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Effects of High-Velocity Circuit Resistance and Treadmill Training on Cardiometabolic Risk, Blood Markers, and Quality of Life in Older Adults

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Complete List of Authors:	Roberson, Kirk; University of Miami, Kinesiology and Sport Sciences Potiaumpai, Melanie ; University of Miami, Kinesiology and Sport Sciences Widdowson, Kayla; University of Miami, Kinesiology and Sport Sciences Jaghab, Annmarie; University of Miami, Kinesiology and Sport Sciences Chowdhari, Sean ; University of Miami, Kinesiology and Sport Sciences Armitage, Catherine; University of Miami, Kinesiology and Sport Sciences Seeley, Afton; University of Miami, Kinesiology Jacobs, Kevin; University of Miami, Kinesiology and Sport Sciences Signorile, Joseph; University of Miami, Kinesiology and Sport Sciences
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1 Effects of High-Velocity Circuit Resistance and Treadmill Training on Cardiometabolic Risk,
2 Blood Markers, and Quality of Life in Older Adults
3 Kirk B. Roberson, MS¹, Melanie Potiaumpai, MS¹, Kayla Widdowson, BS¹, Ann-Marie Jaghab,
4 BS¹, Sean Chowdhari¹, Catherine Armitage, BS¹, Afton Seeley, MS¹, Kevin A. Jacobs, PhD¹,
5 and Joseph F. Signorile, PhD^{1,2}

6
7 ¹ Laboratory of Neuromuscular Research & Active Aging-University of Miami, Department of
8 Kinesiology and Sport Sciences, Coral Gables, FL

9 ² University of Miami-Miller School of Medicine, Center on Aging

10

11 **Corresponding Author: Dr. Joseph F. Signorile**

12 Address: 1507 Levante Ave., Coral Gables, FL, 33146

13 Telephone: (305)-284-3105

14 Fax: (305)-284-4183

15 Email: j.signorile@miami.edu

16

17 Abstract

18 The presence of cardiometabolic syndrome (CMS) infers an increased risk for cardiovascular
19 incidence and mortality, and is associated with reduced health-related quality of life (HRQoL).
20 Although the effects of exercise on biomarkers, HRQoL, and future risk have been studied; no
21 study has measured the effects on all three components. The present study compared the effects
22 of steady-state, moderate-intensity treadmill training (TM) and high-velocity circuit resistance
23 training (HVCRT) on biological markers, HRQoL, and overall CVD risk in adults with CMS and
24 CVD risk factors. Thirty participants (22 F; 8 M) were randomly assigned to one of three groups:
25 HVCRT, TM, or control. Participants in exercise groups attended training 3 days/wk for a total
26 of 12 weeks. Of the thirty participants who began the study, twenty-four (19 F; 5 M) were
27 included in the final analysis. Primary outcome measures included CMS criteria, hemodynamic
28 measures, Framingham Risk Score (FRS), and HRQoL. All variables were measured pre- and
29 post-intervention. CMS z score significantly decreased for HVCRT ($p=0.03$), with no significant
30 changes for TM or control. FRS significantly decreased in HVCRT compared to TM ($p=0.03$)
31 and control ($p=0.03$). Significant decreases in systolic ($p<0.01$) and diastolic blood pressures
32 ($p<0.01$) for HVCRT accompanied significant increases from baseline in stroke volume ($p=0.03$)
33 and end-diastolic volume ($p<0.01$). Systemic vascular resistance significantly decreased
34 ($p=0.05$) for HVCRT compared to control. Emotional well-being significantly improved
35 following HVCRT and TM compared to control ($p=0.04$; $p=0.03$). HVCRT represents a novel
36 training modality that improved factors in each of the three components assessed.

37 **Key Words:** exercise; cardiometabolic syndrome; cardiovascular disease; hemodynamics; high-
38 velocity circuit training

39 Introduction

40 The cardiometabolic syndrome (CMS) represents a cluster of physiological and metabolic
41 abnormalities that confer increased risk for developing cardiovascular disease (CVD) and type 2
42 diabetes mellitus (Grundey et al. 2004). Despite decades of therapeutic advances, CVD remains
43 the leading cause of death in the United States (Xu et al. 2016). Numerous studies have shown
44 that both resistance training and aerobic endurance exercise can promote an increase in physical
45 fitness and successfully impact many of the individual risk factors associated with CMS
46 including blood pressure (BP) (Hagberg et al. 1989, Kelley and Kelley 2000), waist
47 circumference (WC) (Slentz et al. 2004, Church et al. 2009), and blood lipid profile (Halverstadt,
48 Phares et al. 2007, Paoli et al. 2013). Others have also considered the impact of exercise
49 intervention strategies on measures of health-related quality of life (HRQoL) in older adults with
50 and without CMS (Barnett et al. 2003, Oh et al. 2010); however, these results have been
51 inconsistent. Recently, high-intensity circuit and interval training have been suggested to be
52 more effective modalities for improving many dimensions of physical fitness and reducing risk
53 factors compared to moderate-intensity interval training, low-intensity circuit training, and
54 traditional aerobic endurance training in individuals at risk for CVD and those with lifestyle-
55 induced cardiometabolic disease (Paoli et al. 2013, Weston et al. 2014). Furthermore, high-
56 velocity resistance training, often referred to as power training, has been shown to elicit superior
57 improvements in both physical performance and markers of independence in older adults
58 compared to traditional resistance training (Miszko et al. 2003, Henwood and Taaffe 2005,
59 Henwood et al. 2008, Izquierdo and Cadore 2014). Accordingly, the development and
60 implementation of a program that synergistically combines both high-intensity circuit training
61 and high-velocity resistance training would be particularly important and may provide the

greatest opportunity to significantly reduce risk factors associated with CMS and CVD and attenuate the rapid decline in physical and functional performance that occurs with aging. Therefore, the purpose of the present investigation was to compare the effects of steady-state, moderate-intensity treadmill training (TM) and high-velocity circuit-resistance training (HVCRT) on biomarkers, HRQoL, and future risk for developing CVD in older adults with multiple CMS and CVD risk factors.

MATERIAL AND METHODS

Participants

Twenty-two women (age: 69 ± 8 years; height: 161 ± 3 cm; body weight: 81.1 ± 12.5 kg) and eight men (age: 73 ± 5 years; height: 178 ± 9 cm; body weight: 101.4 ± 5.8 kg) with multiple CMS and CVD risk factors were recruited to this study. CMS risk factors include: WC ≥ 102 cm in men and ≥ 88 cm in women, fasting glucose (FG) ≥ 100 mg/dL, triglyceride (TGL) ≥ 150 mg/dL or drug treatment for elevated TGL, high-density lipoprotein cholesterol (HDL-C) < 40 mg/dL in men and < 50 mg/dL in women or drug treatment for low HDL-C, and systolic blood pressure (SBP) ≥ 130 or diastolic blood pressure (DBP) ≥ 85 mmHg or on anti-hypertensive treatment with a history of hypertension. Separate CVD risk factors as defined by the American College of Sports Medicine are: age (men ≥ 45 , women ≥ 55 years), family history of CVD, cigarette smoking, sedentary lifestyle, obesity (body mass index ≥ 30 kg/m²), and dyslipidemia (low-density lipoprotein cholesterol (LDL-C) ≥ 130 mg/dL or total cholesterol > 200 mg/dL). The Framingham Risk Score (FRS) used to calculate predicted future risk for developing heart disease. CVD risk factors included in the FRS are cigarette smoking and total cholesterol. Risk factors for CVD were assessed using the American College of Sports Medicine Risk

Stratification Screening Questionnaire. Participants were excluded if they had regularly participated in a structured physical activity program within the past three months, had any uncontrolled neuromuscular, orthopedic, or cardiovascular disease, were unable to read or speak English, or had significant cognitive impairment (Folstein mini-mental score < 23). Additionally, participants that were currently taking a beta-blocker were excluded from the study. Information regarding physical and mental health, as well as physical activity, was provided by each participant on the Physical Activity Readiness and Health History Questionnaire. Participants were instructed to refrain from any type of structured exercise for the duration of the experimental protocol. The study was approved by the University Institutional Review Board and all participants provided informed written consent.

Participant flow through the study from recruitment-to-analysis is illustrated in Figure 1. Of the 30 individuals recruited to participate in the study, three withdrew due to medical complications unrelated to the study and one voluntarily withdrew, leaving 26 individuals (twenty women; six men) who completed the study. Of the 26 who completed the study, two were excluded from the analysis due to poor protocol adherence, leaving a 24 participants who were included in the final analysis. Participant risk profiles are depicted in Table 1.

Experimental Protocol

To compare the effects of TM, HVCRT, and no exercise (control) on HRQoL, biomarkers, and overall risk for CVD, participants were randomly assigned following simple randomization procedures (computerized random numbers) to one of the three experimental groups. Participants in the training groups visited the laboratory on 42 separate occasions over the course of 14 weeks. Participants in the control group only visited the lab to complete pre-and post-testing measures during weeks one and 14. On day one they completed all necessary

consent forms and questionnaires. Additionally, anthropometric measurements, including body weight and height, fat free mass, and WC were made. For the blood draw, participants reported to the laboratory following a 12-hour fast. Participants returned 72 hours after their final training session for a final blood draw. The RAND-36 Item Health Survey 1.0 (RAND) was used to assess HRQoL and was administered on the first and final day of the study. FRS was calculated with the Framingham equation using information obtained from the American College Of Sports Medicine risk stratification along with relevant blood work. A CMS z score was also calculated for each participant and serves as a continuous score of the five CMS variables. Hemodynamic measures were obtained using impedance cardiography (ICG).

During weeks 2-13, participants in the TM and HVCRT groups underwent a 12-wk supervised exercise program (3 d/wk). Participants were asked not to modify their diet and instructed to maintain a dietary log accounting for caloric intake for 3 d/wk throughout the course of the study. Successful adherence was defined as missing no more than six exercise sessions. Control group participants were given identical dietary instructions and materials.

Primary outcome measures were the following: RAND, FRS, CMS- z score, WC, triglycerides (TGL), HDL-C, SBP, DBP, and FG. Additionally, hemodynamic measures obtained using an ICG device to include cardiac output, stroke volume, ejection fraction, end-diastolic volume, and systemic vascular resistance. Secondary outcome measures included: body mass index, LDL-C, Cholesterol/HDL-C ratio, body weight, fat free mass, very low-density lipoprotein cholesterol, high sensitivity C-reactive protein (CRP), hemoglobin A1C (A1C), and resting HR.

Body weight, fat-free mass, and body mass index were measured using a Tanita BC-418 bioelectrical impedance scale (Tanita, Corporation of America, Inc., Illinois, USA) and height

was measured using a stadiometer that was a component of a medical dual beam scale (Detecto Corp, Webb City, MO, USA). WC was measured with the participant standing, arms at sides, feet together, and abdomen relaxed. A horizontal measure was taken immediately above the iliac crest. Three measurements were taken and the average was recorded.

RAND

Items from the RAND were scored and used to assess eight health concepts: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions (Hays and Morales 2001). Participants were given identical instructions when completing the survey at the beginning and end of the study.

FRS

The FRS for coronary heart disease over 10 years was calculated for each participant using the Framingham equation (Wilson et al. 1998) which consists of a scoring scheme based on age, sex, total cholesterol, smoking, HDL-C, and SBP. A CMS z score was calculated using the equation described by Bateman et al., for each participant using the five defining criteria (Bateman et al. 2011).

CMS z Score

Briefly, a modified z score was calculated for each variable using individual participant's data, CMS criteria, and standard deviations (SD) from the entire sample. Due to differences in criteria for men and women, separate equations and separate standard deviations were calculated. The equations used to calculate the CMS z score were: $[z\text{-score} = [(40 - \text{HDL-C})/\text{SD}] + [(\text{TGL} - 150)/\text{SD}] + [(\text{FG} - 100)/\text{SD}] + [(\text{WC} - 102)/\text{SD}] + [(\text{mean arterial pressure} - 100)/\text{SD}]]$ for men

and $[z\text{-score} = [(50 - \text{HDL-C})/\text{SD}] + [(TGL - 150)/\text{SD}] + [(FG - 100)/\text{SD}] + [(WC - 88)/\text{SD}] + [(mean\ arterial\ pressure - 100)/\text{SD}]]$ for women. SDs based on the baseline data were used to calculate the initial CMS z scores while SDs from the post-intervention data were used to calculate the final z scores.

Blood Collection and Analysis

A fasting venous blood sample was collected before training began and 72 hours after the final training session. All samples were obtained in the morning (7:00 – 9:00 a.m.) in a seated position from an antecubital vein. Samples were subsequently analyzed for FG, A1C, a complete lipid profile, and CRP. Fasting serum glucose was measured photometrically on Roche/Hitachi Cobas C systems (Roche Diagnostics, Indianapolis, IN). A1C was evaluated using ion-exchange high-performance liquid chromatography. total cholesterol, TGL and HDL-C were measured by enzymatic calorimetric methods and LDL-C was calculated using the equation presented by Friedewald et al. (Friedewald et al. 1972). CRP was measured with a turbidimetric enzymatic assay using an automated chemistry analyzer (Roche Diagnostics, Indianapolis, IN). All testing was performed at the University Hospital & Clinical Pathology Laboratory.

Hemodynamics

An ICG device (PhysioFlow Enduro, Manatec, Macheren, France) was used to determine HR, and estimate stroke volume, ejection fraction, end-diastolic volume, and systemic vascular resistance for the participants at rest. Briefly, the PhysioFlow provides information on cardiac function by performing an analysis of trans-thoracic bio impedance recording in association with an ECG signal. It measures changes in impedance by injecting a high frequency alternating electrical current of low magnitude towards the thorax between two electrodes positioned on the

neck and another two on the xiphoid process. The remaining two electrodes are used to record an ECG signal. A more detailed description of the PhysioFlow methodology has been described elsewhere (Charloux et al. 2000). Participants were instructed to abstain from food, cigarette smoking, and caffeine for two hours prior to testing. Participants were tested in a seated position with back supported and both feet flat on the floor. After shaving, abrading, and cleaning the skin with 70% isopropyl alcohol pads, six PF-50 electrodes were applied according to the manufacturer's guidelines. Software calibration was completed prior to each test. After 15 minutes of quiet sitting but prior to PhysioFlow testing, two separate BP measures were obtained electronically (BP TRU, BPM-200, Coquitlam, BC, Canada). Following BP measurements, cardiac parameters were measured continuously with the participant sitting calmly and quietly for five minutes. An average value was calculated for each measure from the data acquired during the final minute of recording.

Treadmill Training

All exercise training was conducted in a supervised laboratory setting with an instructor-to-participant ratio of 1:1. Primary outcome variables from the blood analysis were tested by assessors who were blinded to groups; however, other pre- and post-test assessments were performed by the same assessors. Training sessions were conducted at the same time each day ($\pm$ 1 hr) and participants were instructed not to consume any food, drinks or supplements containing high amounts of caffeine or any other substances that may alter HR prior to each exercise session. One familiarization day was provided prior to the start of the 12-week intervention. Participants were allowed to ask questions regarding the equipment and procedures, and all assessment outcomes were explained in detail. During this time, participants were instructed on the use of the Borg 15-point rating of perceived exertion (RPE) scale to assess effort. All

treadmill exercise was performed three days per week on a motorized Cybex 790T treadmill (Cybex International, Inc., Medway, MA, USA). In accordance with American College Of Sports Medicine guidelines for moderate intensity exercise (Medicine 2013), training was conducted at 55% (± 2 bpm) of each participant's heart rate reserve, as determined by the Karvonen formula using age predicted maximum heart rate values (Camard et al. 2008). HR was continuously monitored throughout training using a Polar portable sensor (H7 Heart Rate Sensor, Lake Success, NY, USA).

Weeks one through three comprised the conditioning phase in which participants steadily increased exercise duration until the target time of 35 min was achieved. Participants were instructed to perform a self-paced warm-up for the first three minutes of each exercise session. Exercise intensity was modulated by either increasing the speed or the percent grade of the treadmill. Participants were instructed to begin increasing the percent grade after they had achieved the fastest walking pace they could maintain for the duration of the workout. A cool-down was conducted at the end of each session, separate from the 35 min of training. During the cool-down, participants were instructed to decrease speed and grade until their HR reached a value of within 10% of resting. At the end of each session, an RPE, average speed, percent grade, and total time were recorded. During weeks 4-12, participants were encouraged to increase intensity once their exercising HR dropped > 2 bpm below their target (55% heart rate reserve).

High-Velocity Circuit Resistance Training

A total of 11 pneumatic resistance exercise machines (Keiser A420, Keiser Corporation, Fresno, CA, USA) were utilized during the study. A one-repetition maximum (1RM) was determined for each participant on all machines using guidelines established by the National Strength and Conditioning Association (Baechele et al. 2008). Following testing, the optimal

220 training load for the production of muscular power was calculated for each exercise, relative to
221 each participants 1RM. The percentages of each 1RM corresponding to the optimal load were
222 previously identified by Potiaumpai et al. (Potiaumpai et al. 2016) in an age-matched population
223 using identical resistance exercise machines.

224 For the circuit training protocol, 11 exercises were completed at the specified optimal
225 load (%1RM) in the following order: chest press (50%), leg press (60%), latissimus dorsi pull-
226 down (40%), hip adduction (70%), overhead press (60%), leg curl (60%), seated row (50%), hip
227 abduction (70%), elbow extension (50%), plantar flexion (60%), and elbow flexion (50%). Each
228 set consisted of 12 repetitions. For the concentric portion of the lift, the participant was asked to
229 “move the load as forcefully and as quickly as possible.” The eccentric phase of the lift consisted
230 of a two-second controlled motion. Rest intervals were self-directed; however, participants were
231 instructed not to begin the next exercise until they were confident that they could complete all
232 assigned repetitions without an intra-set rest period. The duration of each rest-period was
233 measured using a digital stopwatch, and the average time for all rest-periods was calculated.
234 Time began following the completion of the final repetition of one exercise and was stopped at
235 the onset of the first repetition of the next exercise.

236 During the first three weeks of training, the volume of training increased gradually. For
237 week one, participants completed only one full-rotation through the circuit. Week two consisted
238 of two rotations, and weeks 3-12, three full-rotations. HR was obtained at the start and half-way
239 point of each circuit. HR was measured by palpating the radial artery for 20 secs and multiplying
240 the number of beats by three. An average HR for the entire exercise session was calculated from
241 the six recorded values. The total time for the entire workout was also recorded each session.
242 Finally, an RPE was obtained following the completion of the last exercise of the session using

the Borg Category Ratio (Borg CR-10). Participants were asked to provide an RPE that reflected the difficulty of the exercise session as a whole. The Borg CR-10, rather than the Borg 15-point RPE scale was chosen for this protocol. Scores from the Borg 15-point RPE scale have been shown to increase linearly with HR and oxygen consumption (Borg, 1998); thus, due to the steady-state nature of the TM protocol, we believed this to be the appropriate choice. However, during resistance training, particularly circuit resistance training, HR changes suddenly and disproportionately with each set and rest period (Sweet et al., 2004). Therefore, the Borg CR-10 scale was deemed to be more appropriate for resistance training, and its use for this modality is widely accepted. Nonetheless, corresponding values between the two scales are provided below. Total time, average HR, average rest-period, and RPE values were only recorded for weeks 3-12 when three full circuits were completed. Keiser pneumatic resistance machines were interfaced with a laboratory computer, which allowed the transfer and analysis of data including force, velocity, and power. Progression of load was based on significant increases in power output from the previous week: when there was a 5% increase in the average power output of a particular exercise on at least two of the three sessions in a given week. When a significant increase in power was observed, a 10% increase in load was applied for subsequent training sessions.

Dietary Records

Participants were instructed to report their food and drink items and corresponding serving sizes for morning snacks, breakfast, lunch, afternoon snacks, dinner, and evening snacks. Recalls were collected for two out of five weekdays (Monday – Friday) and one out of two weekend days (Saturday – Sunday) for a total of three days. Participants were instructed not to modify their eating or drinking habits going into the study or during the study. This was done to minimize the impact of changes in diet on any of the physical or biomarkers assessed.

Participants were given a set of standardized reporting logs at the beginning of each week and logs from the previous week were collected. All nutrition logs were analyzed using Nutritionist Pro software (version 5.4.0, Axxya Systems-Nutritionist Pro, Stafford, TX).

Statistical Analysis

An analysis of covariance was used to examine between group differences. Pre-test values were used as covariates to improve precision and to control for possible imbalances during the randomization process and between baseline values. This is the preferred approach for analyzing randomized trials with baseline and follow-up measurements since it corrects for baseline values (Vickers and Altman, 2001). Paired t-tests were used to investigate within-group changes. All significance tests were two-tailed and a required significance level of $\alpha \leq 0.05$. In order to obtain a statistical power of 80% with an alpha value set at 0.05, 30 participants were needed. This sample size is based on a calculated effect size ($f = 0.55$) from a similar study comparing circuit resistance training to steady-state endurance training. Effects sizes for Cohen's d are listed as the absolute value and are interpreted as: 0.80 is considered large, 0.50 is considered medium, and 0.20 is considered small. When discussing the main effects, Cohen's f was used to describe the effect size. For Cohen's f , values are interpreted as: 0.40 is considered large, 0.25 is considered medium, and 0.10 is considered small. All statistical analyses were performed with SPSS, version 24 statistical package (IBM SPSS Statistics, Armonk, NY). Data are expressed as mean $\pm$ standard error (SE).

RESULTS

Participant data were included in the data analyses only if criteria for adherence were met. Study adherence was defined as attending 30 of 36 required exercise sessions (83%) and all

pretest and post-test sessions. Based on these criteria, data for 24 (19 F; 5 M) participants were included in the analysis. Descriptive data for the 24 participants are summarized in Table 2. There were no significant differences in baseline characteristics between groups and body weight, fat-free mass, and body mass index did not significantly change from baseline in any group. No differences were observed in total caloric intake during the intervention for the TM, HVCRT, or control groups (Table 3).

RPE was assessed using the Borg CR-10 for HVCRT and the Borg 15-point RPE scale for TM. Average RPE for HVCRT was 6.0 ± 0.2 , which corresponds to a work effort that lies between “Hard” and “Very Hard”, while the average RPE for TM was 10.9 ± 0.5 , which corresponds to a “Light” level of perceived exertion. The difference in average HR between HVCRT (107 ± 4 bpm) and TM (114 ± 3 bpm) was not statistically significant. The average rest interval time for all participants in the HVCRT group for weeks 3-12 of training was 31.7 ± 3.4 s. Total exercise session time for the TM group was $33 \text{ min} \pm 2 \text{ min}$ for weeks 3-12, which was dictated by the protocol. For the HVCRT group, average total exercise session time for weeks 3-12 was $30 \text{ min} \pm 2 \text{ min}$.

Primary Outcome Measures

Within and between-group data for all primary outcome measures are presented in Table 4. Figure 2 depicts the mean change for each group for all CMS criteria, as well as the CMS z score. Hemodynamic measures are depicted in Figure 3. A significant decrease from baseline to 12 weeks was observed in SBP (MD=-19.56, SE=2.33, $p<0.01$, $d=2.80$) and DBP (MD=-9.44, SE=1.68, $p<0.01$, $d=1.87$) for the HVCRT group only (Table 4). Post-hoc analysis revealed that SBP significantly decreased in the HVCRT group when compared to both the TM (MD=-10.01, SE=3.70, $p=0.04$, $d=0.36$) and control (MD=-15.69, SE=3.58, $p=0.01$, $d=0.42$) (Table 4).

311 Additionally, DBP was significantly reduced in the HVCRT group when compared to control
312 (MD=-10.27, SE=2.84, $p < 0.01$, $d=0.39$) (Table 4). Mean arterial pressure significantly
313 decreased from baseline for the HVCRT group (MD=-9.92, SE=3.92, $p=.04$, $d=1.17$), while no
314 differences were detected for TM or control (Figure 2). A significant difference in FG was
315 observed in the HVCRT group (MD=-9.00, SE=3.96, $p=0.05$, $d=0.76$) while no change was
316 observed in the TM or control groups (Table 4). HDL-C significantly increased from baseline for
317 the TM group (MD=4.38, SE=1.76, $p=0.04$, $d=0.88$) (Table 4). Significant within-group
318 differences were detected for CMS z score, showing a decrease from baseline for the HVCRT
319 group (MD=-3.22, SE=0.36, $p < .001$, $d=1.58$) and TM (MD=-1.81, SE=0.73, $p=0.04$, $d=0.52$).
320 Post-hoc analysis revealed a significant difference in CMS z score between the HVCRT group
321 and control (MD=-2.77, SE=0.87, $p=.02$, $d=0.29$) (Table 4). Data revealed a significant decrease
322 in systemic vascular resistance for the HVCRT group when compared to the control group
323 (MD=-161.80, SE=62.82, $p=0.05$, $d=1.74$) (Figure 3). There was a significant main effect for
324 stroke volume ($p=0.03$, $f=0.61$) and systemic vascular resistance ($p=0.03$, $f=0.61$) but not for
325 end-diastolic volume or ejection fraction (Figure 3). Significant within-group differences were
326 detected in the HVCRT group for stroke volume (MD=11.87, SE=4.63, $p=0.03$, $d=2.89$), end-
327 diastolic volume (MD=32.31, SE=10.39, $p=0.01$, $d=4.33$), and ejection fraction (MD=-4.42,
328 SE=5.23, $p=0.04$, $d=1.48$); however, no differences were observed for the TM or control groups
329 (Figure 3). Data for FRS for each group are depicted in Table 4. After accounting for sex, age,
330 total cholesterol, smoking, HDL-C and SBP, a significant decrease in the FRS was observed in
331 the HVCRT group (MD=-4.44, SE=2.46, $p < 0.01$, $d=1.00$). Post-hoc analysis revealed a
332 significant decrease in FRS for the HVCRT group when compared to the TM group (MD=-2.99,
333 SE=1.06, $p=0.03$, $d=0.00$) and the control group (MD=-3.31, SE=1.18, $p=0.03$, $d=0.18$). No

within-group significant differences were detected for any individual components of the RAND for HVCRT, TM, or control groups. Post-hoc analysis revealed a significant increase in the Emotional Well-Being component for HVCRT when compared to control (MD=16.72, SE=6.10, $p=0.04$, $d=1.77$) and for TM when compared to control (MD=18.00, SE=6.25, $p=0.03$, $d=1.27$).

Secondary Outcome Measures

For secondary outcomes, a significant decrease was detected for cholesterol/HDL ratio (MD=-0.48, SE=0.14, $p=0.01$, $d=1.24$) in the TM group. A significant decrease from baseline for A1C was observed in the HVCRT group (MD=-0.30, SE=0.03, $p < 0.001$, $d=1.38$) and TM (MD=-0.06, SE=0.03, $p=0.02$, $d=3.58$). In contrast, a significant increase in A1C was observed in the control group (MD=0.10, SE=0.04, $p=0.03$, $d=0.36$). Post-hoc analysis revealed a significant decrease in A1C in the HVCRT group when compared to the control group (MD=-0.40, SE=0.12, $p=0.01$, $d=0.77$) but the TM group. No significant differences were detected in any groups for resting HR, total cholesterol, very low-density lipoprotein cholesterol, or CRP.

DISCUSSION

The present investigation compared the effects of steady-state, moderate-intensity treadmill training and high-velocity circuit-resistance training on biological markers, HRQoL, and overall risk for developing CVD in older adults with multiple CMS and CVD risk factors. Our results indicate that HVCRT provides a greater benefit in improving FG and A1C. HVCRT also significantly reduced CMS z scores when compared to control, significantly reduced FRS compared to TM and control, and significantly improved HRQoL compared to control. Moreover, hemodynamic parameters including SBP, and DBP were significantly reduced from

355 baseline and stroke volume and end-diastolic volume were significantly increased following
356 HVCRT, but not TM or control.

357 The effects of continuous aerobic and traditional resistance exercise on BP have been
358 well documented (Cornelissen and Smart 2013) with both eliciting positive adaptations in SBP
359 and DBP; likely through different mechanisms. Additionally, Bateman et al. (2011) reported that
360 a combined training model consisting of alternating aerobic and resistance training sessions
361 significantly reduced DBP. When examining the effects of interval training compared to
362 moderate-intensity continuous treadmill training Molmen-Hansen et al. (2012) reported that
363 aerobic interval training was more effective than continuous treadmill training at reducing SBP,
364 although both resulted in significant reductions. In a study similar to ours, Paoli et al. (2013)
365 indicated that high-intensity circuit training was more effective in improving BP than either low-
366 intensity circuit training or moderate-intensity endurance training. While their results for circuit
367 resistance training are consistent with the findings from our study, repetitions per set, work-
368 recovery intervals, and total number of exercises completed differed. Although our findings with
369 regard to BP reflect those generally accepted, participants in the HVCRT group saw markedly
370 greater reductions in SBP (~19 mmHg) when compared to the high-intensity circuit training
371 group in the study by Paoli et al. (2013) (~7 mmHg) and the interval training group in the study
372 by Molman-Hansen et al. (2012) (12 mmHg). The significant reductions in SBP may be
373 explained in part by the reduction, albeit not significant, in systemic vascular resistance seen in
374 the HVCRT group. In contrast, increases in systemic vascular resistance, which did not reach
375 statistical significance, were observed in the TM and control groups. Several studies have
376 reported reductions in systemic vascular resistance following training in both healthy and
377 diseased older adults (Jennings et al. 1986, Hambrecht et al. 2000, Molmen-Hansen et al. 2012).

In agreement with our findings, reductions in SBP, reported by Molman-Hanset et al. (2012) occurred concomitantly with reductions in systemic vascular resistance. Jennings et al. (1986) related the effects of exercise on systemic vascular resistance to potential increases in the cross-sectional area of the vascular beds, particularly those affecting skeletal muscle, and alterations in sympathetic activity and circulating hormones.

Our findings that stroke volume and end-diastolic volume at rest increase with a corresponding decrease in systemic vascular resistance in the HVCRT group are supported by the work of Hambrecht et al. (2000), who reported that systemic vascular resistance and stroke volume at rest were inversely correlated ($r=-0.76$; $p < 0.001$) and that changes in systemic vascular resistance at rest were also significantly related to changes in end-diastolic volume ($r=0.45$, $p < 0.001$). These findings are similar to those obtained by Molmen-Hansen et al. (2012); however, these researchers employed high-intensity treadmill interval training, rather than resistance training. Although the two forms of exercise are different, the intensity pattern is arguably similar. HVCRT employs intervals of maximal effort using high-velocity repetitions, followed by short rest intervals similar to those utilized in their aerobic interval training protocol. Generally, with both training approaches the relative increase in HR and the duration of time that HR is elevated is similar. Thus, we hypothesize that while skeletal muscle adaptations may differ as a result of treadmill vs circuit resistance training, cardiac adaptations may be similar, resulting in similar increases in left-ventricular compliance and end-diastolic volume, and subsequent increases in stroke volume as described by the Frank-Starling mechanism. Our findings for ejection fraction are, however, in contrast to those of other exercise studies (Hambrecht et al. 2000, Molmen-Hansen et al. 2012). Although Molmen-Hansen et al. (2012) saw increases in stroke volume and end-diastolic volume in the interval training group, they also saw a significant increase in

401 ejection fraction. Similar findings for ejection fraction were reported by Hambrecht et al (2000);
402 however, their results were obtained from patients with chronic heart failure. Ejection fraction is
403 defined as stroke volume divided by end-diastolic volume; therefore, the larger improvements in
404 end-diastolic volume compared to stroke volume in our HVCRT group may provide an
405 explanation for a decreased ejection fraction. Similar results were observed for our TM group;
406 however, changes did not reach significance.

407 Another major finding in this study was that HVCRT and TM resulted significant
408 improvements in the CMS z score, which is reflective of a significant reduction in overall CMS
409 and CVD risk. Johnson et al. (2007) were the first to describe and use a CMS z score (described
410 as a MS z score in their work). In a subsequent publication from the Studies of a Targeted Risk
411 Reduction Intervention through Defined Exercise initiative, Bateman et al. (2011) reported no
412 significant changes in CMS z score due to their aerobic training intervention; however, a slight
413 increase was seen in their resistance training group. These findings vary from those of our study,
414 likely due to their use of a more traditional approach that employed 3 sets of 8-12 controlled
415 repetitions three days per week. Our HVCRT group provided an overload distinct from
416 traditional resistance training, where participants maintained an elevated HR and breathing rate,
417 and recovery-periods were kept relatively short, similar to patterns used during aerobic interval
418 training, but using both movement speed and submaximal loading to increase intensity.

419 There were no significant changes in blood lipid profile as a result of HVCRT. This
420 finding is not surprising as a review by Durstine et al. (2002) indicates the need for dietary
421 modifications and body weight loss as important factor for reducing LDL-C and total cholesterol
422 through training. These observations are also supported by Bouchonville et al. (2014) who found
423 superior improvements in cardiometabolic risk factors in an exercise and diet group when

compared to an exercise-only group. Durstine et al. (2002) also suggest that increases in HDL-C occur as a result of exercise prescriptions that elicit sufficiently high caloric expenditure. While we did not measure caloric expenditure for the TM or HVCRT groups, the greater mean exercising HR and longer total exercise time for each session may have resulted in an increased total energy expenditure for the TM group. Significant increases in HDL-C in the TM group coupled with no changes in total cholesterol provide an explanation for the significant reduction in the cholesterol/HDL ratio observed. The results for our HVCRT group are in contrast to those reported by Paoli et al.(2013); however, they are supported by similar findings in studies employing participants of a similar age (Marques et al. 2009) and participants with CMS (Bateman et al. 2011). Our findings demonstrating significant reductions in A1C for HVCRT and TM are consistent with previously reported results (Williams et al. 2007, Yavari et al. 2012); however, data for individuals without type-2 diabetes mellitus are sparse, making our findings unique to this population. Our findings showing a significant reduction in FG following HVCRT are novel, in that no other study, to our knowledge, has reported a similar impact following circuit resistance training or high-velocity exercise. This finding in conjunction with a significant reduction in A1C over control provides a strong argument for the use of HVCRT in lieu of TM.

Given the argument that FRS with has greater predictive value for identifying future risk for CVD and type-2 diabetes mellitus than CMS alone (Stern et al. 2004, Wannamethee et al. 2005), we included it as a separate component when assessing cardiometabolic risk. Our findings for FRS mirror those of the CMS *z* score with respect to within-group changes from baseline for HVCRT, showing a significant reduction in score. This finding was once again unique to the HVCRT group. Moreover, the reduction in FRS for the HVCRT group was significant when

447 compared to both the TM and control groups, a finding which was not present when evaluating
448 the CMS z score alone. The Framingham equation takes into account separate variables that are
449 not defining criteria for CMS; but nonetheless can significantly contribute to CVD risk.
450 Significant reductions in FRS for the HVCRT group may be explained, in part, by the significant
451 decrease in SBP. This decrease was not observed in the TM or control groups. Although the FRS
452 appears to be a better predictor of CVD risk, Wannamethee et al. (2005) suggest that the
453 presence of CMS may be a better predictor for type-2 diabetes mellitus. Therefore, the use of
454 both assessment tools may provide a more comprehensive and well-rounded assessment of
455 morbidity risk when multiple cardiometabolic risk factors are present.

456 The negative impact of CMS risk factors on HRQoL has been well-documented,
457 particularly their effects on emotional and psychological well-being (Sullivan et al. 2007, Oh et
458 al. 2010, Boylan and Ryff 2015). The RAND is a common tool used to assess HRQoL and can
459 also be utilized to detect changes in several dimensions of health and well-being as a result of an
460 exercise intervention. Our findings that both exercise protocols resulted in significant
461 improvements in Emotional-Well Being when compared to control are consistent with those
462 reported by Oh et al. (2010) and present another perspective on how meaningfully CMS and
463 CVD risk factors are to the predicted health of at-risk individuals. We believe that the relatively
464 short length of the intervention may not have been sufficient to alter some of the psychological
465 components assessed by the RAND, as Oh et al. (2010) conducted a six-month intervention
466 study and reported significant findings in many other components. Based on these and other's
467 findings, we believe that it is critical to continue to assess individual perception of overall health
468 and to include HRQoL due to the known connection between CMS risk and its associated
469 impact. Future studies should be conducted using similar interventions, but over a longer period

of time and should attempt to determine any relationships that may exist between improvements in physiological parameters and HRQoL.

Limitations

Possible limitations include a lack of blinded pretest and post-test assessments, with the exception of the blood markers. We understand that this introduces the potential for tester bias. Another limitation was the failure to use an intention-to-treat analysis. This was due to an inability to have those that withdrew from the study, return for post-testing. A lack of evenly distributed men and women in each group was another limitation in our study. However, concerning CVD risk, the FRS accounts for sex differences when determining future risk. Sex related differences in autonomic control of HR and BP have been previously noted, indicating that BP in some cases may be higher in post-menopausal women (Reckelhoff, 2004) and that regulation of SVR and HR may differ as well (Evans et al. 2001). However, by performing an ANCOVA, we have accounted for any baseline differences that may have been due to differences related to sex. The large number of outcome variables and the chosen statistical approach does increase the probability of Type 1 errors. This potentially could have been addressed by using a multivariate analysis of variance (MANOVA); however, this approach would not allow the level of precision when correcting for baseline values provide by our ANCOVA. ANCOVA is the preferred approach for analyzing randomized trials with baseline and follow-up measurements (Vickers and Altman, 2001).

HVCRT represents a novel training modality that successfully improved several CMS and CVD risk factors and reduced the predicted overall risk for CVD and type-2 diabetes mellitus in a population of older men and women. Furthermore, emotional well-being significantly improved in those that exercised compared to their non-exercising counterparts. For

individuals with multiple risk factors for CMS and CVD, it is important not only to assess physiological parameters such as blood markers and cardiovascular function, but also a composite CMS score, FRS, and an overall perception of health. While these factors alone can provide valuable prognostic information, assessing each of the three components should allow for a more thorough evaluation of any physical activity and/or pharmacological intervention.

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621

Table 1. Presence of Risk Factors among Participants

Percentage of Participants Meeting Risk Factor Criteria (%)			
	TM (n=8)	HVCRT (n=9)	CONT (n=7)
Age	100	100	100
BMI	63	89	43
WC	100	100	86
BP	25	78	43
FG	38	33	29
HA1C	38	78	71
TC	56	75	57
HDL-C	25	22	43
LDL-C	63	67	57
TGL	50	11	29
Smoker	0	13	0
Sedentary	100	100	100

BMI = body mass index; BP = blood pressure; FG = fasting blood glucose; HA1C = glycosylated hemoglobin A1C; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; TC = total cholesterol; TGL = triglyceride; WC = waist circumference.

628 Table 2. Baseline Participant Characteristics

	TM (n=8)	HVCRT (n=9)	CONT (n=7)
Age (yrs)	68 ± 3	72 ± 3	70 ± 3
Height (cm)	165 ± 3	167 ± 3	158 ± 3
Weight (kg)	85.6 ± 5.3	91.5 ± 3.0	78.3 ± 7.0
BMI	31.4 ± 1.5	33.0 ± 1.0	31.1 ± 2.4

629 Values ± SE; BMI = body mass index; CONT = control; HVCRT = high-velocity circuit
630 resistance training; TM = moderate-intensity treadmill training. No significant differences were
631 detected between groups.

632

Table 3. Energy Intake in Kilocalories

	Week One	Week Six	Week Twelve
TM	1377 ± 209	1528 ± 212	1470 ± 285
HVCRT	1923 ± 193	1706 ±196	1919 ±269
CONT	1680 ± 229	1819 ± 232	2017 ± 312

Values ± SE; CONT = control; HVCRT = high-velocity circuit resistance training; TM = moderate-intensity treadmill training. No significant differences were detected between groups.

637 Table 4. Baseline and change scores of primary outcome measures for cardiometabolic
638 syndrome

Outcome Measures	Baseline	12 Weeks	Adjusted Mean at 12 Weeks	Group Comparisons	Adjusted Mean Difference (95% CI)	<i>p</i>	Cohen's <i>d</i>
WC (cm)							
TM	104.9 ± 3.9	104.5 ± 4.0	103.4 ± 2.0	HVCRT – TM	-0.3 ± 2.7 (-7.3, 6.7)	0.99	0.15
HVCRT	107.4 ± 3.2	106.0 ± 2.6	103.1 ± 1.9	HVCRT – CONT	-1.4 ± 2.9 (-9, 6.2)	0.95	0.48
CONT	96.7 ± 8.6	99.6 ± 6.6	104.6 ± 2.2	TM – CONT	-1.1 ± 2.9 (-8.8, 6.5)	0.98	0.34
SBP (mmHg)							
TM	119.0 ± 4.6	115.6 ± 4.3	121.9 ± 2.4	HVCRT – TM	-10.0 ± 3.7 (-19.7, -0.4)	0.04*	0.36
HVCRT	139.2 ± 4.7	119.7 ± 3.4*	111.9 ± 2.4	HVCRT – CONT	-15.7 ± 3.6 (-25, -6.4)	0.01*	0.42
CONT	124.3 ± 5.8	124.7 ± 5.1	127.6 ± 2.5	TM – CONT	-5.7 ± 3.4 (-14.5, 3.1)	0.29	0.70
DBP (mmHg)							
TM	74.1 ± 4.4	73.1 ± 4.1	74.4 ± 1.9	HVCRT – TM	-6.7 ± 2.7 (-13.6, 0.2)	0.06	0.18
HVCRT	80.8 ± 2.9	71.3 ± 2.7*	67.6 ± 1.8	HVCRT – CONT	-10.3 ± 2.8 (-17.7, -2.9)	<0.01*	0.39
CONT	71.3 ± 4.2	74.6 ± 3.2	77.9 ± 2.0	TM – CONT	-3.6 ± 2.7 (-10.7, 3.6)	0.51	0.14
FG (mg/dL)							
TM	98.0 ± 14.9	88.9 ± 9.9	87.4 ± 5.9	HVCRT – TM	-1.1 ± 8.1 (-22.1, 20)	0.99	0.09
HVCRT	95.9 ± 7.3	86.9 ± 4.9*	86.3 ± 5.5	HVCRT – CONT	-7.8 ± 8.4 (-29.8, 14.1)	0.74	0.30
CONT	89.0 ± 7.7	91.9 ± 6.7	94.1 ± 6.3	TM – CONT	-6.8 ± 8.7 (-29.4, 15.9)	0.83	0.12
TGL (mg/dL)							
TM	147.5 ± 19.8	138.4 ± 19.9	128.0 ± 14.2	HVCRT – TM	-2.2 ± 19.6 (-53.3, 49)	0.99	0.44
HVCRT	127.9 ± 16.8	117.8 ± 11.3	125.8 ± 13.3	HVCRT – CONT	-18.5 ± 21.0 (-73.5, 36.5)	0.77	0.18
CONT	134.5 ± 30.4	142.5 ± 42.1	144.3 ± 16.3	TM – CONT	-16.3 ± 21.6 (-72.9, 40.2)	0.84	0.07
HDL-C (mg/dL)							
TM	51.5 ± 5.4	55.9 ± 6.6*	56.5 ± 2.6	HVCRT – TM	-0.4 ± 3.6 (-9.7, 8.9)	0.99	0.12
HVCRT	50.2 ± 3.0	54.1 ± 3.6	56.1 ± 2.5	HVCRT – CONT	-1.3 ± 3.9 (-11.5, 9)	0.99	0.56
CONT	55.7 ± 5.2	61.2 ± 6.2	57.4 ± 3.0	TM – CONT	-0.9 ± 4.0 (-11.3, 9.6)	0.99	0.34
FRS (%)							
TM	7.9 ± 2.5	7.0 ± 2.5	7.9 ± 0.8	HVCRT – TM	-3.0 ± 1.1 (-5.8, -0.2)	0.03*	0.00
HVCRT	11.4 ± 1.7	7.0 ± 1.3*	4.9 ± 0.7	HVCRT – CONT	-3.3 ± 1.2 (-6.4, -0.2)	0.03*	0.18
CONT	6.5 ± 2.3	6.2 ± 2.2	8.2 ± 0.9	TM – CONT	-0.3 ± 1.0 (-3.3, 2.7)	0.99	0.13
CMS-z Score							
TM	-0.9 ± 1.2	-2.8 ± 1.2	-2.7 ± 0.6	HVCRT – TM	-1.4 ± 0.8 (-3.4, 0.7)	0.25	0.20
HVCRT	-0.2 ± 0.6	-3.4 ± 0.7*	-4.1 ± 0.5	HVCRT – CONT	-2.8 ± 0.9 (-5.1, -0.5)	0.02*	0.29
CONT	-2.0 ± 1.5	-2.4 ± 1.7	-1.3 ± 0.7	TM – CONT	-1.4 ± 0.9 (-3.7, 0.9)	0.34	0.10

639 Values $\pm$ SE, unless otherwise stated; * $p \leq 0.05$; 95% confidence interval (CI) are derived from
640 analysis of covariance, adjusted for baseline level. CMS = cardiometabolic syndrome; CONT =
641 control; DBP = diastolic blood pressure; FG = fasting glucose; FRS = Framingham risk score;
642 HDL-C = high density lipoprotein cholesterol; HVCRT = high-velocity circuit resistance
643 training; LDL-C = low density lipoprotein cholesterol; SBP = systolic blood pressure; TGL =
644 triglycerides; TM = moderate-intensity treadmill training; WC = waist circumference.

645

Draft

FIGURE CAPTIONS

Figure 1. Participant flow through the study.

Figure 2. Mean change in CMS criteria. (a) Waist circumference, (b) Cardiometabolic syndrome *z* score, (c) Systolic blood pressure, (d) Diastolic blood pressure, (e) Mean arterial pressure, (f) Fasting blood glucose, (g) High-density lipoprotein cholesterol, and (h) Triglyceride. HVCRT: high-velocity circuit resistance training; TM: moderate-intensity treadmill training; CONT: no-exercise. Values $\pm$ SE.* Significantly different from baseline, $p \leq 0.05$.

Figure 3. Effect of exercise modes on hemodynamic variables. (a) Systemic vascular resistance, (b) Stroke volume, (c) End diastolic volume, (d) Ejection fraction. HVCRT: high-velocity circuit resistance training; TM: moderate-intensity treadmill training; CONT: no-exercise. Values $\pm$ SE.* Significantly different from baseline, $p \leq 0.05$.

Figure 1. Participant flow through the study.

279x362mm (300 x 300 DPI)