 (large) and Matched-pairs rank-biserial $|r| < 0.1$ (negligible), 0.1-0.3 (small), 0.3-0.5 (medium), >0.5 (large)
Abbreviations: PLR (passive leg raising)

Supplementary Table S5 - Exercise Intervention - Echocardiographic Responses

Endpoint	Baseline (mean ± SD)	Intervention (mean ± SD)	Mean change (95% CI)	Effect size (95% CI)	Effect_Label	Effect_Magnitude	p_value_adjusted
Systolic Strain Rate	0.72 ± 0.12	0.98 ± 0.21	0.26 [0.18, 0.33]	1.292 [0.807, 1.766]	Cohen's dz	Large	<0.001
End Systolic Pressure	109.05 ± 13.05	132.39 ± 19.74	23.34 [16.53, 30.15]	1.257 [0.767, 1.748]	Rank-biserial r	Large	<0.001
GWJ	1412.97 ± 287.40	1807.48 ± 381.54	394.52 [253.53, 535.50]	1.026 [0.584, 1.458]	Cohen's dz	Large	<0.001
Peak Systolic Strain	14.93 ± 2.01	17.27 ± 3.12	2.34 [1.37, 3.30]	0.884 [0.462, 1.295]	Cohen's dz	Large	<0.001
Arterial Elastance	7.49 ± 1.30	7.80 ± 1.66	0.31 [-0.24, 0.87]	0.207 [-0.151, 0.561]	Cohen's dz	Small	0.259

Primary in response to exercise intervention (n = 31). Values are presented as mean ± standard deviation or mean change [95% confidence interval].

Effect Size: Cohen's dz for paired t-test; rank-biserial r for Wilcoxon signed-rank test.

p_value_adjusted: Holm-Bonferroni corrected p-values for multiple comparisons.

Abbreviations:

CI = confidence interval; GWJ = global work index; SD standard deviation

Supplementary Table S6 - Handgrip Intervention - Echocardiographic Responses

Endpoint	Baseline (mean ± SD)	Intervention (mean ± SD)	Mean change (95% CI)	Effect size (95% CI)	Effect_Label	Effect_Magnitude	p_value_adjusted
End Systolic Pressure	106.14 ± 8.32	115.17 ± 11.59	9.03 [6.00, 12.06]	1.112 [0.649, 1.563]	Cohen's dz	Large	<0.001
Arterial Elastance	5.89 ± 0.98	6.70 ± 1.26	0.81 [0.43, 1.19]	0.791 [0.375, 1.197]	Cohen's dz	Medium	<0.001
GWI	1683.77 ± 275.87	1763.17 ± 265.92	79.40 [-3.93, 162.73]	0.356 [-0.016, 0.722]	Cohen's dz	Small	0.183
Peak Systolic Strain	18.75 ± 2.67	18.19 ± 2.22	-0.57 [-1.23, 0.09]	-0.322 [-0.687, 0.047]	Cohen's dz	Small	0.183
Systolic Strain Rate	0.82 ± 0.10	0.80 ± 0.12	-0.02 [-0.06, 0.02]	-0.196 [-0.573, 0.181]	Rank-biserial r	Medium	0.183

Primary endpoints in response to handgrip intervention (n = 30). Values are presented as mean ± standard deviation or mean change [95% confidence interval].

Effect Size: Cohen's dz for paired t-test; rank-biserial r for Wilcoxon signed-rank test.

p_value_adjusted: Holm-Bonferroni corrected p-values for multiple comparisons.

Abbreviations:

CI = confidence interval; GWI = global work index, SD standard deviation

Supplementary Table S7 - PLR Intervention - Echocardiographic Responses

Endpoint	Baseline (mean ± SD)	Intervention (mean ± SD)	Mean change (95% CI)	Effect size (95% CI)	Effect_Label	Effect_Magnitude	p_value_adjusted
End Systolic Pressure	106.14 ± 8.32	114.75 ± 8.31	8.61 [5.95, 11.27]	1.207 [0.728, 1.674]	Cohen's dz	Large	<0.001
Arterial Elastance	5.89 ± 0.98	6.62 ± 0.99	0.73 [0.37, 1.08]	0.766 [0.353, 1.170]	Cohen's dz	Medium	0.001
Peak Systolic Strain	18.75 ± 2.67	17.76 ± 2.06	-0.99 [-1.79, -0.20]	-0.465 [-0.838, -0.084]	Cohen's dz	Small	0.066
GWl	1683.77 ± 275.87	1767.90 ± 213.09	84.13 [-11.91, 180.17]	0.327 [-0.043, 0.692]	Cohen's dz	Small	0.186
Systolic Strain Rate	0.82 ± 0.10	0.79 ± 0.08	-0.02 [-0.06, 0.02]	-0.228 [-0.589, 0.136]	Cohen's dz	Small	0.222

Primary endpoints in response to passive leg raising (PLR) intervention (n = 30). Values are presented as mean ± standard deviation or mean change [95% confidence interval].

Effect Size: Cohen's dz for paired t-test; rank-biserial r for Wilcoxon signed-rank test.

p_value_adjusted: Holm-Bonferroni corrected p-values for multiple comparisons.

Abbreviations:

CI = confidence interval; PLR = passive leg raising; PLR= passive leg raising; SD standard deviation

Supplementary Table S8 - Comprehensive Sensitivity Analyses Results

Intervention	Endpoint	Outliers	Original p	Effect Size	Winsorized p	Permutation p	Bootstrap CI≠0	Concordance	Verdict
HANDGRIP N=30	Arterial Elastance	0	<0.001	0.791	<0.001	<0.001	Yes	4/4	ROBUST
	Systolic strain rate	0	0.129	-0.320	0.133	0.2890	No	0/4	ROBUST
	End-syst Pressure	0	<0.001	1.112	<0.001	<0.001	Yes	4/4	ROBUST
	Peak Systolic strain	0	0.088	-0.322	0.069	0.0720	No	0/4	ROBUST
	GWl	1	0.061	0.356	0.021	0.0600	No	1/4	SENSITIVE
PLR N=30	Arterial Elastance	0	<0.001	0.766	<0.001	0.0010	Yes	4/4	ROBUST
	Systolic strain rate	0	0.222	-0.228	0.148	0.2055	No	0/4	ROBUST
	End-syst Pressure	0	<0.001	1.207	<0.001	<0.001	Yes	4/4	ROBUST
	Peak Systolic strain	0	0.016	-0.465	0.012	0.0165	Yes	4/4	ROBUST
	GWl	0	0.084	0.327	0.104	0.0900	No	0/4	ROBUST
EXERCISE N=31	Arterial Elastance	0	0.259	0.207	0.229	0.2440	No	0/4	ROBUST
	Systolic strain rate	0	<0.001	1.292	<0.001	<0.001	Yes	4/4	ROBUST
	End-syst Pressure	1	<0.001	0.977	<0.001	<0.001	Yes	4/4	ROBUST
	Peak Systolic strain	0	<0.001	0.884	<0.001	0.0010	Yes	4/4	ROBUST
	GWl	1	<0.001	1.026	<0.001	<0.001	Yes	4/4	ROBUST

Concordance represents the proportion of methods showing statistical significance (out of 4: original test, winsorization, permutation, bootstrap CI). ROBUST = all methods agree; SENSITIVE = result depends on outlier treatment. Bold p-values indicate $p < 0.05$. Effect sizes are Cohen's d_z for normally distributed data and rank-biserial correlation for non-normally distributed data. Bootstrap CI≠0 indicates the 95% bootstrap confidence interval excludes zero. Permutation testing used 1,999 permutations; bootstrap used 1,999 resamples.

Abbreviations: GWl= global work index; End-Syst Pressure= End-Systolic Pressure

Supplementary Table S9 - Exploratory Analysis of Secondary Endpoints

EXPLORATORY ANALYSIS: This analysis was not pre-specified for multiple comparison correction. P-values are nominal and provided for descriptive purposes. Interpretation should focus on effect sizes and physiological patterns. Findings are hypothesis-generating and require confirmation in future studies.

Intervention	Category	Parameter	Baseline	Change [95% CI]	% Change	Effect Size [95% CI]	Magnitude
Handgrip	Loop Morphology	ED_fiber stress	0.05 ± 0.01	0.00 (-0.00 to 0.01)	+2.2%	-0.135 (-0.498 to 0.267)	Negligible
		Time to peak Strain	376.80 ± 27.03	-0.93 (-6.40 to 4.54)	-0.2%	0.008 (-0.381 to 0.395)	Negligible
	Myocardial Work	GCW	2014.87 ± 311.54	120.13 (32.04 to 208.23)	+6.0%	0.509 (0.124 to 0.886)	Medium
		GWW	99.43 ± 43.11	20.17 (-9.75 to 50.09)	+20.3%	0.178 (-0.225 to 0.530)	Negligible
		GWE	0.95 ± 0.02	-0.00 (-0.01 to 0.01)	-0.4%	-0.110 (-0.468 to 0.250)	Negligible
	Strain Rate	EDSR_global	0.68 ± 0.36	0.05 (-0.13 to 0.22)	+6.9%	0.092 (-0.307 to 0.464)	Negligible
	Hemodynamics	HR	64.77 ± 10.34	8.20 (5.19 to 11.21)	+12.7%	1.000 (1.000 to 1.000)	Large
		SBP	117.93 ± 9.24	10.03 (6.66 to 13.40)	+8.5%	1.112 (0.649 to 1.563)	Large
		DBP	71.47 ± 8.99	5.50 (1.80 to 9.20)	+7.7%	0.556 (0.166 to 0.937)	Medium
		Pressure_min	8.61 ± 0.67	0.73 (0.49 to 0.98)	+8.5%	1.112 (0.649 to 1.563)	Large
	Diastolic Timing	IVRT	100.23 ± 8.32	2.00 (-2.32 to 6.32)	+2.0%	0.236 (-0.167 to 0.572)	Small
		Filling Time	571.83 ± 149.25	-109.71 (-148.51 to -70.90)	-19.2%	-0.995 (-0.998 to -0.990)	Large
		Total diastolic time	672.07 ± 146.66	-107.71 (-147.09 to -68.32)	-16.0%	-0.991 (-0.996 to -0.979)	Large
		IVRT proportion	0.11 ± 0.02	0.02 (0.01 to 0.02)	+15.1%	0.941 (0.871 to 0.974)	Large
		Filling time proportion	0.59 ± 0.05	-0.05 (-0.07 to -0.03)	-8.7%	-0.995 (-0.998 to -0.990)	Large

Intervention	Category	Parameter	Baseline	Change [95% CI]	% Change	Effect Size [95% CI]	Magnitude
Passive Leg Raising	Loop Morphology	ED_fiber stress	0.05 ± 0.01	0.00 (-0.00 to 0.00)	+3.1%	0.028 (-0.364 to 0.412)	Negligible
		Time to peak Strain	376.80 ± 27.03	0.73 (-5.27 to 6.73)	+0.2%	0.046 (-0.313 to 0.403)	Negligible
	Myocardial Work	GCW	2014.87 ± 311.54	85.30 (-19.99 to 190.59)	+4.2%	0.303 (-0.066 to 0.666)	Small
		GWW	99.43 ± 43.11	17.03 (-3.08 to 37.14)	+17.1%	0.316 (-0.053 to 0.681)	Small
		GWE	0.95 ± 0.02	-0.01 (-0.02 to 0.00)	-0.6%	-0.229 (-0.590 to 0.136)	Small
	Strain Rate	EDSR_global	0.68 ± 0.36	-0.06 (-0.19 to 0.08)	-8.3%	-0.157 (-0.515 to 0.205)	Negligible
	Hemodynamics	HR	64.77 ± 10.34	-0.17 (-2.30 to 1.97)	-0.3%	-0.029 (-0.387 to 0.329)	Negligible
		SBP	117.93 ± 9.24	9.57 (6.61 to 12.53)	+8.1%	1.207 (0.728 to 1.674)	Large
		DBP	71.47 ± 8.99	9.13 (6.07 to 12.20)	+12.8%	1.113 (0.650 to 1.565)	Large
		Pressure_min	8.61 ± 0.67	0.70 (0.48 to 0.91)	+8.1%	1.207 (0.728 to 1.674)	Large
	Diastolic Timing	IVRT	100.23 ± 8.32	1.13 (-1.10 to 3.37)	+1.1%	0.191 (-0.213 to 0.539)	Negligible
		Filling Time	571.83 ± 149.25	2.24 (-27.86 to 32.35)	+0.4%	0.028 (-0.330 to 0.386)	Negligible
		Total diastolic time	672.07 ± 146.66	3.38 (-27.26 to 34.01)	+0.5%	0.041 (-0.317 to 0.399)	Negligible
		IVRT proportion	0.11 ± 0.02	0.00 (-0.00 to 0.00)	+0.8%	0.090 (-0.269 to 0.448)	Negligible
		Filling time proportion	0.59 ± 0.05	0.00 (-0.01 to 0.02)	+0.4%	0.050 (-0.309 to 0.407)	Negligible
Exercise	Loop Morphology	ED_fiber stress	0.04 ± 0.01	0.00 (-0.00 to 0.00)	+2.2%	0.152 (-0.203 to 0.505)	Negligible
		Time to peak Strain	379.35 ± 32.62	-62.13 (-78.01 to -46.25)	-16.4%	-1.435 (-1.933 to -0.924)	Large
	Myocardial Work	GCW	1780.45 ± 345.72	567.94 (394.78 to 741.09)	+31.9%	1.203 (0.733 to 1.662)	Large
		GWW	179.26 ± 107.17	76.74 (28.51 to 124.98)	+42.8%	0.591 (0.269 to 0.794)	Medium

Intervention	Category	Parameter	Baseline	Change [95% CI]	% Change	Effect Size [95% CI]	Magnitude
	Myocardial Work	GWE	0.90 ± 0.04	-0.00 (-0.02 to 0.01)	-0.5%	-0.101 (-0.453 to 0.253)	Negligible
	Strain Rate	EDSR_global	0.41 ± 0.20	0.17 (0.06 to 0.28)	+40.9%	0.562 (0.179 to 0.938)	Medium
	Hemodynamics	HR	73.13 ± 11.64	16.97 (13.19 to 20.74)	+23.2%	1.649 (1.098 to 2.187)	Large
		SBP	121.16 ± 14.50	25.94 (18.37 to 33.50)	+21.4%	0.977 (0.949 to 0.990)	Large
		DBP	71.42 ± 8.01	-1.19 (-4.25 to 1.86)	-1.7%	-0.143 (-0.496 to 0.212)	Negligible
		Pressure_min	8.84 ± 1.06	1.89 (1.34 to 2.45)	+21.4%	0.986 (0.969 to 0.994)	Large
		IVRT	101.23 ± 4.49	-3.26 (-6.65 to 0.13)	-3.2%	-0.458 (-0.715 to -0.091)	Small
	Diastolic Timing	Filling Time	463.60 ± 141.09	-102.00 (-141.13 to -62.88)	-22.0%	-0.923 (-0.965 to -0.835)	Large
		Total diastolic time	564.83 ± 141.65	-105.26 (-145.13 to -65.39)	-18.6%	-0.923 (-0.965 to -0.835)	Large
		IVRT proportion	0.12 ± 0.02	0.02 (0.02 to 0.03)	+19.3%	1.315 (0.826 to 1.792)	Large
		Filling time proportion	0.54 ± 0.06	-0.01 (-0.03 to 0.01)	-1.8%	-0.193 (-0.546 to 0.164)	Negligible

† P-values are NOMINAL (unadjusted for multiple comparisons) and provided for descriptive purposes only. ‡ Effect sizes: Cohen's d for normally distributed endpoints, rank-biserial correlation for non-normal endpoints. Magnitude categories: Negligible ($|dz| < 0.2$), Small ($0.2 \leq |dz| < 0.5$), Medium ($0.5 \leq |dz| < 0.8$), Large ($|dz| \geq 0.8$). Baseline values shown as mean ± SD. All analyses used paired comparisons (paired t-test or Wilcoxon signed-rank test). Color coding indicates effect size magnitude for rapid visual pattern identification. Data are organized by intervention (Exercise, Handgrip, Passive Leg Raising) then by physiological category within each intervention.

These exploratory analyses were not pre-specified in the primary analysis plan and should be interpreted as hypothesis-generating observations requiring prospective validation.

Abbreviations: ED_strain, end-diastolic strain (preload marker); Time to peak Strain, time to peak strain from aortic valve closure (ms); GCW, Global Constructive Work (mmHg·%); GWW, Global Wasted Work (mmHg·%); GWE, Global Work Efficiency (%); EDSR_global, Early Diastolic Strain Rate (s^{-1}); HR, Heart Rate (bpm); SBP, Systolic Blood Pressure (mmHg); DBP, Diastolic Blood Pressure (mmHg); Pressure_min, Minimum Pressure (mmHg); IVRT, Isovolumetric Relaxation Time (ms); Filling Time, Ventricular Filling Duration (ms); Total diastolic time, Total Diastolic Time (ms); IVRT proportion, IVRT as Proportion of Diastole (%); Filling time proportion, Filling Time as Proportion of Diastole (%).