

# Change in Metabolic Syndrome and Cardiorespiratory Fitness Following Exercise Training – The Ball State Adult Fitness Longitudinal Lifestyle Study (BALL ST)

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**Purpose:** To evaluate how the changes in directly measured cardiorespiratory fitness (CRF) relate to the changes in metabolic syndrome (MetS) status following 4–6 months of exercise training.

**Methods:** Maximal cardiopulmonary exercise (CPX) tests and MetS risk factors were analyzed prospectively from 336 adults (46% women) aged  $45.8 \pm 10.9$  years. MetS was defined according to the National Cholesterol Education Program-Adult Treatment Panel III criteria, as updated by the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI). Pearson correlations, chi-squares, and dependent 2-tail t-tests were used to assess the relationship between the change in CRF and the change in MetS risk factors, overall number of MetS risk factors, and a MetS severity score following 4–6 months of participation in a self-referred, community-based exercise program.

**Results:** Overall prevalence of MetS decreased from 23% to 14% following the exercise program ( $P < 0.05$ ), while CRF improved 15% ( $4.7 \pm 8.4$  mL/kg/min,  $P < 0.05$ ). Following exercise training, the number of positive risk factors declined from  $1.4 \pm 1.3$  to  $1.2 \pm 1.2$  in the overall cohort ( $P < 0.05$ ). The change in CRF was inversely related to the change in the overall number of MetS risk factors ( $r = -0.22$ ;  $P < 0.05$ ) and the MetS severity score ( $r = -0.28$ ;  $p < 0.05$ ).

**Conclusion:** This observational cohort study indicates an inverse relationship between the change in CRF and the change in MetS severity following exercise training. These results suggest that participation in a community-based exercise program yields significant improvements in CRF, MetS risk factors, the prevalence of the binary MetS, and the MetS severity score. Improvement in CRF through exercise training should be a primary prevention strategy for MetS.

**Keywords:** cardiorespiratory fitness, metabolic syndrome, exercise training, abdominal obesity

## Introduction

Metabolic Syndrome (MetS) is defined as the clustering of multiple risk factors associated with an increased risk for cardiovascular disease (CVD) and type II diabetes.<sup>1</sup> The metabolic disorder was first described by Reaven in 1988 as “Syndrome X”<sup>2</sup> which was characterized by insulin resistance and hyperinsulinemia resulting in additional metabolic and hemodynamic abnormalities. The metabolic risk factors associated with MetS are commonly recognized as dyslipidemia (high fasting triglycerides and depressed HDL), hypertension, elevated plasma glucose, and abdominal obesity. MetS affects roughly one-third of the US population and has been linked to an increased risk of chronic disease, placing a significant burden on the US health-care system and economy.<sup>3</sup> The prevalence has been observed to be 65% in cardiac rehabilitation populations.<sup>4</sup>

Traditionally, the MetS risk factors have been viewed as a set of binary variables with measurement thresholds that were based on established opinion.<sup>1</sup> However, a continuous scale methodology using the sum of risk factor Z scores was recommended by Brage et al<sup>5</sup> with children, and this concept was employed in adults by Franks et al<sup>6</sup> and others.<sup>7–11</sup> The MetS Z score equations in each study were generated using within study subject data for the risk factors. DeBoer and Gurka<sup>11</sup> proposed a set of continuous scale risk factor equations based on data from the National Health and Nutrition Examination Survey (NHANES). Use of these equations could help transition MetS analyses from a binary to continuous scale, and use of equations from NHANES may prove more appropriate for the general population.

Substantial evidence supports the beneficial effects of exercise training or enhanced cardiorespiratory fitness (CRF) on the individual<sup>12–15</sup> and collective MetS risk factors,<sup>16</sup> including lowering blood pressure (BP) and improving BP control, regulating fat and glucose metabolism, and also increasing insulin action. Numerous cross-sectional and prospective cohort studies have associated presence or development of MetS with a more sedentary lifestyle,<sup>17–20</sup> and/or low CRF.<sup>21–25</sup> Kelley et al found that individuals with low CRF in the Ball State Adult Fitness Longitudinal Lifestyle Study (BALL ST) cohort were 20 times more likely to have MetS, compared to the most-fit individuals.<sup>25</sup>

Adoption of a regular exercise routine,<sup>26–29</sup> and/or improvements in CRF through regular exercise training<sup>23</sup> have been shown to reduce both individual and collective risk factors associated with MetS. A report from the HERITAGE Family Study showed exercise training three times per week on a leg cycle ergometer resulted in a significant drop in the number of individuals with MetS (16.9% to 11.8%).<sup>26</sup> Dalleck et al reported that a community-based exercise training program resulted in a significant reduction in prevalence of MetS after training (22.3% to 13.5%).<sup>27</sup> While these studies showed favorable results on MetS risk factors, they employed a binary version of the MetS, and there were significant differences across studies in risk factors and testing/training procedures.

Research examining the influence of the change in directly measured CRF following exercise training on the change in collective MetS risk factors is limited. Therefore, the purpose of this study was to evaluate whether the changes in CRF were associated with the changes in MetS status and severity following 4–6 months of exercise training. The study hypothesis is that the change in the MetS Z score following training will be related to the change in CRF.

## Methodology

### Subjects and Study Design

Subjects completed laboratory assessments as part of BALL ST, an ongoing population-based program initiated in 1970 to promote healthy lifestyles and physical fitness. This was a retrospective analysis of individuals who completed 4–6 months of exercise training between 1970 and 2018. All participants provided written informed consent for their information to be used for research. This analysis included 336 self-referred, middle-aged adult men (n = 183) and women (n = 153) who completed fitness assessments, including a maximal cardiopulmonary exercise test (CPX) before and after exercise training. Inclusion criteria consisted of being  $\geq 18$  years of age, having complete data for all MetS risk factors (see below), and attainment of  $\geq 1.0$  respiratory exchange ratio during both CPX. All subjects volunteered to engaged in the program, completed a Ball State University approved informed consent prior to testing and training, and all data were de-identified therefore the Ball State University Institutional Review Board determined the study to be “exempt”. This research was conducted in accordance with the Declaration of Helsinki.

### Clinical Measurements

All subjects were instructed to continue their regular medication routines, as well as refrain from exercise, caffeine, food, and alcohol for 12 hours prior to laboratory testing. Subjects completed a health history questionnaire, which provided self-reported information about medical history, lifestyle habits (eg, smoking, physical activity, diet, etc.), and medications.<sup>30</sup> For analyses purposes, cigarette smoking was characterized as either current or non-smoker. Each subject then completed a series of assessments including anthropometric measurements (height, weight, waist circumference), body composition, resting heart rate (HR) and blood pressure (BP), fasting blood chemistry, and a resting 12-lead electrocardiogram. Standardized laboratory techniques were used for all assessments and have been described in detail elsewhere.<sup>30–32</sup>

## Metabolic Markers

Metabolic syndrome risk factors were measured pre- and post-training and defined according to the National Cholesterol Education Program (NCEP-ATP III as updated by the AHA/NHLBI).<sup>1,33</sup> Markers and thresholds included abdominal obesity (AO) (Waist circumference (WC)  $\geq 102$  cm for men or  $\geq 88$  cm for women), elevated fasting plasma triglycerides ( $\geq 150$  mg/dL), low HDL-C ( $< 40$  mg/dL for men or  $< 50$  mg/dL for women), elevated fasting plasma glucose (FBG) ( $\geq 100$  mg/dL), hypertension ( $\geq 130$  mm Hg systolic BP or 85 mmHg diastolic BP), or pharmacologic treatment for diagnosed hypertriglyceridemia, low HDL-C, diabetes, or hypertension. WC was taken in the horizontal plane at the smallest circumference in the abdominal region, generally 2–4 inches above the umbilicus. Plasma lipids were measured following a 12-hr fast, and resting BP was measured in the seated position following  $\geq 5$ -minutes of rest. A minimum of two BP measurements were recorded, with an additional measurement taken if the 2nd differed from the first by  $\geq 6/4$  mmHg for systolic or diastolic BP, respectively. The present study employed both binary and continuous scale metrics of MetS, with a severity score<sup>11</sup> serving as the continuous variable.

## Exercise Testing and Cardiorespiratory Fitness

All subjects completed a maximal CPX on a treadmill as part of their physical examination. Exercise test protocols varied and included Bruce,<sup>34</sup> BSU Bruce Ramp,<sup>35</sup> modified Balke<sup>36</sup> or other non-standardized protocols. In most cases, selection of test protocol was individualized, based on subject characteristics, with a goal to achieve maximal effort within 8–12 minutes. Subjects were asked to refrain from structured exercise the day of testing. Exercise HR was measured using electrocardiography and recorded each minute, at peak exercise, and during recovery from the exercise test. Exercise BPs were monitored manually during exercise and recovery. Gas exchange data were collected using open circuit spirometry with methods described previously.<sup>30,32</sup> Standardized procedures for metabolic cart calibration were followed for all tests, and CPXs were supervised by clinical exercise physiologists, with additional medical supervision when appropriate.<sup>37</sup> Subjects were verbally encouraged to exercise to volitional fatigue. CRF was indicated by  $VO_{2peak}$ , defined as the average of 2 or 3 consecutive  $VO_2$  values within 2 mL/kg/min, typically occurring in the last 2 minutes of the CPX.

## Exercise Training

Following the initial laboratory assessment, each subject engaged in an individualized exercise training program described previously.<sup>38</sup> In brief, exercise training consisted of aerobic exercise at least 4 days per week, for approximately 45 minutes, at an intensity equal to approximately 50–80% of pretraining  $VO_{2peak}$ . Adherence to 4 days per week represented inclusion criteria for the second laboratory assessment. Exercise training intensity was monitored using a target HR which was assessed several times per session. The standard training period was 4–6 months. The exercise routine was progressive in nature, following national guidelines.<sup>37</sup> The second laboratory assessment was completed following completion of the exercise training program. As with testing, subjects were instructed to take their medications as normal throughout the exercise program. The fundamental goals of the exercise training program were improvement of CRF.

## Statistical Analysis

As the operational definition of the MetS includes  $\geq 3$  abnormal risk factors or the use of medication to control the risk factor, we defined the incidence of MetS using both criteria. However, we assessed the exercise training adaptation using the measured score for each risk factor. Analyses were performed in R version 3.6.3 (R Core Team, Vienna, Austria). Descriptive statistics are reported to summarize pre- and post-training characteristics of the participants. We used repeated measures ANOVA test to examine gender and/or time differences in changes in CRF and MetS risk factors across the training program. Chi-squared tests were also performed when appropriate for the comparisons. The linear associations between the change in CRF and the change in the measured risk factor values were assessed using Pearson product-moment correlations. Pearson correlations were also determined to examine the linear associations between the change in CRF and the change in the number of MetS risk factors, as well as the overall MetS severity score.<sup>11</sup> The correlation coefficients were compared between sexes using the Fisher's transformation in the "cocor" package in

R. Cohen's *d* effect sizes were calculated to examine the standardized difference between means pre/post. Statistical significance was set at  $P < 0.05$ .

## Results

Baseline and follow-up data for risk factors, prevalence of the MetS, the severity score, and CRF are presented in Table 1, Supplementary Tables 1 and 2. The pretraining CRF reflected a cohort that was below the national average for sex and age-matched men and women from the FRIEND database (46th percentile).<sup>39</sup> Twenty-three percent of the cohort had MetS at baseline and there was a significant difference between men (30%) and women (15%) ( $P < 0.05$ ). The baseline number of MetS risk factors for the cohort was  $1.4 \pm 1.3$ , with men having a greater number of MetS risk factors compared to women ( $1.7 \pm 1.4$  and  $1.1 \pm 1.2$ , respectively;  $P < 0.05$ ).

Following an average of  $5.1 \pm 1.3$  months of structured exercise training, the cohort averaged a 15% improvement in CRF (men  $5.0 \pm 4.9$  mL/kg/min; women  $4.3 \pm 3.8$  mL/kg/min), while total body weight was reduced by  $2.4 \pm 4.3$  kg (men  $2.7 \pm 4.2$  kg; women  $2.1 \pm 4.3$  kg) ( $P < 0.05$ ). Using data from the FRIEND Registry,<sup>39</sup> the cohort improved CRF from the 46th percentile at baseline to the 65th percentile following the exercise training program ( $P < 0.05$ ). These changes are within the expected ranges for these variables after exercise training.<sup>37</sup>

Following exercise training, the overall prevalence of MetS (ie, binary variable) decreased from 23% to 14% ( $P < 0.05$ ) (Table 1). The number of overall positive MetS risk factors declined 14% for the whole cohort (1.4 to 1.2), and also decreased significantly within both sexes (Table 1) ( $P < 0.05$ ). As shown in Table 1, all risk factors except FBG were improved following exercise training for the whole cohort ( $P < 0.05$ ). The mean FBG was within the normal range for both men and women at baseline, and this did not further improve following training. Table 2 shows the changes in prevalence of

**Table 1** Changes in Metabolic Risk Factors and Measures of CRF Following Training. (Mean  $\pm$  S.D.)

Characteristic	Men (n = 183)		Women (n = 153)		Total (n = 336)	
	Baseline	Post-Training	Baseline	Post-Training	Baseline	Post-Training
Age (years)	45.9 $\pm$ 10.6		45.7 $\pm$ 11.2		45.8 $\pm$ 10.9	
Body Weight (kg)	86.7 $\pm$ 13.7	84.0 $\pm$ 12.9*	72.7 $\pm$ 16.8 <sup>†</sup>	70.6 $\pm$ 15.3* <sup>†</sup>	80.3 $\pm$ 16.7	77.9 $\pm$ 15.5*
BMI (kg/m <sup>2</sup> )	27.1 $\pm$ 4.1	26.2 $\pm$ 3.8*	26.7 $\pm$ 6.1	25.8 $\pm$ 5.5*	26.9 $\pm$ 5.1	26.0 $\pm$ 4.7*
Fasting Blood Glucose (mg/dL)	97.3 $\pm$ 17.8	98.8 $\pm$ 12.4	92.1 $\pm$ 11.6 <sup>†</sup>	93.5 $\pm$ 14.1 <sup>†</sup>	94.9 $\pm$ 12.5	96.4 $\pm$ 13.5*
Waist Circumference (cm)	96.0 $\pm$ 10.5	92.7 $\pm$ 9.4*	81.8 $\pm$ 13.5 <sup>†</sup>	79.8 $\pm$ 12.6* <sup>†</sup>	89.5 $\pm$ 13.9	86.8 $\pm$ 12.7*
Resting sBP (mmHg)	123.0 $\pm$ 11.9	118.3 $\pm$ 11.8*	118.0 $\pm$ 13.9 <sup>†</sup>	114.0 $\pm$ 12.5* <sup>†</sup>	120.8 $\pm$ 13.1	116.3 $\pm$ 12.3*
Resting dBP (mmHg)	80.7 $\pm$ 8.6	77.2 $\pm$ 9.2*	75.9 $\pm$ 10.4 <sup>†</sup>	73.4 $\pm$ 10.2* <sup>†</sup>	78.5 $\pm$ 9.7	75.5 $\pm$ 9.8*
HDL-C (mg/dL)	45.4 $\pm$ 10.6	49.0 $\pm$ 12.3*	59.7 $\pm$ 14.4 <sup>†</sup>	59.8 $\pm$ 13.7 <sup>†</sup>	51.9 $\pm$ 14.5	53.9 $\pm$ 14.0*
Triglycerides (mg/dL)	131.2 $\pm$ 70.3	118.2 $\pm$ 63.0*	95.2 $\pm$ 46.3 <sup>†</sup>	90.9 $\pm$ 37.2 <sup>†</sup>	114.8 $\pm$ 63.1	105.8 $\pm$ 54.5*
MS Risk Factors (#)	1.7 $\pm$ 1.4	1.4 $\pm$ 1.2*	1.1 $\pm$ 1.2 <sup>†</sup>	0.9 $\pm$ 1.1* <sup>†</sup>	1.4 $\pm$ 1.3	1.2 $\pm$ 1.2*
CRF (mL/kg/min)	35.5 $\pm$ 7.8	40.5 $\pm$ 8.0*	26.7 $\pm$ 6.2 <sup>†</sup>	31.1 $\pm$ 7.0* <sup>†</sup>	31.5 $\pm$ 8.3	36.2 $\pm$ 8.9*
FRIEND (%)	43.3 $\pm$ 23.5	61.4 $\pm$ 22.1*	49.4 $\pm$ 25.2 <sup>†</sup>	68.3 $\pm$ 21.4* <sup>†</sup>	46.4 $\pm$ 24.4	64.5 $\pm$ 22.0*
MetS Prevalence (%)	30	17*	15 <sup>†</sup>	9* <sup>†</sup>	23	14*
MetS Severity Score	0.145 $\pm$ 0.661	-0.070 $\pm$ 0.635*	-0.566 $\pm$ 0.755 <sup>†</sup>	-0.623 $\pm$ 0.700 <sup>†</sup>	-0.179 $\pm$ 0.789	-0.332 $\pm$ 0.719*
Change in MetS Severity Score (%)	-148		-10		-79	

**Notes:** \*Denotes a significant difference from baseline ( $P < 0.05$ ), <sup>†</sup>Denotes a significant difference from men at the respective baseline/post-training test ( $P < 0.05$ ), <sup>‡</sup>Denotes the degree of change from baseline to post-training was significantly different compared to men ( $P < 0.05$ ).

**Abbreviations:** BMI, body mass index; sBP, systolic blood pressure; dBP, diastolic blood pressure; HDL-C, high-density lipoprotein-cholesterol; CRF, cardiorespiratory fitness; FRIEND, fitness registry and the importance of exercise national database; MetS, metabolic syndrome.

**Table 2** Change in Prevalence of MS Risk Factors Following Exercise Training Using NCEP/ATP III Thresholds – N (%)

MS Risk Factor	Men		Women		Total	
	Baseline	Post-Training	Baseline	Post-Training	Baseline	Post-Training
Abdominal Obesity	47 (26)	31 (17)*	42 (27)	31 (20)*	89 (26)	62 (18)*
Impaired Fasting Glucose	71 (39)	79 (43)	29 (19) <sup>†</sup>	32 (21) <sup>†</sup>	100 (30)	111 (33)
Hypertension	86 (47)	61 (33)*	44 (29) <sup>†</sup>	31 (20)* <sup>†</sup>	130 (39)	92 (27)*
Low HDL-C	55 (30)	42 (23)*	40 (26)	40 (26)	95 (28)	82 (24)
Elevated Triglycerides	55 (30)	45 (25)	18 (12) <sup>†</sup>	11 (7) <sup>†</sup>	73 (22)	56 (17)*

**Notes:** \*Denotes a significant difference from baseline ( $P < 0.05$ ), <sup>†</sup>Denotes a significant difference from men at the respective baseline/post-training test ( $P < 0.05$ ).

**Abbreviations:** HDL-C, high-density lipoprotein-cholesterol; MetS, metabolic syndrome.

**Table 3** Pearson Correlations Between Change in CRF and Change in MetS Risk Factors

	Men	Women	Total
Abdominal Obesity	−0.43*	−0.24* <sup>†</sup>	−0.36*
Impaired Fasting Glucose	−0.04	−0.10	−0.06
Resting Systolic BP	−0.03	0.09	0.02
Resting Diastolic BP	−0.15*	−0.00	−0.09
Low HDL-C	0.17*	0.13	0.17*
Elevated Triglycerides	−0.24*	−0.14	−0.21*
Number of MetS Risk Factors	−0.22*	−0.20*	−0.22*
MetS Severity Score	−0.33*	−0.18*	−0.28*

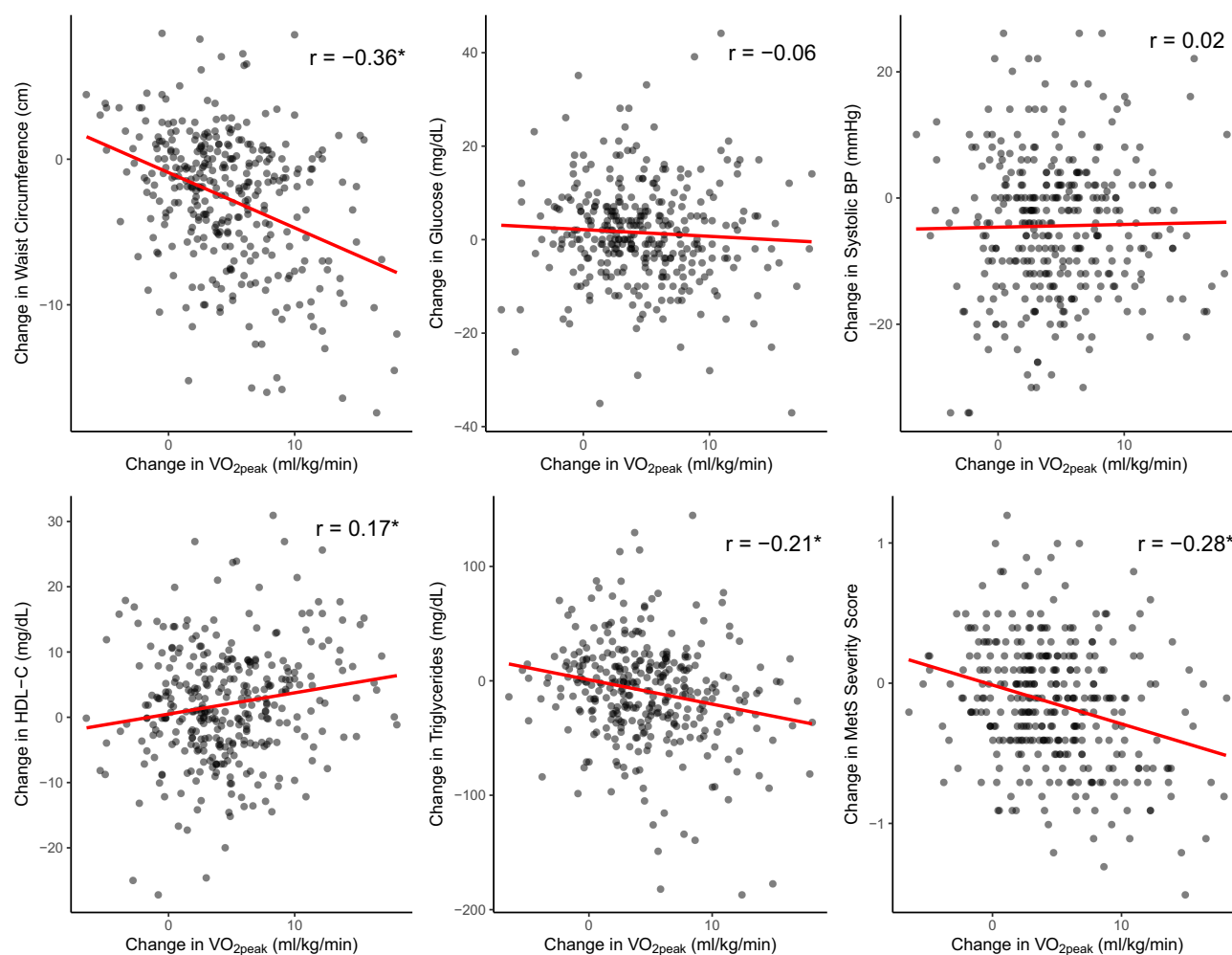
**Notes:** \*Denotes a significant relationship ( $P < 0.05$ ), <sup>†</sup>Denotes a significantly different correlation coefficient compared to men ( $P < 0.05$ ).

the individual risk factors when employing the binary NCEP/ATP MetS thresholds. A significant change in classification for abdominal obesity, hypertension, and serum triglycerides was observed following exercise training ( $P < 0.05$ ). There was a significant improvement in the continuous MetS severity score within the whole cohort (−79%) and for men (−149%) but not for women (−10%) (Table 1) ( $P < 0.05$ ).

The relationship between exercise-training-induced change in CRF and changes in the MetS risk factors and severity scores is presented in Table 3 and Figure 1. The primary study hypothesis was that the change in MetS severity score (Z score) following exercise training would be related to the change in CRF. As shown in Table 3, the overall correlation was −0.28 ( $P < 0.05$ ), and it was statistically significant for both men and women ( $P < 0.05$ ). Furthermore, for the overall cohort, improvements in CRF following the training program were correlated with favorable changes in abdominal obesity, serum triglycerides, HDL-C, and the number of MetS risk factors. The correlation between change in CRF and change in abdominal obesity was stronger for men compared to women (Table 3) ( $P < 0.05$ ).

## Discussion

The major finding of this study was the inverse association between the improvement in directly measured CRF and the overall reduction in the MetS severity score following exercise training. The improvement of CRF was inversely related to both the change in the number of abnormal MetS risk factors (binary thresholds), and to the MetS severity score as constructed using the equations from DeBoer and Gurka.<sup>11</sup> The mean cohort scores for most MetS risk factors were considered within normal limits at entry into the program, however there was significant variability in these scores, with almost two-thirds of participants possessing values below thresholds used in defining binary MetS.<sup>1</sup> Only 23% of the subjects in the present study met the binary criteria for MetS at baseline. This is lower than the 34% prevalence estimate



**Figure 1** Scatter plots of change in CRF and change in MetS risk factors and MetS severity score. \*Denotes a significant correlation coefficient.

of MetS for the adult population in the United States.<sup>3</sup> The lower prevalence in the present study is likely related to the self-referred cohort. However, even with a lower prevalence, the improvement in CRF following the exercise program was associated with a significant decline in binary MetS, and a 79% reduction in the severity score. As the majority of our cohort did not meet the binary threshold for MetS, the changes in the severity scores may help to identify a group of individuals that can benefit from exercise training and more aggressive risk factor reduction prior to development of the binary MetS.

A reduction in the incidence of MetS following formal exercise training is not a new finding as others have reported this following exercise training and/or secondary to an improved CRF following training.<sup>8,16,26–29</sup> Myers et al reviewed a large number of studies and concluded that regular exercise training and/or improvement in CRF was beneficially related to both the incidence and prevalence of the MetS.<sup>16</sup> The exercise training intervention trials reviewed by Myers et al had significant differences in cohort characteristics, prevalence of MetS at pre- and post-training, and different exercise training regimens. Regardless of these differences, each study that incorporated a measure of CRF concluded that regular exercise training improved CRF and reduced the incidence of MetS, demonstrating the powerful benefits of exercise training and improving CRF across diverse populations.

Two of these studies characterized their cohort's MetS status before and after training using a version of a continuous scale metric (Z-score). Johnson et al<sup>8</sup> used an overweight sample ( $n = 117$ ; age 40–65 yr) from the STRRIDE trial that exercise trained for 6 months. Forty percent of the subjects met the binary MetS criteria at baseline. The investigators reported that moderate-intensity continuous exercise training (40–55% VO<sub>2peak</sub>) was associated with improvements in

MetS binary status and Z-score. Morales-Palomo et al<sup>28</sup> recruited an older group ( $n = 121$ ; mean age 58 yr) with binary MetS and randomly assigned them to one of four groups. Subjects exercise trained 3 days per week for 4 months on stationary leg cycle ergometers. Exercise training groups included one that engaged in moderate continuous training, two that engaged in different versions of high-intensity interval training (HIIT), and a control group. The authors reported that their post-training MetS Z-scores were significantly lower (better) for their moderate continuous training ( $-52\%$ ) and longer HIIT training ( $-41\%$ ) groups. Strengths of the above studies included women, adequate exercise training regimens, and directly measured CRF, and a continuous scale MetS metric. However, it should be noted that both used Z scores developed within their own samples, and used mean arterial pressure (MAP) as opposed to resting systolic pressure. The present investigation used the Z score developed on the NHANES study group,<sup>11</sup> and resting systolic pressure in the MetS Z score. The use of the NHANES data for development of the Z score formula within the present study should enhance generalizability of the results.

The cohorts studied by Johnson et al<sup>8</sup> and Morales-Palomo et al<sup>28</sup> had higher MetS risk factor measurements at baseline compared to the cohort in the present study. Their cohorts were older (mean age  $\approx 8$  + yrs older) so may have had more years to accumulate the metabolic abnormalities.<sup>10</sup> Some of the subjects in the present study were taking medications related to controlling MetS risk factors (eg, 13% taking antihypertensives, 7% dyslipidemics, and  $<1\%$  hyperglycemics), and these medications could have affected exercise training and MetS results. Morales-Palomo<sup>28</sup> reported a significantly higher use of medications related to MetS risk factors in their cohort ( $\geq 60\%$  on hypertensive;  $\geq 22\%$  on glucose lowering, etc), whereas Johnson et al<sup>8</sup> recruited subjects that were not on medications common to the MetS. These significant differences among the studies in medication usage are a factor that should not be taken lightly, but as each study showed improvements in CRF and MetS severity scores, the influence of medications may be less important. Suffice it to say that the use of medications in the present study, and in that by Morales-Palomo, are likely similar to that seen in the general population, and furthermore, did not prevent the overall improvements in the MetS observed in these studies following exercise training.

National datasets have suggested that the MetS is a considerable health-care problem for both adult men and women,<sup>3,40</sup> but the more recent analysis suggested women may have a higher prevalence compared to men (35.6% compared to 30.3%).<sup>3</sup> As shown in Table 1, the present study had a higher incidence of binary MetS in men compared to women who referred themselves into the community-based exercise program between 1970 and 2019. The men in the present study also had more abnormal risk factors compared to women (Tables 1 and 2). This sex difference was also reported by Johnson et al for prevalence of MetS and levels of individual risk factors at baseline and follow-up.<sup>8</sup> The present analyses included a cohort that was self-referred, so these sex differences are not intended to match national norms, nor are they particularly critical to the overall results of the study.

The reduction in incidence of binary MetS and the severity scores following  $\sim 4$ –6 months of exercise training has clinical importance in that these risk factors are highly associated with non-communicable disease and premature mortality.<sup>41</sup> The severity of metabolic risk factors as assessed using the MetS severity score increases over time within individuals and predicts diagnosis of ATP-III MetS.<sup>10</sup> As a result, clinicians should prescribe exercise as a therapeutic modality to improve health and longevity, especially as MetS prevalence increases on the national scale. While the results of the present study align with previous research documenting an inverse relationship between the change in CRF and change in prevalence of MetS,<sup>8,26,28,29</sup> the current study adds additional information about the improvement in a continuous scale MetS severity score in a self-referred adult population that included both men and women, and across a wide age range (21–78 yr).

This study was not without limitations, as it was retrospective in design and did not include a non-exercise control group. While some of the most relevant literature included studies with non-exercise control groups,<sup>8,28,29</sup> other papers did not mention control groups.<sup>26,27</sup> As our report comes from a longitudinal cohort where individuals were tested at different times, we did not have a non-exercise control group across the decades. Although, subjects' baseline measurements were compared to the training response, therefore serving as their own control. We do not feel that the omission of a non-exercise control group diminishes our findings. Furthermore, as mentioned in the methods section, this report included only those participants who completed approximately 4 training sessions per week during the training program. While subjects were encouraged to consume a heart-healthy diet while in the program, there was no formal monitoring of this. It is possible that some subjects started the exercise

program with a heart-healthy diet, or modified their diets during the program, but there are no nutritional data for analysis. As some of the cohort completed the exercise program before the invention of physical activity monitors, the present study focused on the improvement in  $\text{VO}_{2\text{peak}}$  and risk factors for those who completed the formal exercise program. It is likely that some subjects participated in physical activities (eg, recreational sports, walking a pet in the neighborhood, etc.) outside of the formal exercise training, but this was not captured for analyses of overall physical activity. It should also be mentioned that our cohort consisted of a predominantly white (99%) population. As a result, our findings may not be generalizable to other racial groups. We also acknowledge that there were several metabolic systems used across the study period (1970–2018) but the metabolic system used for each subject was the same. Finally, some participants in the BALLST cohort may have also participated in resistance training, which has also been shown to favorably influence MetS,<sup>42</sup> but resistance training equipment was not available within the program during the years when ~ 75% of the subjects completed their training. Therefore, while it is possible that subjects who completed any additional resistance training may have incurred additional beneficial changes in CVD risk factors, a parsing of these results is not possible.

## Conclusion

The change in CRF was inversely associated with the change in binary MetS status and the MetS severity score in this cohort of adult men and women following 4–6 months of participation in an exercise training program. Overall, the exercise training program resulted in a significant improvement in CRF. Further, positive changes in CRF were significantly associated with improvements in abdominal obesity, HDL-C, and serum triglycerides.

In conclusion, the results of this study demonstrate that participating in a community-based exercise program yields significant improvements in CRF, the MetS risk factors, prevalence of the MetS, and the MetS severity score. Given the strong evidence supporting the health benefits of CRF, exercise should be highly emphasized as a primary prevention strategy for MetS, the associated risk of chronic disease, and mortality.<sup>15</sup> Future research should assess the relationship between differences in exercise volume and its associations with changes in measured CRF and MetS risk factors.

## Disclosure

The authors report no conflicts of interest in this work.

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