Supplemental Material

Table S1. Participant characteristics.

Variable		
Age (years)	23 ± 1	
Height (cm)	175 ± 3	
Body mass (kg)	71 ± 2	
$VO_{2\ max}$ (ml O_2 min^{-1})	3263 ± 218	
$VO_{2\ max}$ (ml O_2 min^{-1} kg^{-1})	48 ± 2	
Systolic blood pressure (mmHg)	112 ± 3	
Diastolic blood pressure (mmHg)	67 ± 2	
Hemoglobin (mmol L^{-1})	8.6 ± 0.2	
Thrombocytes (10^9 L^{-1})	277 ± 16	
Glycated hemoglobin (mmol L^{-1})	5.3 ± 0.1	
Total cholesterol (mmol L^{-1})	4.2 ± 0.4page s	
High-density lipoprotein (mmol L^{-1})	1.4 ± 0.2	
Low-density lipoprotein (mmol L^{-1})	2.6 ± 0.3	
Triglycerides (mmol L^{-1})	1.0 ± 0.1	
Female sex hormones	Ischemic preconditioning (n=5)	Hand-grip exercise (n=4)
Estrogen (nmol L^{-1})	0.17 ± 0.03	0.22 ± 0.13
Progesterone (nmol L^{-1})	0.60 ± 0.00	0.63 ± 0.03

$VO_{2\ max}$, maximal oxygen uptake. Data are presented as mean ± SEM (n=12).

Table S2. Baseline hemodynamics and venous plasma 6-keto prostaglandin $F_{1\alpha}$ and norepinephrine levels.

Leg	Ischemic preconditioning (n=12)			ANOVA P values	Hand-grip exercise (n=10)			ANOVA P values
Variable	*Pre*	*Post+5*	*Post+90*	*Time*	*Pre*	*Post+5*	*Post+90*	*Time*
Leg blood flow (ml min^{-1})	276 ± 42	306 ± 34	349 ± 47	P=0.8704	330 ± 43	321 ± 36	351 ± 40	P=1.0
Leg vascular conductance (ml min^{-1} $mmHg^{-1}$)	3.6 ± 0.5	4.0 ± 0.4	4.4 ± 0.6	P=1.0	4.4 ± 0.5	4.1 ± 0.4	4.6 ± 0.5	P=1.0
Mean arterial pressure (mmHg)	81 ± 2	80 ± 2	81 ± 2	P=1.0	79 ± 2	80 ± 2	79 ± 2	P=0.9532
Venous pressure (mmHg)	3 ± 1	2 ± 0 *	2 ± 0 *	P<0.0001	4 ± 1	3 ± 0	3 ± 1	P=1.0
Heart rate (bpm)	63 ± 3	63 ± 3	61 ± 2	P=1.0	63 ± 3	63 ± 3	62 ± 4	P=1.0
Venous norepinephrine (nmol l^{-1})	0.9 ± 0.1	1.1 ± 0.2	1.0 ± 0.1	P=1.0	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	P=1.0
Venous 6-keto $PGF_{1\alpha}$ (pg ml^{-1})	61 ± 4	59 ± 7	-	P=1.0	75 ± 4	72 ± 6	-	P=1.0
Forearm	Ischemic preconditioning (n=12)			ANOVA P values	Hand-grip exercise (n=10)			ANOVA P values
Variable	*Pre*	*Post+5*	*Post+90*	*Time*	*Pre*	*Post+5*	*Post+90*	*Time*
Forearm blood flow (ml min^{-1})	94 ± 18	60 ± 8	81 ± 12	P=0.0762	79 ± 15	146 ± 17 *	92 ± 13 #	P<0.0001
Forearm vascular conductance (ml min^{-1} $mmHg^{-1}$)	1.3 ± 0.3	0.8 ± 0.1	1.0 ± 0.2	P=0.0947	1.0 ± 0.2	1.9 ± 0.2 *	1.2 ± 0.2 #	P<0.0001

Mean arterial pressure (mmHg)	80 ± 2	79 ± 2	80 ± 2	P=0.6088	78 ± 2	78 ± 2	78 ± 2	P=1.0
Venous pressure (mmHg)	3 ± 0	2 ± 1	2 ± 0	P=0.2116	4 ± 1	3 ± 0	2 ± 1 *	P=0.0030
Venous norepinephrine (nmol l-1)	1.0 ± 0.1	1.4 ± 0.1 *	1.3 ± 0.1 *	P=0.0040	1.0 ± 0.1	1.1 ± 0.2	1.0 ± 0.1	P=1.0
Venous 6-keto PGF1α (pg ml-1)	56 ± 5	76 ± 10 *	-	P=0.0084	77 ± 8	60 ± 5	-	P=0.2277

Data are presented as mean ± SEM. * denotes post-hoc significantly different from Pre within intervention; # denotes post-hoc significantly different from Post+5 within intervention.

Table S3. Absolute changes in hemodynamics with intra-arterial infusion of acetylcholine.

Leg	Ischemic preconditioning (n=12)			ANOVA P values		Hand-grip exercise (n=10)			ANOVA P values	
Variable	*Pre*	*Post+5*	*Post+90*	*Time*	*Time x Dose*	*Pre*	*Post+5*	*Post+90*	*Time*	*Time x Dose*
Δ LBF (Ach; 10 μg min^{-1} L^{-1})	914 ± 121	1206 ± 132 *	1152 ± 185 *	P=0.0163	P=1.0	1259 ± 184	1118 ± 199	1216 ± 200	P=1.0	P=1.0
Δ LBF (Ach; 25 μg min^{-1} L^{-1})	1214 ± 168	1709 ± 178 *	1513 ± 201 *			1495 ± 230	1440 ± 253	1551 ± 243		
Δ MAP (Ach; 10 μg min^{-1} L^{-1})	-1.9 ± 0.5	-3.7 ± 0.8 *	-3.8 ± 1.0 *	P=0.0027	P=1.0	-3.6 ± 0.9	-4.4 ± 1.1	-3.5 ± 0.9	P=0.6056	P=1.0
Δ MAP (Ach; 25 μg min^{-1} L^{-1})	-2.0 ± 0.6	-3.6 ± 0.7 *	-5.0 ± 1.2 *			-2.2 ± 1.0	-4.3 ± 1.4	-2.8 ± 1.0		
Δ VP (Ach; 10 μg min^{-1} L^{-1})	-0.2 ± 0.4	0.1 ± 0.1	0.1 ± 0.3	P=0.2930	P=1.0	0.1 ± 0.2	0.0 ± 0.3	-0.2 ± 0.2	P=1.0	P=1.0
Δ VP (Ach; 25 μg min^{-1} L^{-1})	-0.4 ± 0.4	0.4 ± 0.3	0.0 ± 0.3			-0.1 ± 0.3	-0.3 ± 0.4	-0.2 ± 0.3		
Forearm	Ischemic preconditioning (n=12)			ANOVA P values		Hand-grip exercise (n=10)			ANOVA P values	
Variable	*Pre*	*Post+5*	*Post+90*	*Time*	*Time x Dose*	*Pre*	*Post+5*	*Post+90*	*Time*	*Time x Dose*
Δ FBF (Ach; 10 μg min^{-1} L^{-1})	77 ± 14	68 ± 12	96 ± 13	P=0.6141	P=1.0	46 ± 12	118 ± 19 *	91 ± 19 *	P<0.0001	P=1.0
Δ FBF (Ach; 25 μg min^{-1} L^{-1})	99 ± 19	127 ± 18	134 ± 24			98 ± 14	185 ± 19 *	157 ± 27 *		
Δ MAP (Ach; 10 μg min^{-1} L^{-1})	-2.8 ± 0.7	-3.4 ± 0.9	-4.3 ± 0.9	P=0.0853	P=1.0	-3.7 ± 0.6	-4.6 ± 0.8	-3.5 ± 0.9	P=0.7396	P=1.0
Δ MAP (Ach; 25 μg min^{-1} L^{-1})	-3.7 ± 0.5	-4.1 ± 0.9	-5.9 ± 0.9			-3.3 ± 0.8	-5.2 ± 1.1	-3.7 ± 1.1		

Δ VP (Ach; 10 µg min-1 L-1)	0.5 ± 0.3	0.2 ± 0.3	0.1 ± 0.4			0.2 ± 0.2	0.6 ± 0.2 *	0.5 ± 0.3		
Δ VP (Ach; 25 µg min-1 L-1)	0.5 ± 0.3	0.7 ± 0.3	0.3 ± 0.4			0.4 ± 0.3	1.0 ± 0.2 *	1.0 ± 0.4		

LBF, leg blood flow; FBF, forearm blood flow; MAP, mean arterial pressure; VP, venous pressure; Ach, acetylcholine. Data are presented as mean ± SEM. * denotes post-hoc overall significantly different from Pre within *intervention*.

Table S4. Absolute changes in hemodynamics with intra-arterial infusion of sodium nitroprusside.

Leg	Ischemic preconditioning (n=12)			ANOVA P values		Hand-grip exercise (n=10)			ANOVA P values	
Variable	*Pre*	*Post+5*	*Post+90*	*Time*	*Time x Dose*	*Pre*	*Post+5*	*Post+90*	*Time*	*Time x Dose*
Baseline LVC (ml min^{-1} $mmHg^{-1}$)	3.2 ± 0.4	3.6 ± 0.4	4.5 ± 0.5 *#	P<0.0001	-	4.3 ± 0.5	3.3 ± 0.4	3.9 ± 0.4	P=0.2958	-
Δ LVC (SNP; 3 µg min^{-1} L^{-1})	9.6 ± 1.1	10.6 ± 1.3	9.3 ± 1.3	P=0.4828	-	11.9 ± 1.0	12.1 ± 1.4	12.3 ± 1.9	P=1.0	-
Baseline LBF (ml min^{-1})	252 ± 28	285 ± 36	362 ± 38 *#	P<0.0001	-	321 ± 38	248 ± 27	301 ± 36	P=0.3524	-
Δ LBF (SNP; 3 µg min^{-1} L^{-1})	651 ± 77	714 ± 83	626 ± 85	P=0.8164	-	740 ± 60	810 ± 98	814 ± 124	P=1.0	-
Baseline MAP (mmHg)	81.7 ± 2.1	80.2 ± 1.9	81.3 ± 2.0	P=0.9896	-	78.7 ± 3.2	78.7 ± 2.8	79.9 ± 2.1	P=1.0	-
Δ MAP (SNP; 3 µg min^{-1} L^{-1})	-7.8 ± 0.7	-7.8 ± 0.8	-7.5 ± 0.9	P=1.0	-	-9.0 ± 1.3	-7.3 ± 0.6	-7.4 ± 1.3	P=1.0	-
Baseline VP (mmHg)	2.8 ± 0.4	1.5 ± 0.4 *	1.6 ± 0.5 *	P<0.0001	-	3.9 ± 0.7	2.4 ± 0.4 *	2.7 ± 0.5 *	P=0.0035	-
Δ VP (SNP; 3 µg min^{-1} L^{-1})	-0.3 ± 0.3	0.0 ± 0.3	0.1 ± 0.3	P=1.0	-	-0.5 ± 0.5	-0.2 ± 0.2	-0.1 ± 0.2	P=1.0	-
Forearm	IPC (n=12)			ANOVA P values		Hand-grip exercise (n=10)			ANOVA P values	
Variable	*Pre*	*Post+5*	*Post+90*	*Time*	*Time x Dose*	*Pre*	*Post+5*	*Post+90*	*Time*	*Time x Dose*
Baseline FVC (ml min^{-1} $mmHg^{-1}$)	1.3 ± 0.2	1.0 ± 0.1	1.0 ± 0.1	P=0.7328	-	1.3 ± 0.3	1.2 ± 0.1	1.1 ± 0.2	P=1.0	-

Δ FVC (SNP; 3 µg min-1 kg-	1.7 ± 0.3	1.7 ± 0.3	1.8 ± 0.3	P=1.0	-	1.6 ± 0.3	2.0 ± 0.2	1.6 ± 0.1	P=1.0	-
Baseline FBF (ml min-1)	96 ± 17	77 ± 10	82 ± 9	P=0.7612	-	94 ± 20	90 ± 14	87 ± 16	P=1.0	-
Δ FBF (SNP; 3 µg min-1 L-	102 ± 18	107 ± 19	116 ± 18	P=1.0	-	90 ± 16	120 ± 16	99 ± 7	P=0.8980	-
Baseline MAP (mmHg)	80.5 ± 2.1	79.5 ± 1.8	80.5 ± 2.0	P=1.0	-	78.0 ± 3.2	78.0 ± 2.7	78.8 ± 1.9	P=1.0	-
Δ MAP (SNP; 3 µg min-1 L-	-9.6 ± 0.7	-9.5 ± 0.8	-9.4 ± 1.0	P=1.0	-	-10.7 ± 1.2	-8.9 ± 0.6	-8.5 ± 1.4	P=1.0	-
Baseline VP (mmHg)	2.9 ± 0.5	2.0 ± 0.6 *	1.5 ± 0.5 *	P=0.0024	-	3.6 ± 0.6	2.5 ± 0.6 *	2.2 ± 0.6 *	P<0.0001	-
Δ VP (SNP; 3 µg min-1 L-1)	-0.6 ± 0.2	0.1 ± 0.2 *	0.5 ± 0.1 *	P<0.0001	-	-0.5 ± 0.3	0.0 ± 0.2	0.0 ± 0.3	P=0.1502	-

LVC, leg vascular conductance; FVC, forearm vascular conductance; LBF, leg blood flow; FBF, forearm blood flow; MAP, mean arterial pressure; VP, venous pressure; SNP, sodium nitroprusside. Data are presented as mean ± SEM. * denotes post-hoc significantly different from Pre within *intervention*; # denotes post-hoc significantly different from Post+5 within *intervention*.

Table S5. Absolute changes in hemodynamics with intra-arterial infusion of epoprostenol.

Leg	Ischemic preconditioning (n=12)			ANOVA P values		Hand-grip exercise (n=10)			ANOVA P values	
Variable	*Pre*	*Post+5*	*Post+90*	*Time*	*Time x Dose*	*Pre*	*Post+5*	*Post+90*	*Time*	*Time x Dose*
Baseline LVC (ml min^{-1} $mmHg^{-1}$)	3.2 ± 0.4	3.9 ± 0.5	4.9 ± 0.8 *	P=0.0136	-	4.4 ± 0.5	3.9 ± 0.5	4.3 ± 0.3	P=1.0	-
Baseline LBF (ml min^{-1})	247 ± 32	310 ± 40	400 ± 73 *	P=0.0155	-	326 ± 38	290 ± 36	325 ± 29	P=1.0	-
Δ LBF (Epo; 25 µg min^{-1} L^{-1})	243 ± 39	255 ± 50	187 ± 47	P=1.0	P=1.0	286 ± 44	268 ± 58	216 ± 42	P=1.0	P=1.0
Δ LBF (Epo; 50 µg min^{-1} L^{-1})	352 ± 50	339 ± 53	334 ± 68			389 ± 45	416 ± 60	365 ± 61		
Baseline MAP (mmHg)	81.3 ± 2.1	81.2 ± 1.8	82.1 ± 1.7	P=1.0	-	78.2 ± 2.5	77.9 ± 2.3	78.9 ± 2.0	P=1.0	-
Δ MAP (Epo; 25 µg min^{-1} L^{-1})	-2.3 ± 0.9	-4.2 ± 0.9	-3.1 ± 0.7	P=0.3572	P=1.0	-1.6 ± 0.9	0.3 ± 1.3	-2.0 ± 0.7	P=0.5364	P=1.0
Δ MAP (Epo; 50 µg min^{-1} L^{-1})	-4.5 ± 1.1	-5.6 ± 0.9	-4.1 ± 0.9			-3.6 ± 1.2	-2.5 ± 1.4	-2.5 ± 1.0		
Baseline VP (mmHg)	3.4 ± 0.4	2.1 ± 0.4 *	1.8 ± 0.4 *	P<0.0001	-	4.4 ± 0.8	3.0 ± 0.5	3.2 ± 0.7	P=0.1879	-
Δ VP (Epo; 25 µg min^{-1} L^{-1})	-0.4 ± 0.2	-0.1 ± 0.1	0.0 ± 0.2	P=0.1600	P=1.0	-0.2 ± 0.3	-0.4 ± 0.2 *	0.0 ± 0.2 #	P=0.0347	P=1.0
Δ VP (Epo; 50 µg min^{-1} L^{-1})	-0.2 ± 0.2	0.0 ± 0.2	0.2 ± 0.2			0.1 ± 0.3	-0.5 ± 0.2 *	0.0 ± 0.2 #		
Forearm	IPC (n=12)			ANOVA P values		Hand-grip exercise (n=10)			ANOVA P values	
Variable	*Pre*	*Post+5*	*Post+90*	*Time*	*Time x Dose*	*Pre*	*Post+5*	*Post+90*	*Time*	*Time x Dose*

Baseline FVC (ml min^{-1} $mmHg^{-1}$)	1.1 ± 0.2	1.0 ± 0.1	1.0 ± 0.1	P=1.0	-	1.2 ± 0.2	1.2 ± 0.2	0.9 ± 0.2	P=1.0	-
Baseline FBF (ml min^{-1})	83 ± 14	78 ± 11	79 ± 9	P=1.0	-	88 ± 16	91 ± 15	70 ± 12	P=1.0	-
Δ FBF (Epo; 25 µg min^{-1} L^{-1})	70 ± 10	72 ± 6	58 ± 8	P=0.5784	P=1.0	73 ± 14	84 ± 10	78 ± 13	P=1.0	P=1.0
Δ FBF (Epo; 50 µg min^{-1} L^{-1})	106 ± 12	103 ± 9	96 ± 9			109 ± 16	116 ± 16	113 ± 13		
Baseline MAP (mmHg)	80.5 ± 2.1	80.5 ± 1.8	81.6 ± 1.6	P=1.0	-	77.6 ± 2.4	77.3 ± 2.2	78.6 ± 1.9	P=1.0	-
Δ MAP (Epo; 25 µg min^{-1} L^{-1})	-4.0 ± 1.1	-6.0 ± 0.9	-4.6 ± 0.8	P=0.1672	P=1.0	-3.2 ± 0.9	-1.3 ± 1.4	-3.6 ± 0.7	P=0.7300	P=1.0
Δ MAP (Epo; 50 µg min^{-1} L^{-1})	-7.4 ± 1.1	-8.7 ± 0.9	-6.8 ± 0.9			-6.4 ± 0.9	-5.2 ± 1.5	-5.2 ± 1.1		
Baseline VP (mmHg)	3.3 ± 0.4	2.2 ± 0.5	2.0 ± 0.6	P=0.1100	-	3.1 ± 0.6	2.7 ± 0.6	2.2 ± 0.7	P=0.0757	-
Δ VP (Epo; 25 µg min^{-1} L^{-1})	0.0 ± 0.5	0.3 ± 0.2	0.1 ± 0.2	P=0.8820	P=1.0	0.6 ± 0.3	0.3 ± 0.1	0.4 ± 0.3	P=0.9056	P=1.0
Δ VP (Epo; 50 µg min^{-1} L^{-1})	0.0 ± 0.5	0.6 ± 0.2	0.3 ± 0.2			0.7 ± 0.4	0.3 ± 0.3	0.8 ± 0.4		

LVC, leg vascular conductance; FVC, forearm vascular conductance; LBF, leg blood flow; FBF, forearm blood flow; MAP, mean arterial pressure; VP, venous pressure; Epo, epoprostenol. Data are presented as mean ± SEM. * denotes post-hoc overall significantly different from Pre within *intervention*; # denotes post-hoc overall significantly different from Post+5 within *intervention*.