SUPPLEMENTAL MATERIAL

Reversing the Cardiac Effects of Sedentary Aging in Middle Age, A Randomized Controlled Trial: Implications For Heart Failure Prevention

Authors: Erin J. Howden, PhD[1,2,3], Satyam Sarma, MD[1,2], Justin S. Lawley, PhD[1,2], Mildred Opondo, MD[1,4], William Cornwell, MD[1,5], Douglas Stoller, MD, PhD[1,2], Marcus A. Urey, MD[1,2], Beverley Adams-Huet, MS[2], Benjamin D. Levine, MD[1,2]

[1] Institute for Exercise and Environmental Medicine, Texas Health Presbyterian Hospital, Dallas TX 75231, United States

[2] University of Texas Southwestern Medical Center, Dallas, TX 75390, United States

[3] The Baker Heart and Diabetes Institute, Melbourne VIC 3004, Australia

[4] Stanford University, Stanford CA 94305, United States

[5] University of Colorado Anschutz Medical Campus, Aurora, CO 80045, United States

Supplemental Methods

Measurements

Exercise Testing. Measurements of maximal oxygen uptake were performed at baseline, 10 months (after the peak training phase, described in detail above) and two years. At each testing session, VO_2, hemodynamics and blood pressures were determined at the following treadmill conditions: 1) quiet standing rest, 2) low-intensity (≈30—45% of VO_2max; SS1) steady-state submaximal exercise, 3) moderate-intensity (≈60—75% of VO_2max; SS2) steady-state

submaximal exercise, and 4) maximal exercise. Two participants were tested on an upright cycle at the same conditions because of orthopedic limitations. Gas fractions were analyzed by mass spectrometry and ventilatory volumes by a Tissot spirometer, as previously reported.[1] Maximal oxygen uptake (VO_2max) was defined as the highest oxygen uptake measured from at least a 30 second Douglas bag.

Total blood volume. Total blood volume (TBV) was measured using the carbon monoxide rebreathing method, modified from that described by Burge and Skinner,[2] and has been reported in detail previously.[3] The typical error of this measurement expressed as a coefficient of variation (%) for test-retest reproducibility for hemoglobin mass, the primary calculation derived from the carbon monoxide distribution, is ≈3% for repeated measures in our laboratory.[3] To reduce the confounding effect of body size and composition on TBV, absolute values were scaled relative to total body mass (ml/kg).

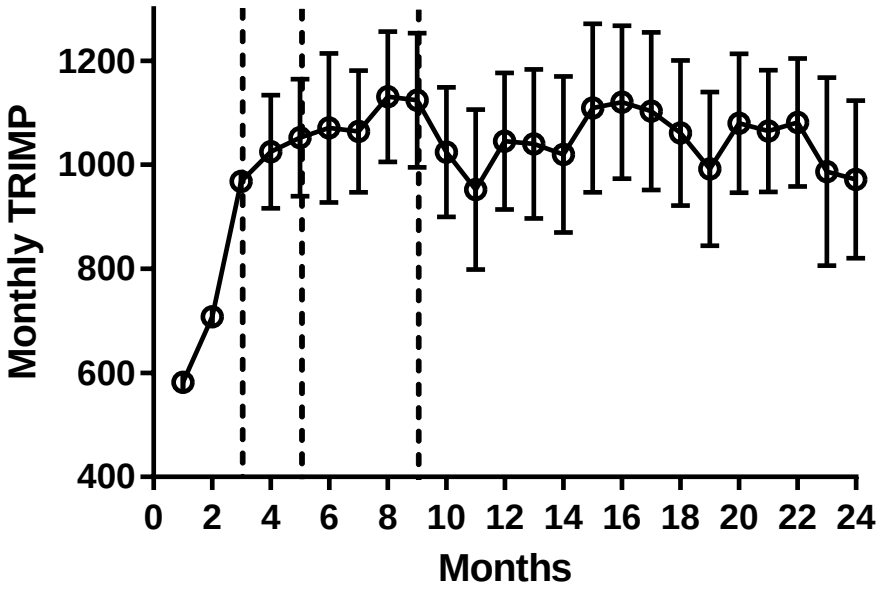
Supplemental Results

Compliance with Prescribed Exercise Training

Participants in the ExT group maintained excellent compliance with the two-year exercise intervention (mean 88±11%). Six participants maintained almost perfect compliance to the prescribed training (completing ≥97% of prescribed sessions). Supplemental Figure 1 depicts the average monthly training load over the course of the study. As expected, TRIMPs increased in response to the progressive increase in training volume from month 1 – 6, before remaining relatively stable during the peak training phase (months 6 - 9). After completion of the peak phase, participants maintained a relatively constant training load, which equated to approximately 3 hours/week of aerobic exercise.

Supplemental Table 1. Effect of Exercise Training on Hemodynamic Response to Preload Manipulation

	HR bpm		MAP mmHg		SV mL		PCWP mmHg	
	Pre	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**
Control Group								
Baseline	63 (60 -66)	62 (59-64)	83 (80 -85)	82 (79 -85)	76 (71 – 80)	78 (73 -83)	12.0 (11.2 – 12.8)	11.8 (10.9-12.6)
LBNP - 15mmHg	64 (61 -67)	64 (61-68)	80 (77-83)	84 (82-86)	67 (61 – 73)	68 (62 -74)	7.4 (6.8 -8.0)	7.8 (7.1 – 8.5)
LBNP - 30mmHg	72 (67-76)	71 (66-76)	82 (79 -85)	82 (78 -85)	54 (49-60)	60 (54 – 66)	5.3 (4.7 – 6.0)	5.7 (5.1 – 6.3)
Baseline	68 (65 – 70)	68 (64-72)	78 (76-80)	79 (76-82)	78 (72-84)	80 (74 – 86)	10.5 (9.7 -11.3)	10.1 (9.4 – 10.8)
NS 15 ml/kg	756 (72 – 79)	76 (71-80)	80 (77-83)	81 (78-83)	87 (81 -95)	91 (84 -97)	16.2 (15.4 – 16.9)	15.9 (15.1 – 16.7)
NS 30 ml/kg	81 (76 – 85)	79 (74-83)	84 (80-88)	83 (81-86)	91 (84 -99)	93 (86 101)	19.6 (19.0 – 20.3)	19.3 (18.5 – 20.2)
ExT Group								
Baseline	61 (58 – 64)	56 (53-59)	80 (78-83)	80 (77-83)	78 (72 -85)	84 (76 -92)	11.6 (11.1 -12.2)	11.8 (11.2 – 12.5)
LBNP - 15mmHg	63 (60-66)	59 (55-62)	80 (79-82)	79 (76-81)	70 (64 – 76)	74 (66 -82)	7.1 (6.5 – 7.7)	7.3 (6.5 – 8.1)
LBNP - 30mmHg	71 (68-75)	65 (61-68)	79 (76-81)	80 (77-82)	59 (52 -65)	62 (54 – 69)	5.0 (4.6 – 5.5)	5.0 (4.4 – 5.6)
Baseline	67 (63-70)	63 (59-66)	78 (76-79)	76 (73-78)	79 (73 -85)	90 (82 -99)	10.4 (9.8 – 10.9)	10.5 (10.0 – 11.0)
NS 15 ml/kg	75 (71 – 79)	69 (64-74)	80 (77-82)	76 (73-79)	91 (84 -97)	102(93– 111)	15.8 (15.3 – 16.3)	15.9 (15.3 – 16.5)
NS 30 ml/kg	76 (71-81)	72 (67-77)	81 (79-84)	80 (77-82)	91 (85 – 98)	104 (95 -114)	19.6 (19.0 – 20.2)	18.9 (18.2 -19.7)



Supplemental Figure 1. Training impulse (mean 95% CI). Mean monthly training load recorded in ExT participants over the two-years. Note the progressive increase in training volume over the first 6 months of the study, before participants completed a 4 month peak phase (6-9months), followed by 14 months of "maintenance training" were training load was kept constant.

References

1. Arbab-Zadeh A, Dijk E, Prasad A, Fu Q, Torres P, Zhang R, Thomas JD, Palmer D and Levine BD. Effect of aging and physical activity on left ventricular compliance. *Circulation*. 2004;110:1799-805.
2. Burge CM and Skinner SL. Determination of hemoglobin mass and blood volume with CO: evaluation and application of a method. *J Appl Physiol (1985)*. 1995;79:623-31.
3. Gore CJ, Rodriguez FA, Truijens MJ, Townsend NE, Stray-Gundersen J and Levine BD. Increased serum erythropoietin but not red cell production after 4 wk of intermittent hypobaric hypoxia (4,000-5,500 m). *J Appl Physiol (1985)*. 2006;101:1386-93.