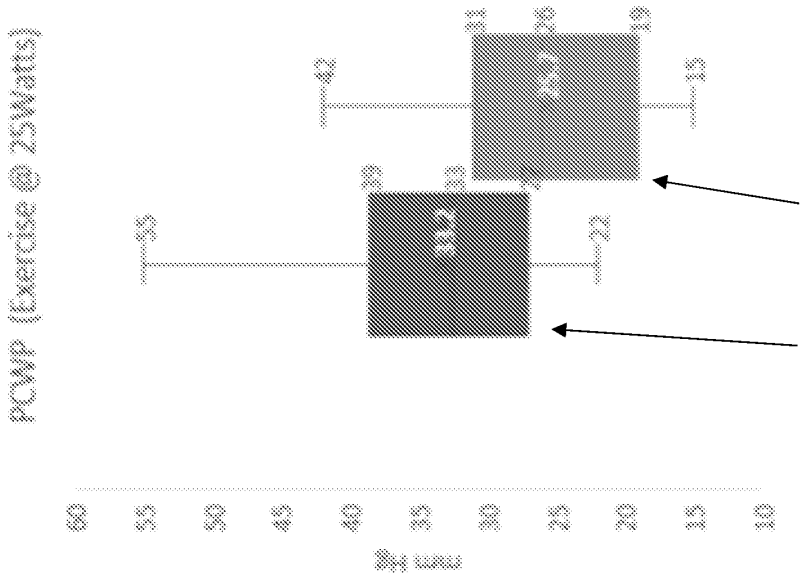
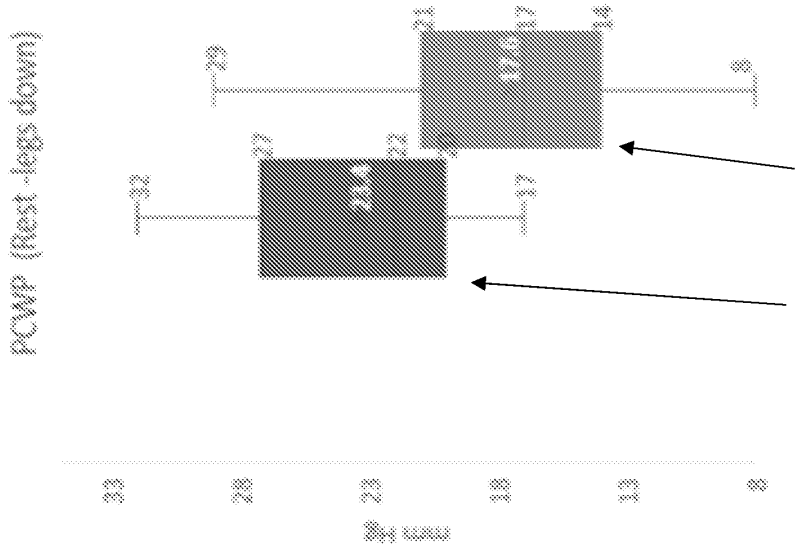


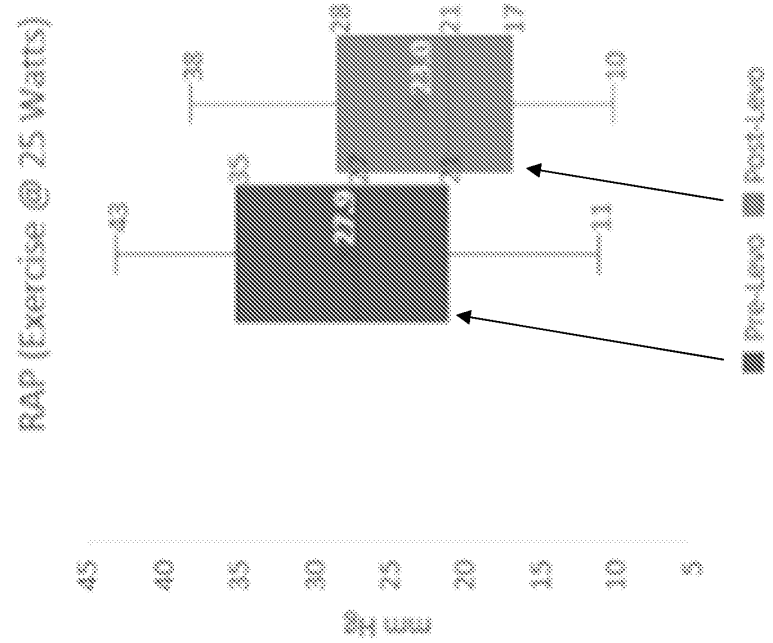
P<0.0000000001

Figure 1B



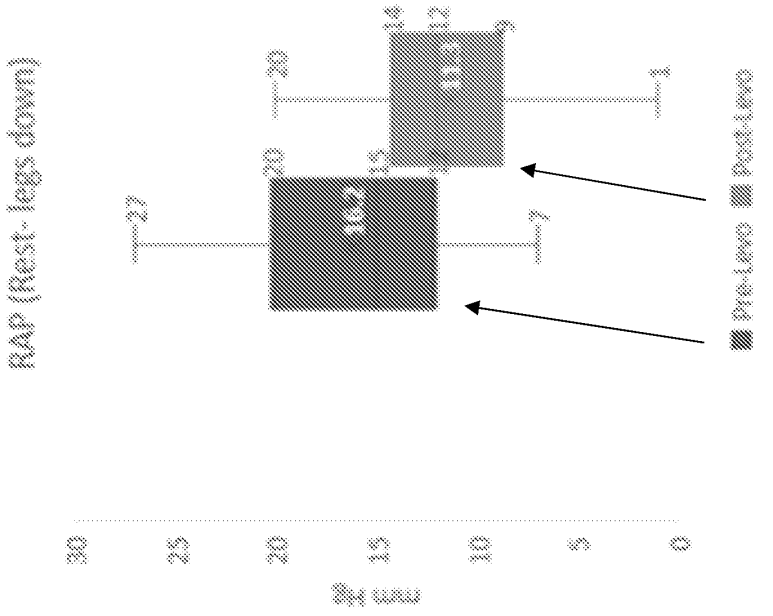
P<0.00001

Figure 1A



P<0.0001

Figure 2B



P<0.00001

Figure 2A

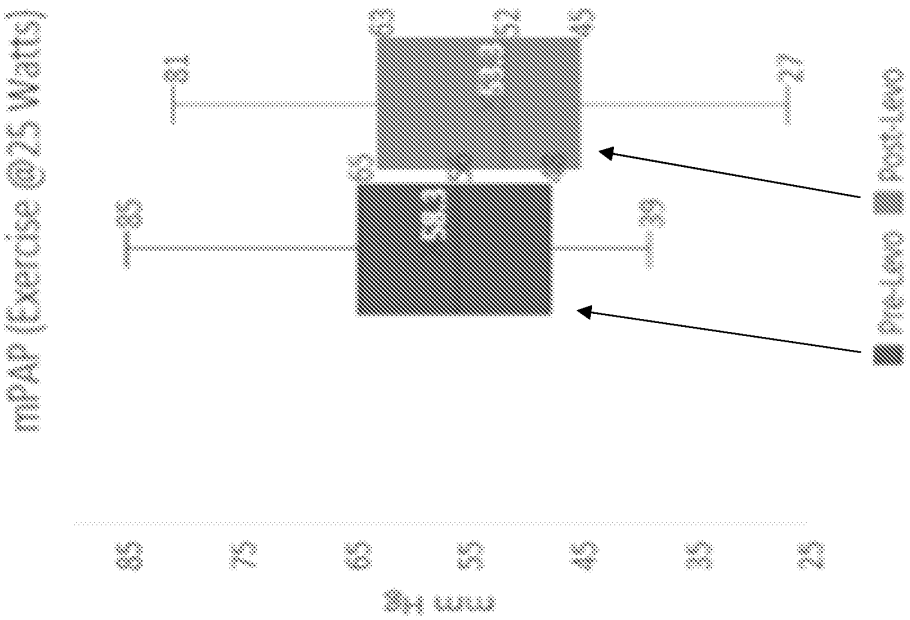


Figure 3B

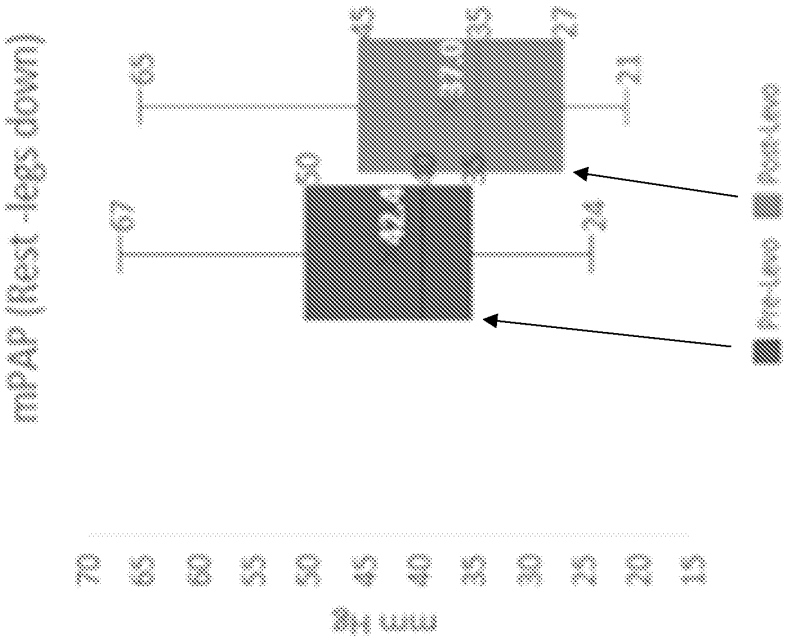
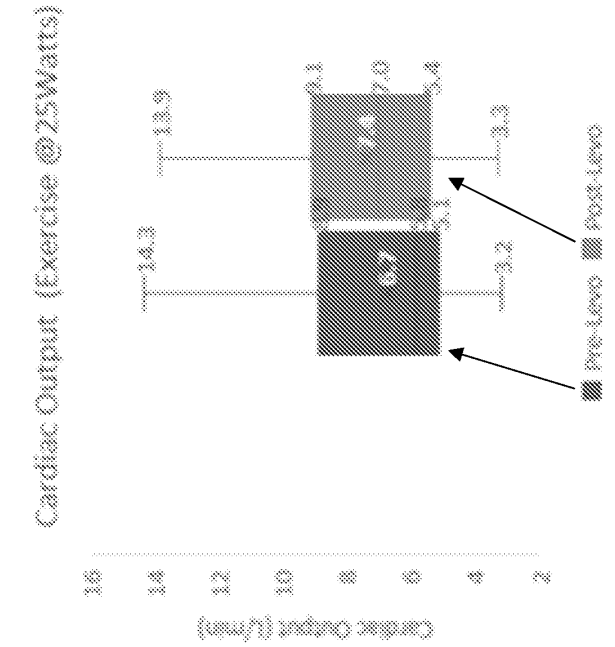
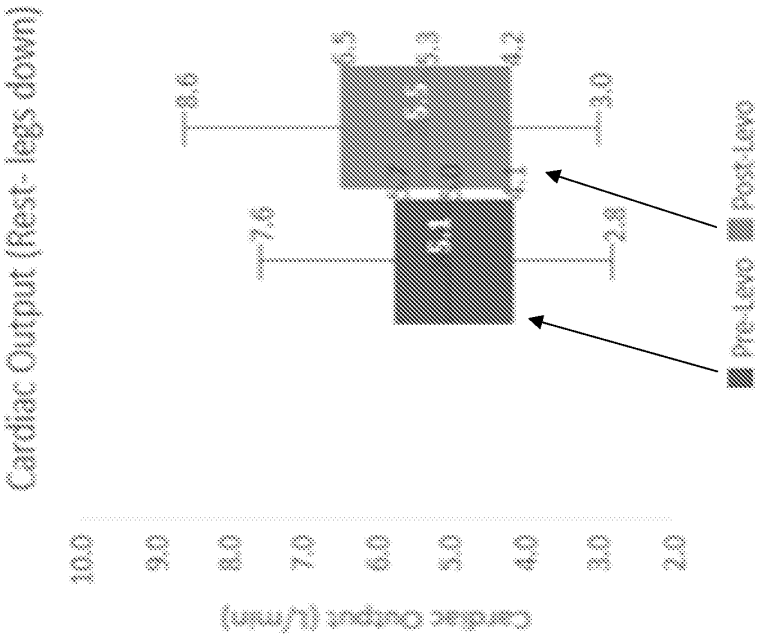


Figure 3A



P<0.01

Figure 4B



P<0.05

Figure 4A

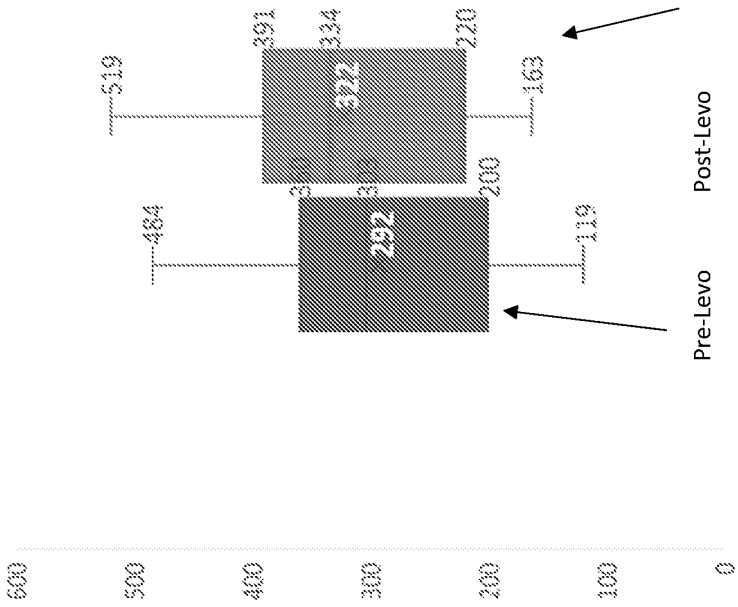

391
334
220
519
322
163
Post-Levo
200
484
292
119
Pre-Levo
600
500
400
300
200
100
0

Figure 5

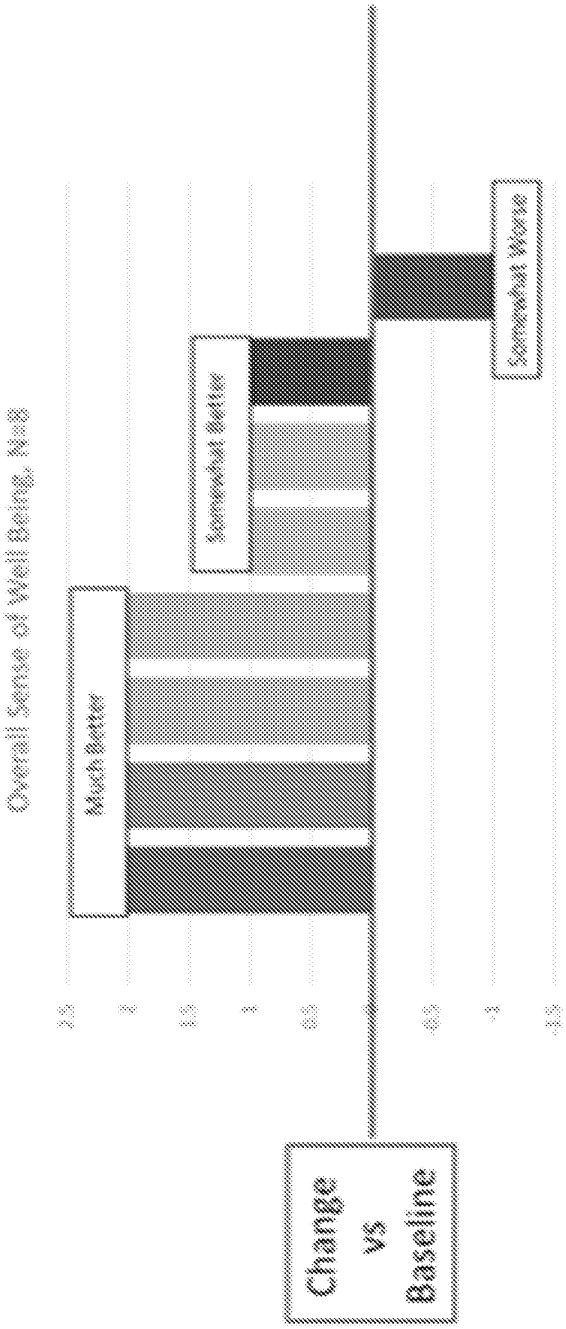

Overall Sense of Well Being, N=8
Much Better
Somewhat Better
Somewhat Worse
2.5
2
1.5
1
0.5
-0.5
-1
-1.5
Change vs Baseline

Figure 6

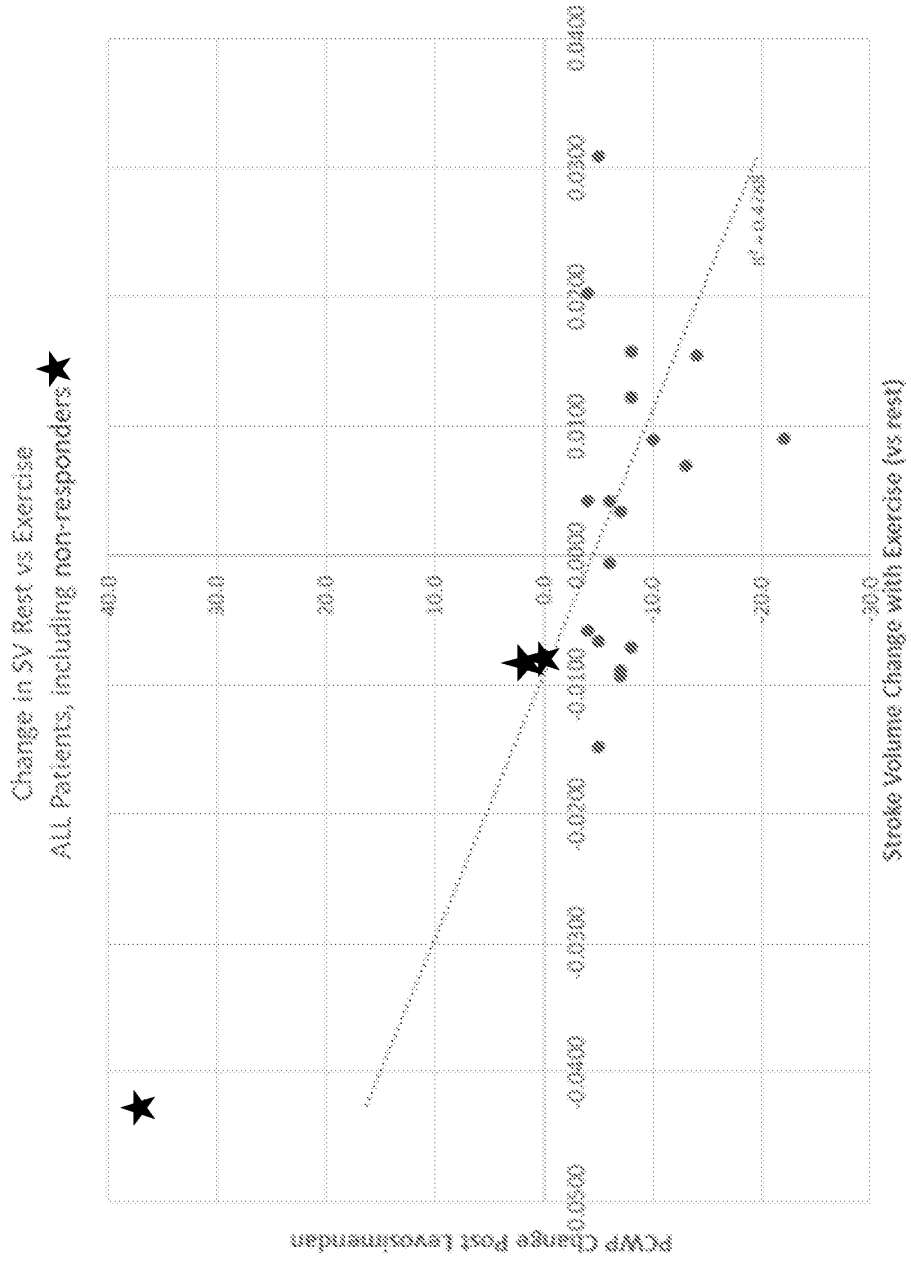

Change in SV Rest vs Exercise
ALL Patients, including non-responders
Stroke Volume Change with Exercise (vs rest)
PCWP Change Post Levosimendan
40.0
30.0
20.0
10.0
0.0
-10.0
-20.0
-30.0
0.0400
0.0300
0.0200
0.0100
0.0000
-0.0100
-0.0200
-0.0300
-0.0400
-0.0500
R² = 0.4281

Figure 7

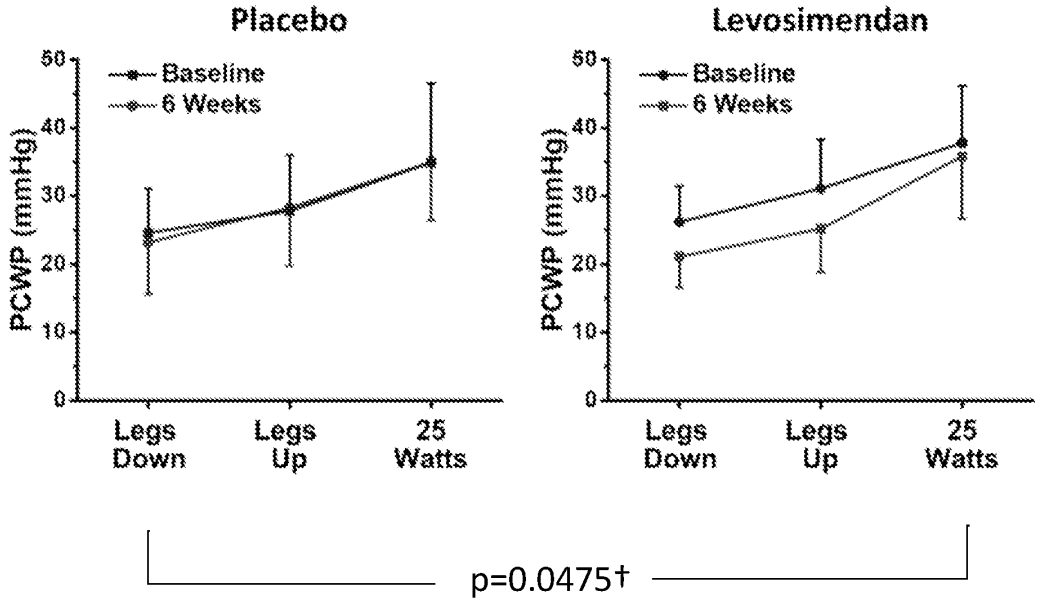

Placebo
Levosimendan
Baseline
6 Weeks
PCWP (mmHg)
0
10
20
30
40
50
Legs Down
Legs Up
25 Watts
p=0.0475†

Figure 8

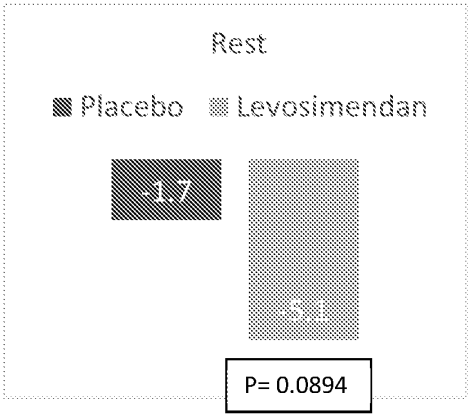


Figure 9A

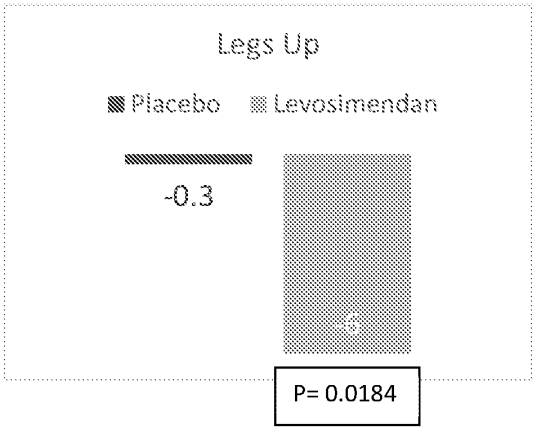


Figure 9B

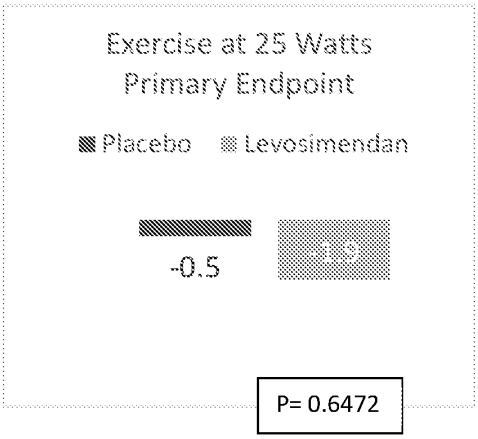


Figure 9C

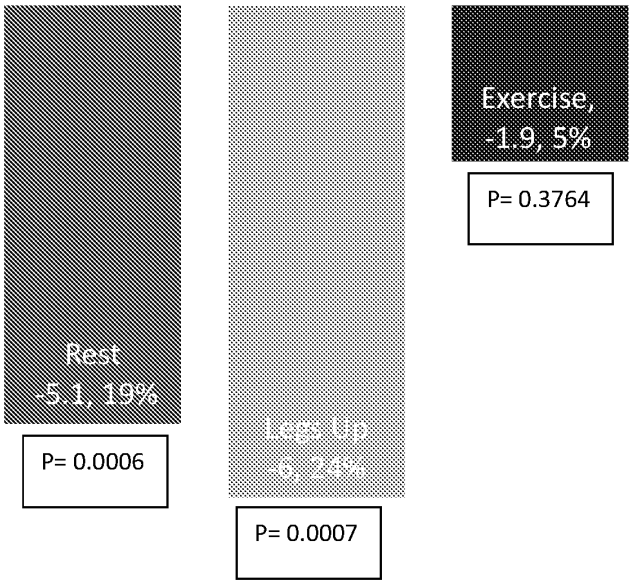


Figure 10

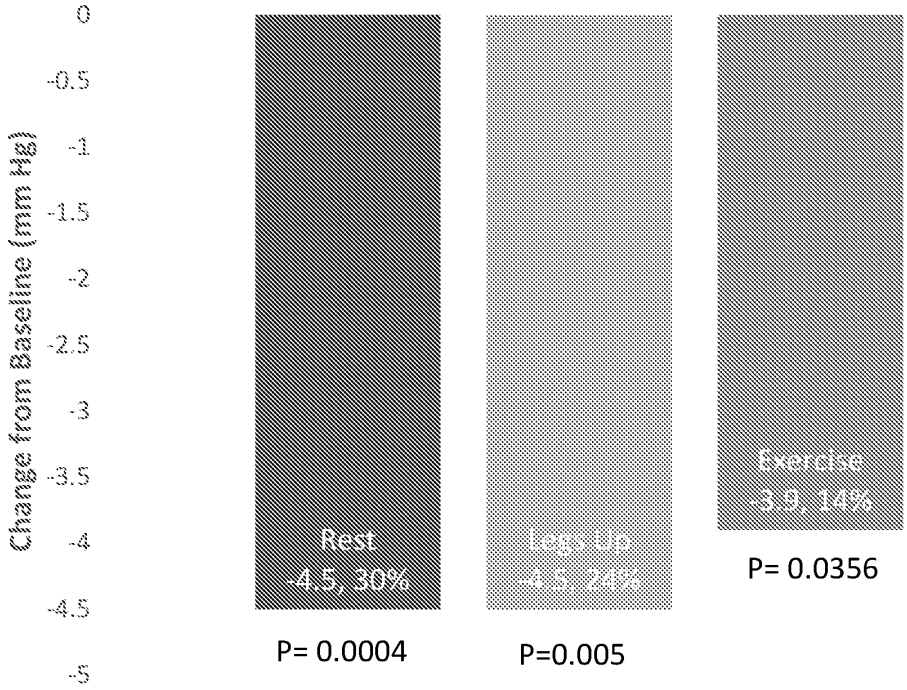

Change from Baseline (mm Hg)
0
-0.5
-1
-1.5
-2
-2.5
-3
-3.5
-4
-4.5
-5
Rest
-4.5, 30%
Legs Up
-4.5, 24%
Exercise
-3.9, 14%
P= 0.0004
P=0.005
P= 0.0356

Figure 11

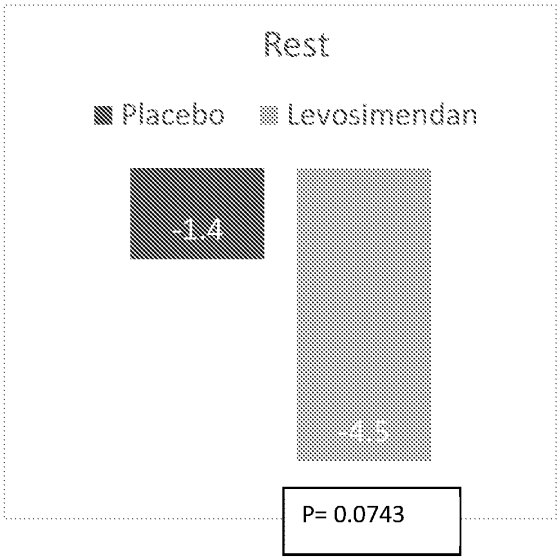


Figure 12A

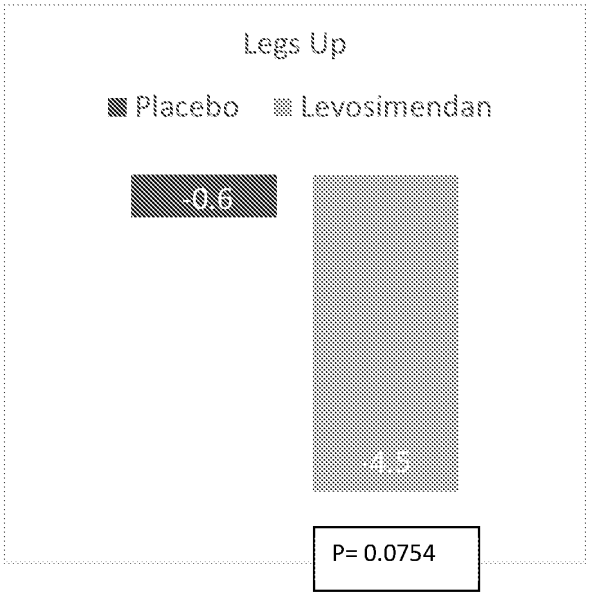


Figure 12B

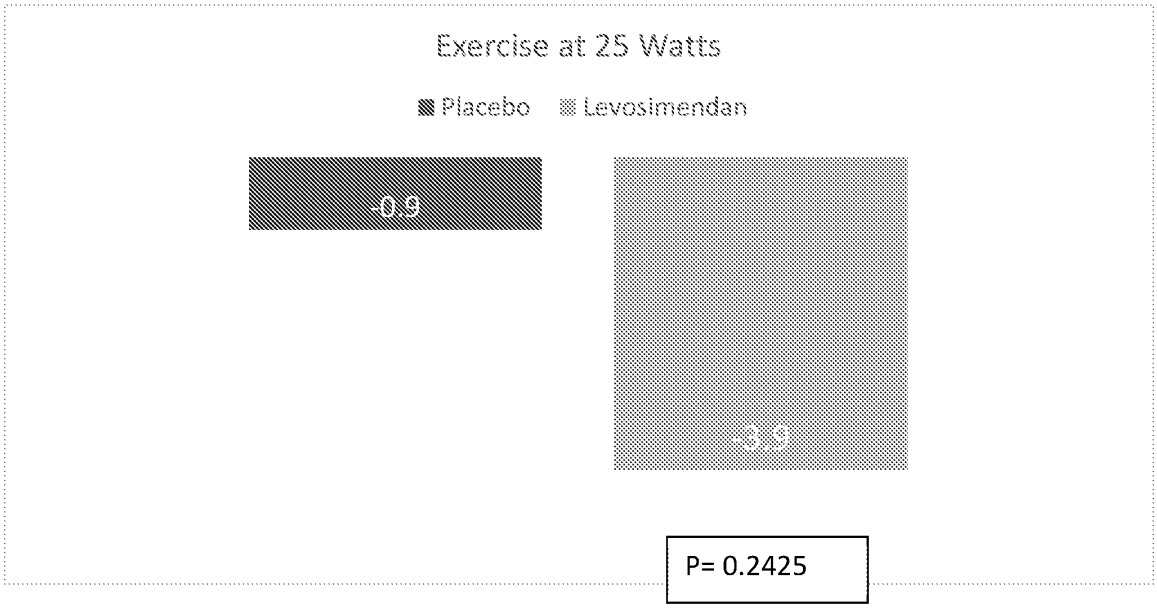


Figure 12C

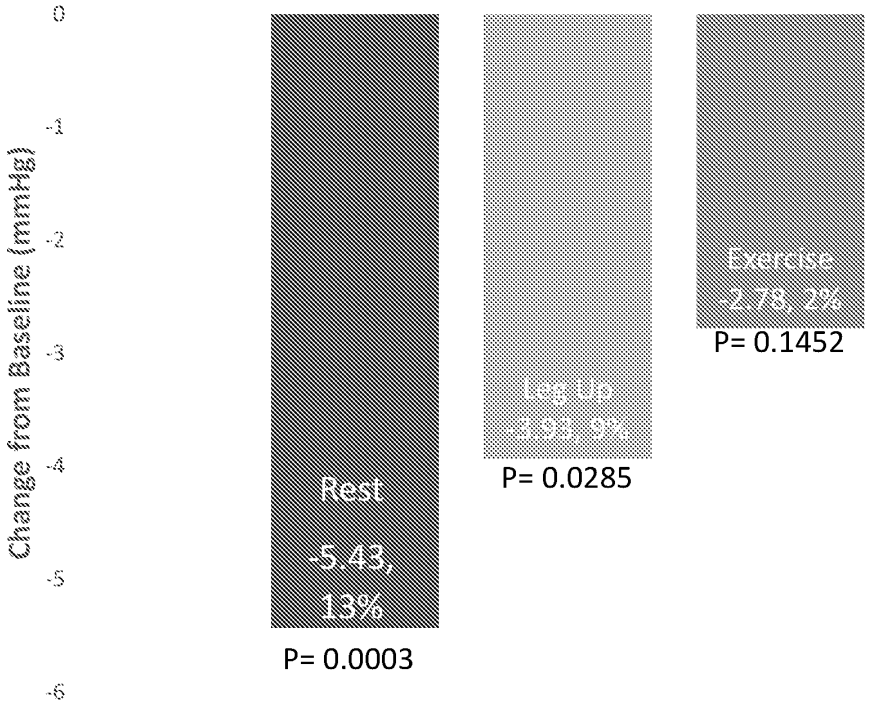

Change from Baseline (mmHg)
0
-1
-2
-3
-4
-5
-6
Rest
-5.43,
13%
P= 0.0003
Leg Up
-3.93, 9%
P= 0.0285
Exercise
-2.78, 2%
P= 0.1452

Figure 13

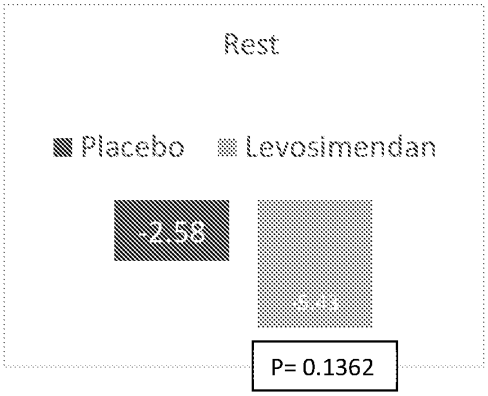


Figure 14A

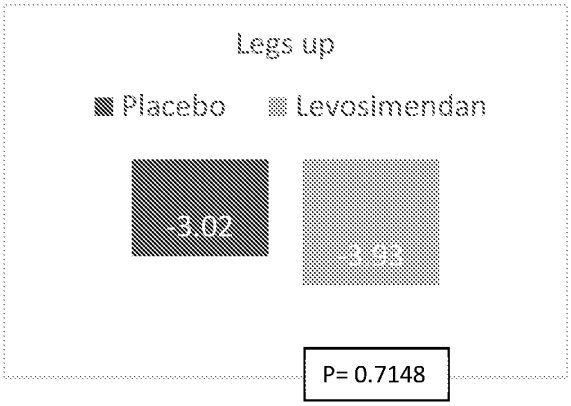


Figure 14B

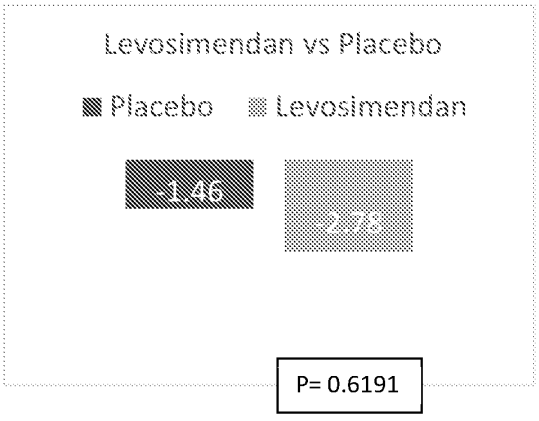


Figure 14C

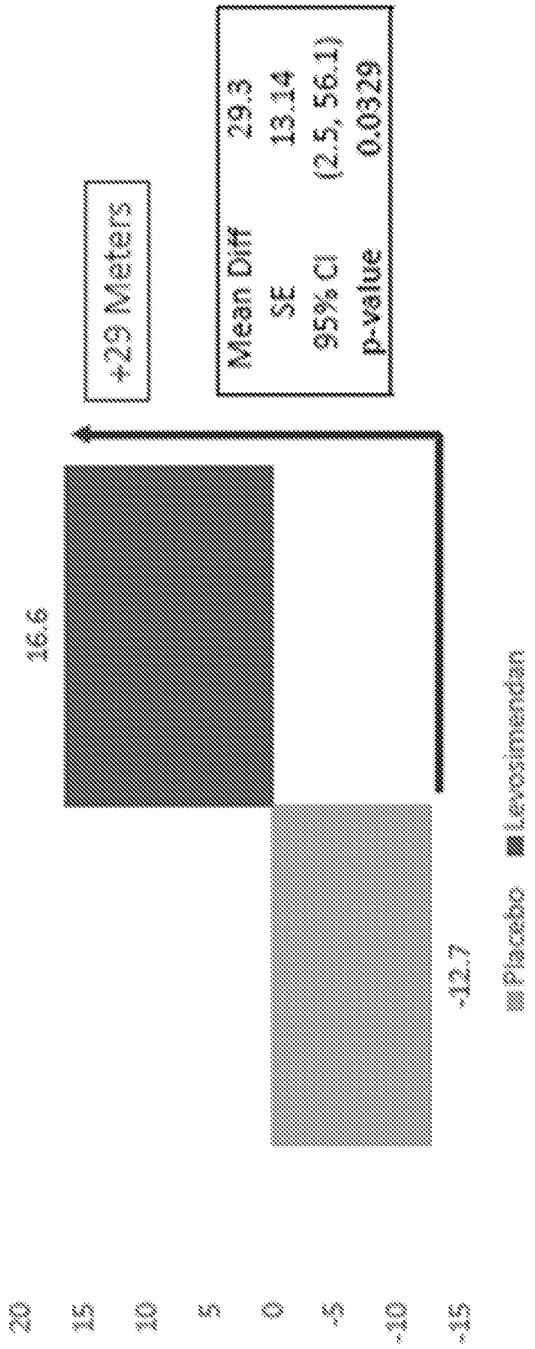

+29 Meters
Mean Diff 29.3
SE 13.14
95% CI (2.5, 56.1)
p-value 0.0329
16.6
-12.7
Placebo
Levosimendan
20
15
10
5
0
-5
-10
-15

Figure 15

	Placebo n=18	*Levosimendan n=18*
Any Treatment Emergent AEs (TEAEs)	8 (44%)	13 (72%)
TEAEs by Severity **Mild** **Moderate** **Severe**	 5 (28%) 2 (11%) 1 (6%)	 9 (50%) 2 (11%) 2 (11%)
Any Drug-Related TEAEs	5 (28%)	9 (50%)
TEAEs of Special Interest †	0	0
Serious TEAEs	1 (6%)	3 (17%)

† hypotension, atrial fibrillation, other significant arrhythmia, resuscitated death, stroke

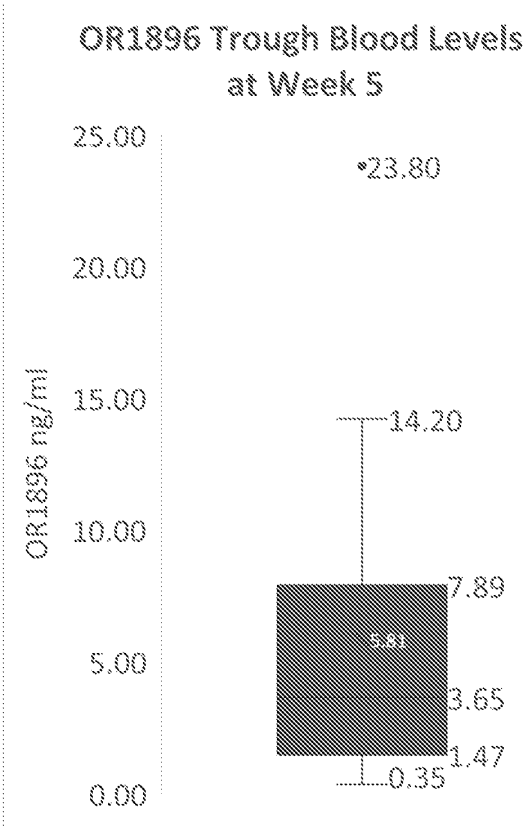
Figure 16

	Placebo n=18	*Levosimendan n=18*
Headache	1 (6%)	3 (17%)
Heart Rate Increased	0 (0%)	2 (11%)
Fatigue	2 (11%)	1 (6%)
Cardiac Failure Acute	1 (6%)	2 (11%)
Dyspnea	1 (6%)	2 (11%)
Vascular Access Site Pain	2 (11%)	0 (0%)
Muscle Spasms	0 (0 %)	2 (11%)
Hypokalaemia	1 (6%)	2 (11%)

Figure 17

Event on Levosimendan	*Severity*	*Relatedness/ Change in Dose*
Infections and Infestations, Device related infection	severe	not related, dose interrupted
Infections and Infestations, Bacteremia	moderate	not related, dose not changed
Cardiac disorders, Cardiac failure acute	mild	not related, dose not changed
Cardiac disorders, Cardiac failure acute	moderate	not related, dose not changed

Figure 18



Patient	OR1896 ng/ml
1	2.64
2	23.80
3	14.20
4	13.80
5	13.30
6	6.08
7	4.59
8	4.43
9	4.16
10	4.02
11	3.27
12	3.22
13	3.06
14	1.64
15	0.98
16	0.61
17	0.40
18	0.35
Mean	5.807833

Figure 19

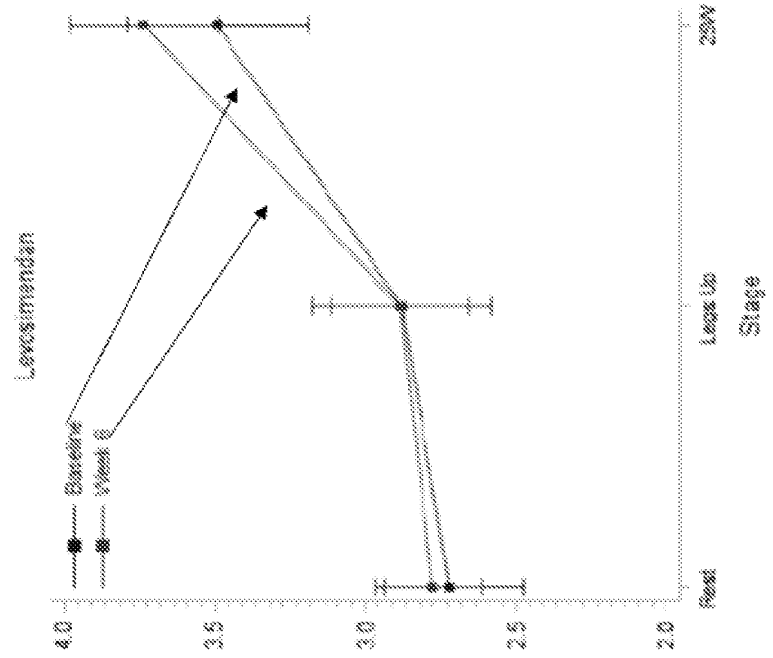


Figure 20B

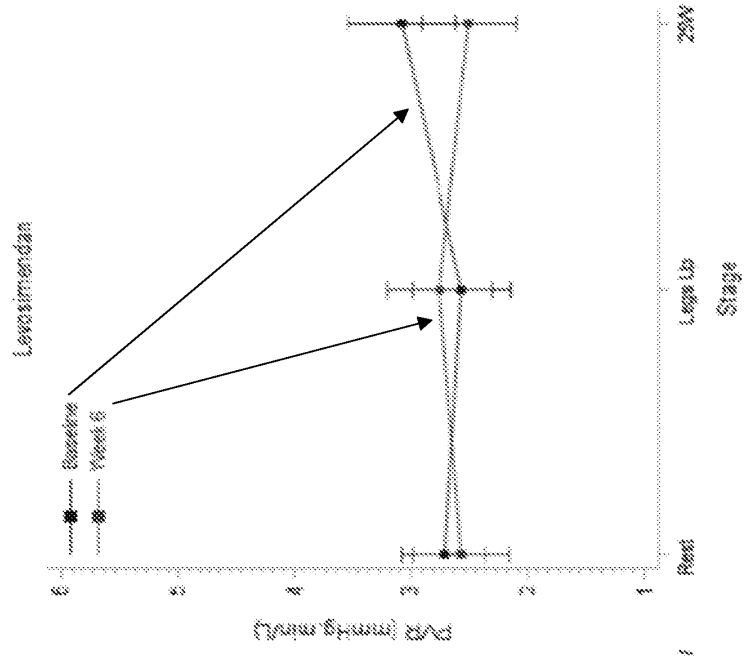


Figure 20A

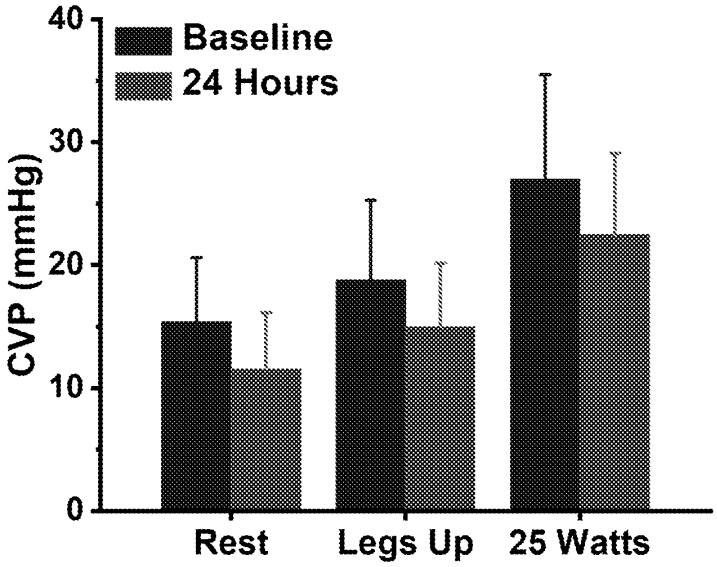


Figure 21A

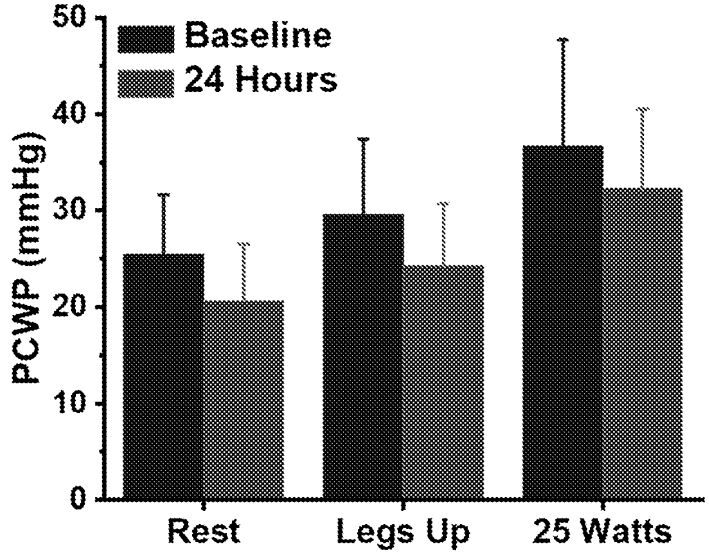


Figure 21B

Characteristic	All Randomized (N=37)	Placebo (N=19)	Treatment (N=18)	p Placebo vs Treatment
Age (years)	68.1 ± 9.3	67.4 ± 11.0	68.8 ± 7.5	0.65
Male Gender, n (%)	14 (37.8)	6 (31.6)	8 (44.4)	0.42
Race, n (%)				0.51
White	32 (86.5)	16 (84.2)	16 (88.9)	
Black or African American	3 (8.1)	2 (10.5)	1 (5.6)	
American Indian or Alaska Native	1 (2.7)	1 (5.3)	0 (0.0)	
Other	1 (2.7)	0 (0.0)	1 (5.6)	
Weight (kg)	98.2 ± 20.5	95.9 ± 20.8	100.6 ± 20.4	0.50
Height (cm)	169.9 ± 10.21	170.5 ± 9.27	169.3 ± 11.36	0.72
BSA	2.14 ± 0.25	2.12 ± 0.25	2.16 ± 0.23	0.6
BMI (kg/m^2)	34.3 ± 8.2	33.0 ± 7.2	35.6 ± 9.2	0.35
Medical History				
Atrial Fibrillation, % of time	29.7 ± 46.3	15.8 ± 37.4	44.4 ± 51.1	0.06
Atrial Fibrillation (history)	28 (75.7)	12 (63.2)	16 (88.9)	0.07
Obesity, n (%)	8 (21.6)	4 (21.1)	4 (22.2)	0.93
DM, n (%)	6 (16.2)	2 (10.5)	4 (22.2)	0.33
HTN, n (%)	19 (51.4)	10 (52.6)	9 (50.0)	0.87
CAD, n (%)	11 (29.7)	5 (26.3)	6 (33.3)	0.64
CKD, n (%)	11 (29.7)	5 (26.3)	6 (33.3)	0.64
Obstructive Sleep Apnea, n (%)	24 (64.9)	12 (63.2)	12 (66.7)	0.82
COPD, n (%)	7 (18.9)	2 (10.5)	5 (27.8)	0.16
Interstitial Lung Disease, n (%)	2 (5.4)	0 (0.0)	2 (11.1)	0.14
Pulmonary Embolism/DVT, n (%)	2 (5.4)	2 (10.5)	0 (0.0)	0.16
NYHA, n (%)				
I	0 (0.0)	0 (0.0)	0 (0.0)	0.68
II	5 (13.5)	3 (15.8)	2 (11.1)	
III	32 (86.5)	16 (84.2)	16 (88.9)	
Vital Signs				
HR	71.2 ± 10.76	68.5 ± 10.36	74.1 ± 10.71	0.12
SBP	130.3 ± 16.47	129.9 ± 15.12	130.7 ± 17.90	0.89
DBP	69.2 ± 11.02	70.4 ± 11.40	67.9 ± 10.78	0.50
RR	16.9 ± 2.17	17.4 ± 1.98	16.4 ± 2.30	0.17
6-Minute Walk Distance	284.6 ± 106.24	279.8 ± 85.24	289.7 ± 127.12	0.78
Echocardiogram				
LVEF	58.4 ± 7.5	58.8 ± 8.2	58.1 ± 6.9	0.80
LA Dimension	92.0 ± 40.1	82.4 ± 33.3	102.2 ± 44.9	0.13
TAPSE	1.8 ± 0.4	1.7 ± 0.5	1.8 ± 0.3	0.76

Figure 22

Parameter	Baseline, mean (SD)		Δ24Hr, mean (95% CI)			
	Legs Down	Legs Up	25 Watts	Legs Down	Legs Up	25 Watts
HR (bpm)	69.6 (16.4)	71.0 (15.9)	86.3 (18.0)	+5.7 (2.9,8.4)*	+6.7 (3.6,9.7)*	+4.8 (0.2,9.3)*
CVP (mmHg)	15.5 (5.2)	18.9 (6.5)	27.1 (8.6)	-3.9 (-5.3,-2.6)*	-3.3 (-4.8,-1.7)*	-4.7 (-6.8,-2.6)*
PA Mean (mmHg)	41.0 (9.3)	46.4 (9.6)	57.3 (13.3)	-4.2 (-6.4,-1.9)*	-4.3 (-6.6,-2.1)*	-2.7 (-5.9,0.4)
PCWP (mmHg)*	25.7 (6.3)	29.7 (7.8)	36.8 (11.3)	-4.9 (-7.0,-2.9)*	-5.3 (-7.3,-3.3)*	-3.9 (-6.8,-0.9)*
AoS (mmHg)	135.0 (18.8)	138.4 (18.7)	155.7 (34.7)	-4.7 (-12.2,2.8)	-1.4 (-8.5,5.7)	-7.2 (-17.5,3.1)
CI (L/min/M2)	2.5 (0.8)	2.6 (0.9)	3.2 (1.1)	0.1 (-0.0,0.3)	0.1 (-0.0,0.3)	0.2 (-0.0,0.4)
SVR (Wood Units)	15.5 (4.2)	15.3 (5.2)	12.5 (5.6)	-1.1 (-2.2,0.0)	-0.4 (-1.8,1.0)	-1.0 (-2.7,0.8)
PVR (Wood Units)	3.3 (2.6)	2.7 (1.6)	3.6 (2.9)	-0.1 (-0.6,0.3)	0.2 (-0.3,0.7)	0.0 (-0.4,0.5)

Figure 23

		Baseline, mean (SD)			Placebo-Corrected Effect of Change from Baseline at 6 Weeks, LS mean (95% CI)			
Parameter	Group	Legs Down	Legs Up	25 Watts	Legs Down	Legs Up	25 Watts
HR (bpm)	Placebo	66.6 (9.6)	66.8 (10.0)	79.1 (11.2)	4.1 (-0.4, 8.7)	2.8 (-3.5, 9.2)	9.3 (-0.4, 19.0)
	Treatment	70.6 (14.4)	70.7 (15.0)	88.3 (18.4)			
CVP (mmHg)	Placebo	16.6 (5.4)	19.9 (5.0)	28.4 (6.8)	-3.1 (-6.4, 0.3)	-3.9 (-8.2, 0.4)	-3.0 (-8.1, 2.1)
	Treatment	14.9 (5.2)	18.8 (8.1)	27.7 (10.2)			
PAS (mmHg)	Placebo	67.2 (21.2)	75.6 (20.9)	87.6 (24.9)	-2.3 (-8.3, 3.7)	0.4 (-7.1, 7.8)	-0.9 (-9.7, 7.9)
	Treatment	64.8 (19.0)	70.7 (18.7)	90.7 (21.2)			
PAD (mmHg)	Placebo	28.9 (6.9)	32.3 (7.0)	39.6 (10.4)	-3.1 (-6.4, 0.3)	-1.6 (-6.2, 3.1)	-1.2 (-6.3, 3.8)
	Treatment	28.6 (5.6)	32.3 (8.17)	40.5 (6.6)			
PA Mean (mmHg)	Placebo	41.7 (10.8)	46.7 (11.0)	55.6 (14.8)	-2.9 (-6.7, 0.1)	-1 (-5.9, 4.1)	-1.3 (-6.7, 4.1)
	Treatment	40.7 (9.3)	45.1 (10.1)	57.4 (10.8)			
PCWP (mmHg)*	Placebo	24.9 (6.5)	28.6 (7.6)	35.5 (11.8)	-3.4 (-7.3, 0.5)	-5.6 (-10.3, -1.0)	-1.4 (-7.7, 4.8)
	Treatment	26.2 (5.3)	31.1 (7.2)	37.8 (8.3)			
AoS (mmHg)	Placebo	141.5 (18.4)	141.1 (16.8)	151.4 (31.1)	1.6 (-11.6, 14.8)	0.4 (-13.9, 14.7)	-2.4 (-25.0, 20.1)
	Treatment	132.4 (19.1)	137.1 (18.1)	148.8 (30.7)			
CI (L/min/M2)	Placebo	2.3 (0.6)	2.5 (0.5)	3.0 (0.9)	0.2 (-0.2, 0.6)	0.10 (-0.5, 0.7)	0.2 (-0.4, 0.8)
	Treatment	2.7 (1.0)	2.9 (1.1)	3.5 (1.3)			
SVR (Wood Units)	Placebo	16.8 (3.4)	15.3 (3.2)	12.7 (3.2)	-1.0 (-4.2, 0.3)	0.04 (-3.5, 3.5)	-2.1 (-5.0, 1.1)
	Treatment	14.0 (4.6)	13.2 (4.8)	10.8 (3.9)			
PVR (Wood Units)	Placebo	4.1 (3.6)	2.2 (1.0)	3.99 (3.8)	-0.24 (-1.46, 0.98)	-0.05 (-1.46, 1.35)	-0.3 (-1.5, 0.9)
	Treatment	2.7 (1.5)	2.6 (1.5)	3.1 (1.9)			

Figure 24

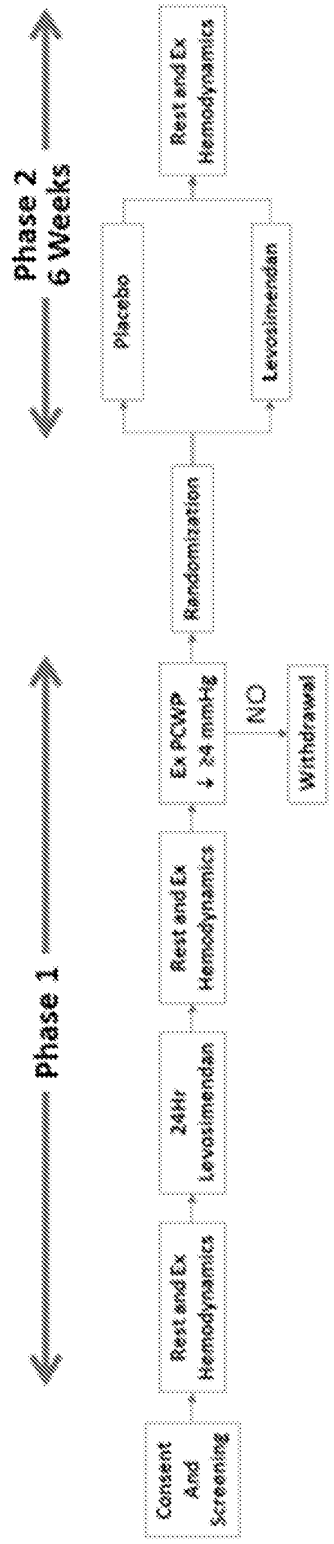

Phase 1
Phase 2
6 Weeks
Consent And Screening
Rest and Ex Hemodynamics
24Hr Levosimendan
Rest and Ex Hemodynamics
Ex PCWP ↓ ≥4 mmHg
NO
Withdrawal
Randomization
Placebo
Levosimendan
Rest and Ex Hemodynamics

Figure 25

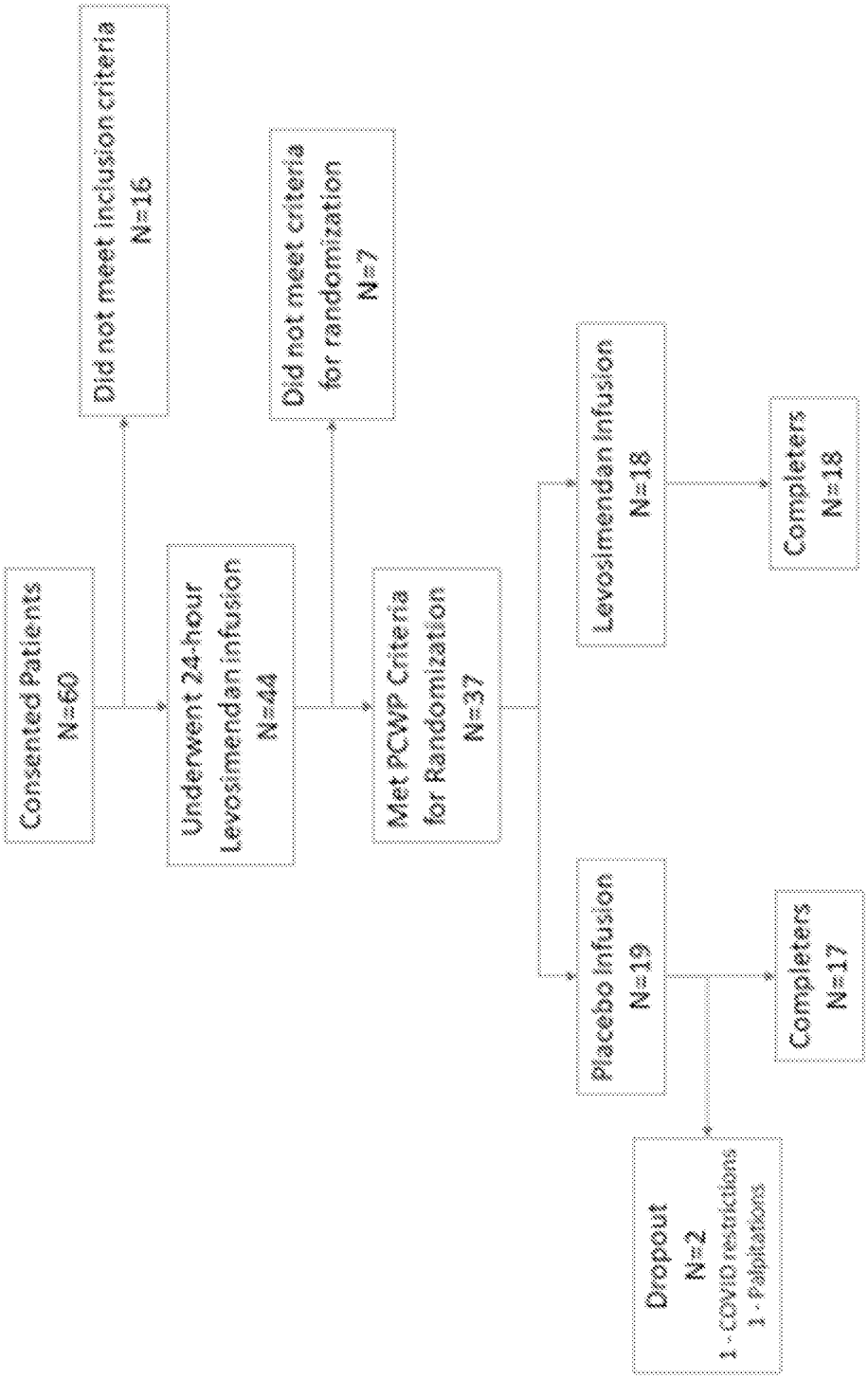

Consented Patients
N=60
Did not meet inclusion criteria
N=16
Underwent 24-hour
Levosimendan infusion
N=44
Did not meet criteria
for randomization
N=7
Met PCWP Criteria
for Randomization
N=37
Levosimendan Infusion
N=18
Completers
N=18
Placebo Infusion
N=19
Completers
N=17
Dropout
N=2
1 - COVID restrictions
1 - Palpitations

Figure 26

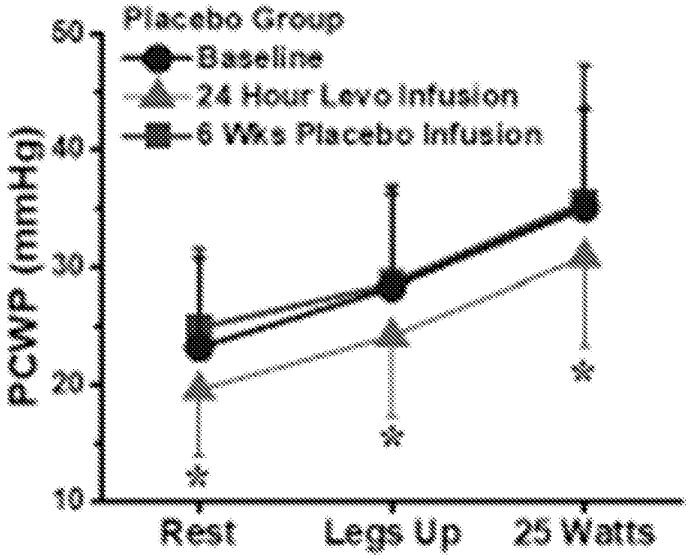


Figure 27A

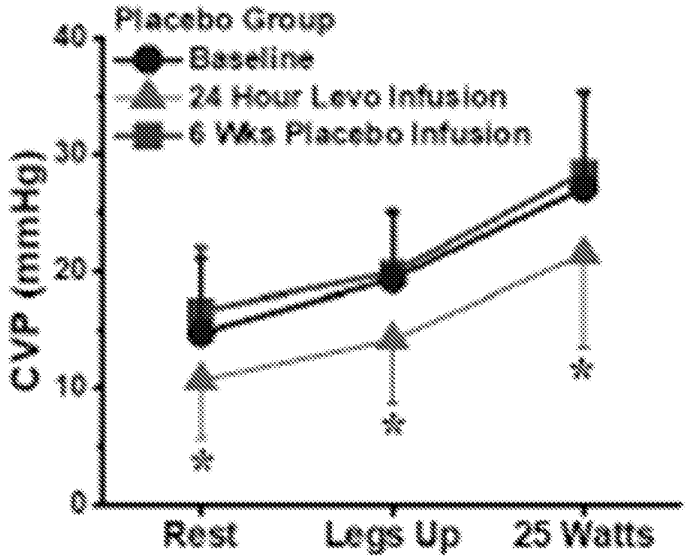


Figure 27B

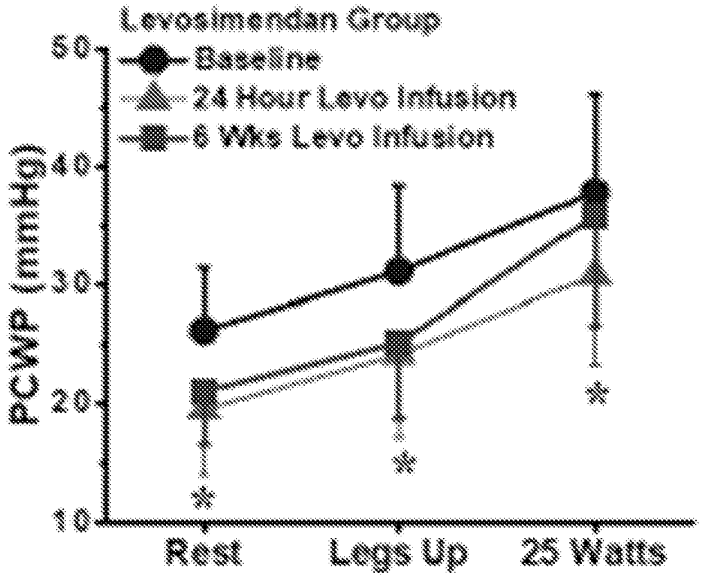


Figure 27C

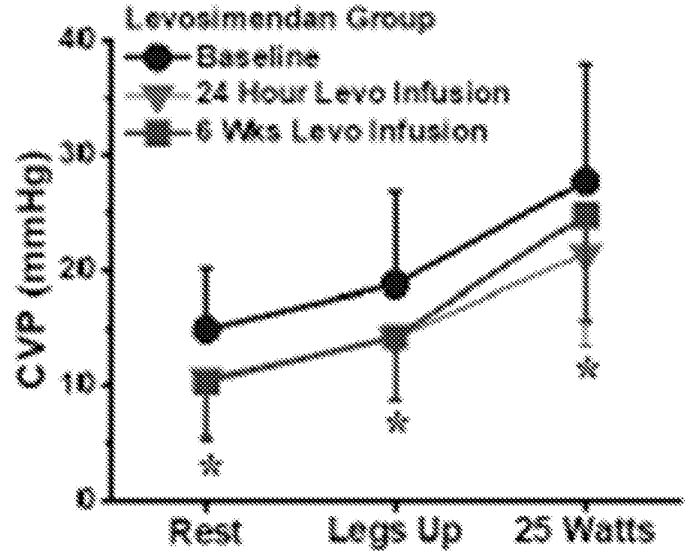


Figure 27D

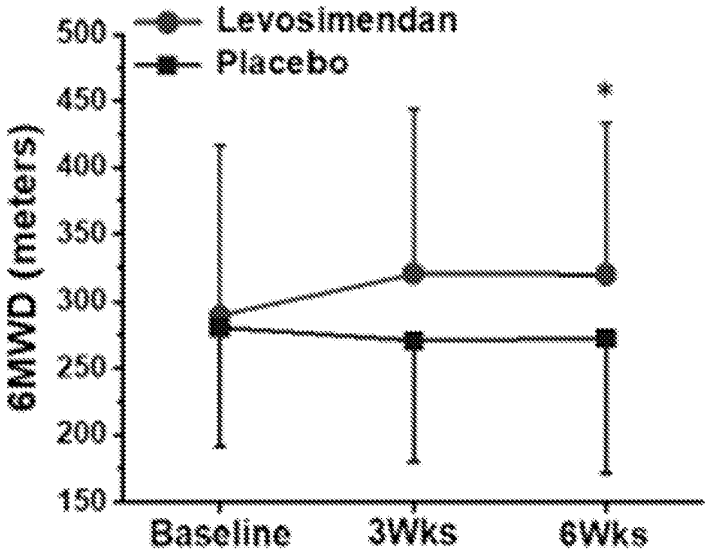


Figure 28A

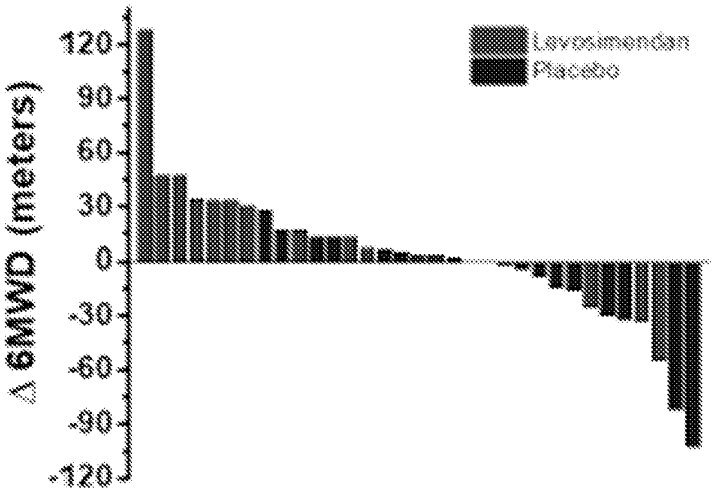


Figure 28B