Study Protocol and Statistical Analyses

"The impact of blood flow restriction (BFR) on exercise and hemodynamic responses"

NCT03540147

February 7, 2019

Study Protocol

Participants

A total of 20 young, apparently healthy adults between the ages of 18 and 35 participated in this study (Table 1). Exclusion criteria included 1) smoking within the past 6 months; 2) uncontrolled hypertension; 3) a history of heart disease, peripheral artery disease, kidney disease, or other known cardiovascular problems; 4) a history of diabetes, gout, or other metabolic disease; 5) obesity, defined as a body mass index (BMI) >30 kg/m^2; 6) major surgeries or changes in health within the last 6 months; 7) have been told by physicians to refrain from exercise; and 8) vulnerable populations (pregnant women, children, unable to consent, etc.). All participants where novice yoga practitioners. The Institutional Review Board reviewed and approved this study, and all participants provided written informed consent. This study meets ethical standards enforced by the journal [10].

Protocols

Participants visited the laboratory on 2 separate occasions for 2 hours per visit. During the first visit, anthropometric measures of height, body weight, and body fatness were taken. Prior to all visits, participants fasted for a minimum of 6 hours, abstained from alcohol and caffeine for the previous 12 hours, and from strenuous physical activity for the previous 24 hours [11]. After 20 minutes of supine rest, baseline measurements consisting of blood pressure, heart rate, blood lactate, endothelial function, and arterial stiffness were taken.

After baseline measurements, a randomized crossover study design was implemented, where participants acted as their own control and performed 20 yoga poses for 30 seconds each with blood flow restriction (BFR) bands and without (non-BFR) inflation of BFR bands placed on the upper thighs (BStrong^{Tm}, Park City, Utah). The BFR bands were inflated to the pre-

determined pressures recommended by the manufacturer according to BFR band size (44.5-60 cm thigh circumference band was inflated to 250 mmHg and 60-78.5 cm thigh circumference band was inflated to 300 mmHg; both bands measured 6 cm in width). During the non-BFR condition, BFR bands were worn, but the bands were not inflated. The sequence started with taking baseline hemodynamic measurements while standing at anatomical neutral. Following baseline, the yoga poses were performed in the following sequential order: 1) Warrior I, 2) Warrior II, 3) Reversed warrior, 4) Extended side angle, 5) Forward fold, 6) Halfway lift, 7) High plank, 8) Up dog, 9) Down dog, 10) Wide-legged forward fold, 11) Goddess, 12) Crescent lunge, 13) Half moon, 14) Chair pose, 15) Mountain pose, 16) Camel, 17) Easy pose, 18) Bridge pose, 19) Happy baby, and 20) Savasana [12] (Supplemental Figure).

The order of these sessions, with inflated and deflated BFR bands, were randomized between the visits. Each testing session was separated by at least 2-3 days to control for potential fatigue or training effects. All yoga sessions were led by a certified yoga instructor. Blood pressure and heart rate were measured continuously throughout the session using beat-by-beat, finger plethysmography (Portapress Finger Plethysmograph, Finapres Medical Systems BV, Amsterdam, Netherlands) as previously described [8]. Participants were asked to keep the hand with the finger plethysmography at heart level during the entire exercise session. Participants performed a familiarization session in order to learn and accommodate minor modifications to yoga poses, which restricted the movement of one arm to place the plethysmography at the heart level. Physiocal was turned on during the measurement. Double products or rate pressure products were calculated by systolic blood pressure multiplied by heart rate. Additionally, participants gave a rating of perceived exertion (RPE: the original Borg Scale) that corresponded

to the perceived difficulty of the exercise task after every 5 yoga postures. Measurements were repeated immediately post yoga performance.

Measurements

Arterial stiffness was measured noninvasively using the cardio-ankle vascular index (CAVI) (Vasera, VS-1500AU, Fukuda Denshi Co., Ltd, Tokyo, Japan) as previously described [13, 14]. Blood pressure cuffs were placed on both arms and both ankles for the measurements of blood pressure and arterial stiffness. Electrocardiogram electrodes were attached to both wrists of the participant. Finally, a heart sound microphone was attached to the sternum of the participant between the second ribs to monitor electrocardiogram and phonocardiogram. CAVI score was calculated from vascular length (distance) divided by the time taken from the pulse wave to propagate from the aorta to the ankle (calculated from the difference between the aortic valve closure sound (taken from the phonocardiogram) and the rise of the ankle pulse wave) [14].

After 20 minutes of supine rest, endothelial function was measured via flow-mediated dilation (FMD) technique [15] by measuring the brachial artery's diameter increase following a brief period of occlusion using an automated diagnostic ultrasound system (UNEXEF-38G, UNEX Corp., Nagoya, Japan)[16]. A blood pressure cuff was placed on the forearm with the proximal edge of the cuff above with the participant's antecubital fossa and a second blood pressure cuff was placed on the contralateral arm for standard blood pressure measurements. Two cross-sectional images of the artery were acquired utilizing the automated ultrasound probe (equipped with 3 linear-array ultrasound probes with a frequency of 10 MHz) proximal to the antecubital fossa. Once a clear cross-sectional image was acquired, a novel stereotactic probe-holding device with a probe self-adjusted automatically to provide a clear longitudinal image of

the artery and begin baseline measurements. Images of the brachial artery were obtained at the end of diastole from each of 10 cardiac cycles. The baseline brachial artery diameter was calculated by taking the average diameter obtained from the 10 cardiac cycles. Pulsed doppler velocity signals were additionally obtained for 10 cardiac cycles at baseline. Following baseline metrics, the cuff was inflated to 50 mmHg above resting systolic blood pressure for 5 minutes to occlude blood flow. After 5 minutes of occlusion, the cuff was deflated, and both brachial artery diameter and blood flow velocity were measured simultaneously and continuously for two-minutes immediately post occlusion. These obtained digitized images generated the maximum diameters of the brachial artery from which the absolute change from baseline and percentage brachial FMD was computed using online semi-automatic analysis software provided by the machine manufacturer (UNEXEF-38G, UNEX Corp., Nagoya, Japan) [17, 18]. FMD measurement was repeated at 1-hour post exercise to evaluate residual hemodynamic effects. FMD was calculated as a percent increase in brachial artery diameter at the post-blood flow occlusion compared with the pre-blood flow occlusion [15].

Blood samples were taken using standard aseptic techniques; sterilizing the finger with an alcohol swab, followed by pricking a finger with a lancet and taking a 0.3 µL sample volume of blood. The blood sample is collected onto a testing strip that is inserted into a blood lactate meter (Blood Lactate Pro, Arkray; Kyoto, Japan).

Statistical Analyses

Two-way ANOVA with repeated measures was used to identify significant differences in hemodynamic variables during the yoga exercise. The Greenhouse-Geisser correction of degrees of freedom was used when sphericity assumptions were violated. Normality and homogeneity assumptions were not violated after inspection of skewness, kurtosis and Shapiro-Wilk analyses.

Cardiovascular responses to each yoga posture must have met the following steady state criteria; 10 consecutive beat-by-beat measurements where heart rate did not vary by more than 10 beats per minute and systolic blood pressure did not vary by more than 20 mmHg to be valid for analyses [8]. All yoga postures achieved steady state and peak blood pressure was used for analysis. A 2x2 repeated measures ANOVA was used to compare blood lactate concentrations between BFR and non-BFR groups. Significance was set at $p<0.05$, and the data were reported as mean±SD.

References

1. Pope ZK, Willardson JM, Schoenfeld BJ. Exercise and blood flow restriction. The Journal of Strength & Conditioning Research 2013; 27: 2914-2926
2. Spranger MD, Krishnan AC, Levy PD et al. Blood flow restriction training and the exercise pressor reflex: a call for concern. American Journal of Physiology-Heart and Circulatory Physiology 2015; 309: H1440-H1452
3. Takarada Y, Sato Y, Ishii N. Effects of resistance exercise combined with vascular occlusion on muscle function in athletes. European Journal of Applied Physiology 2002; 86: 308-314
4. Reeves GV, Kraemer RR, Hollander DB et al. Comparison of hormone responses following light resistance exercise with partial vascular occlusion and moderately difficult resistance exercise without occlusion. Journal of Applied Physiology 2006; 101: 1616-1622
5. VanWye WR, Weatherholt AM, Mikesky AE. Blood flow restriction training: Implementation into clinical practice. International Journal of Exercise Science 2017; 10: 649
6. Patterson SD, Brandner CR. The role of blood flow restriction training for applied practitioners: A questionnaire-based survey. Journal of Sports Sciences 2018; 36: 123-130
7. Renzi CP, Tanaka H, Sugawara J. Effects of leg blood flow restriction during walking on cardiovascular function. Medicine and Science in Sports and Exercise 2010; 42: 726
8. Miles SC, Chou C-C, Lin H-F et al. Arterial blood pressure and cardiovascular responses to yoga practice. Alternative Therapies in Health and Medicine 2013; 19: 38
9. Hietanen E. Cardiovascular responses to static exercise. Scand J Work Environ Health 1984; 10: 397-402
10. Harriss DJ, Macsween A, Atkinson G. Ethical Standards in Sport and Exercise Science Research: 2020 Update. International Journal of Sports Medicine 2019; 40: 813-817. doi:10.1055/a-1015-3123
11. Thijssen DHJ, Bruno RM, van Mil ACCM et al. Expert consensus and evidence-based recommendations for the assessment of flow-mediated dilation in humans. European Heart Journal 2019; 40: 2534-2547.

12. Kaminoff L, Matthews A, Ellis S. Yoga anatomy: Human Kinetics Champaign, IL; 2007

13. Harrison ML, Lin H-F, Blakely DW et al. Preliminary assessment of an automatic screening device for peripheral arterial disease using ankle–brachial and toe–brachial indices. Blood Pressure Monitoring 2011; 16: 138-141

14. Shirai K, Utino J, Otsuka K et al. A novel blood pressure-independent arterial wall stiffness parameter; cardio-ankle vascular index (CAVI). Journal of Atherosclerosis and Thrombosis 2006; 13: 101-107

15. Fico BG, Zhu W, Tanaka H. Does 24-h ambulatory blood pressure monitoring act as ischemic preconditioning and influence endothelial function? Journal of Human Hypertension 2019. 33: 817-820.

16. Tomiyama H, Kohro T, Higashi Y et al. Reliability of measurement of endothelial function across multiple institutions and establishment of reference values in Japanese. Atherosclerosis 2015; 242: 433-442

17. Tomiyama H, Kohro T, Higashi Y et al. A multicenter study design to assess the clinical usefulness of semi-automatic measurement of flow-mediated vasodilatation of the brachial artery. International Heart Journal 2012; 53: 170-175

18. Iwata T, Mori T, Tanno Y et al. Impaired brachial flow-mediated dilatation may predict symptomatic intracranial arterial dissections. Journal of Stroke and Cerebrovascular Diseases 2018; 27: 2691-2695

19. Nelson RR, Gobel FL, Jorgenson CR et al. Hemodynamic predictors of myocardial oxygen consumption during static and dynamic exercise. Circulation 1974; 50: 1179-1189

20. Hunt JE, Walton LA, Ferguson RA. Brachial artery modifications to blood flow-restricted handgrip training and detraining. Journal of Applied Physiology 2011; 112: 956-961

21. Cortez-Cooper MY, Anton MM, DeVan AE et al. The effects of strength training on central arterial compliance in middle-aged and older adults. European Journal of Cardiovascular Prevention & Rehabilitation 2008; 15: 149-155

22. Yamamoto K, Kawano H, Gando Y et al. Poor trunk flexibility is associated with arterial stiffening. American Journal of Physiology-Heart and Circulatory Physiology 2009; 297: H1314-H1318

23. Gainey A, Himathongkam T, Tanaka H et al. Effects of Buddhist walking meditation on glycemic control and vascular function in patients with type 2 diabetes. Complementary Therapies in Medicine 2016; 26: 92-97

24. Vempati RP, Telles S. Yoga-based guided relaxation reduces sympathetic activity judged from baseline levels. Psychological Reports 2002; 90: 487-494.

25. Tang YY, Ma Y, Fan Y et al. Central and autonomic nervous system interaction is altered by short-term meditation. Proceedings of the National Academy of Sciences 2009; 106: 8865-8870.

26. Godfrey RJ, Madgwick Z, Whyte GP. The exercise-induced growth hormone response in athletes. Sports Medicine 2003; 33: 599-613

27. Takarada Y, Nakamura Y, Aruga S et al. Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. Journal of Applied Physiology 2000; 88: 61-65

28. Thomas H, Scott B, Peiffer J. Acute physiological responses to low-intensity blood flow restriction cycling. Journal of Science and Medicine in Sport 2018; 21: 969-974

29.   Kim E, Gregg LD, Kim L et al. Hormone responses to an acute bout of low intensity blood flow restricted resistance exercise in college-aged females. Journal of Sports Science & Medicine 2014; 13: 91

30.   Sugawara J, Tomoto T, Tanaka H. Impact of leg blood flow restriction during walking on central arterial hemodynamics. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology 2015; 309: R732-R739

31.   Loenneke JP, Kearney ML, Thrower AD et al. The acute response of practical occlusion in the knee extensors. Journal of Strength & Conditioning Research 2010; 24: 2831-2834

32.   Fahs CA, Rossow LM, Seo D-I et al. Effect of different types of resistance exercise on arterial compliance and calf blood flow. European Journal of Applied Physiology 2011; 111: 2969-2975

33.   Cook SB, Clark BC, Ploutz-Snyder LL. Effects of exercise load and blood-flow restriction on skeletal muscle function. Medicine and Science in Sports and Exercise 2007; 39: 1708-1713

34.   Laurentino GC, Ugrinowitsch C, Roschel H et al. Strength training with blood flow restriction diminishes myostatin gene expression. Med Sci Sports Exerc 2012; 44: 406-412

35.   Cristina-Oliveira M, Meireles K, Spranger MD et al. Clinical safety of blood flow-restricted training? A comprehensive review of altered muscle metaboreflex in cardiovascular disease during ischemic exercise. American Journal of Physiology-Heart and Circulatory Physiology 2020; 318: H90-H109

36.   Loenneke JP, Thiebaud RS, Fahs CA et al. Effect of cuff type on arterial occlusion. Clinical Physiology and Functional Imaging 2013; 33: 325-327

37.   Loenneke JP, Fahs CA, Rossow LM et al. Blood flow restriction pressure recommendations: a tale of two cuffs. Frontiers in Physiology 2013; 4: 249

38.   Mcgowan CL, Levy AS, Mccartney N et al. Isometric handgrip training does not improve flow-mediated dilation in subjects with normal blood pressure. Clinical Science 2007; 112: 403-409

39.   Loenneke JP, Fahs CA, Rossow LM et al. Effects of cuff width on arterial occlusion: implications for blood flow restricted exercise. European Journal of Applied Physiology 2012; 112: 2903-2912