

Cardiorespiratory Fitness Is Inversely Associated With Clustering of Metabolic Syndrome Risk Factors: The Ball State Adult Fitness Program Longitudinal Lifestyle Study

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Abstract

Objective: The focus of this study was the association between the metabolic syndrome (MetSyn) and cardiorespiratory fitness (CRF) defined as maximal oxygen uptake (VO_{2max}). Although previous research has shown a relationship between MetSyn and CRF, most studies are based on *less objective* measures of CRF and different cardiometabolic risk factor *thresholds* from earlier guidelines.

Participants and Methods: The metabolic markers included in the present study were central obesity, elevated plasma triglycerides, elevated fasting high-density lipoprotein cholesterol, impaired fasting plasma glucose, hypertension, or pharmacologic treatment for diagnosed hypertension, hypertriglyceridemia, low high-density lipoprotein cholesterol, or diabetes. A cohort of 3636 adults (1629 women, 2007 men; mean \pm SD age, 44.7 \pm 12.3 years) completed CRF and metabolic risk factor assessment between January 1, 1971, and November 1, 2016. The CRF was defined as a measured VO_{2max} from a cardiopulmonary exercise test on a treadmill, with a respiratory exchange ratio value of 1.0 or more.

Results: Prevalence of MetSyn (\geq 3 factors) was 26% (n=953) in the cohort, with men having a greater likelihood for MetSyn compared with women (*P*<.001). The difference in VO_{2max} between those individuals with MetSyn and those without was approximately 2.3 (2.0-2.5) metabolic equivalents. Logistic regression analyses showed a significant inverse and graded association between quartiles of CRF and MetSyn for the group overall (*P*<.001), with odds ratios (95% CI) using the lowest fitness group as the referent group of 0.67 (0.55-0.81), 0.41 (0.34-0.51), and 0.10 (0.07-0.14) for VO_{2max} (*P*<.001). The sex-specific odds ratios were 0.25 (0.18-0.34), 0.05 (0.02-0.10), and 0.02 (0.01-0.09) for women and 0.43 (0.31-0.59), 0.19 (0.14-0.27), and 0.03 (0.02-0.05) for men (*P*<.001).

Conclusion: These results with current risk factor thresholds and a large number of women demonstrate that low VO_{2max} is associated with MetSyn.

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he metabolic syndrome (MetSyn) is a high-risk phenotype characterized by the combination of cardiometabolic risk factors, including obesity, dyslipidemia, hypertension, impaired fasting glucose, proinflammatory state, and a prothrombotic state.¹ First described by Reaven,² MetSyn is believed to be a common physiologic predecessor for chronic diseases including cardiovascular disease,³⁻⁵ type 2 diabetes mellitus,⁶ and premature mortality.^{4,7} Defining criteria for MetSyn have been established by multiple agencies over time,^{1,8-11} but the most frequently used are those published by the National Cholesterol Education Program (NCEP)/Adult Treatment Panel¹² and the International Diabetes Foundation.^{9,11} The prevalence of MetSyn has varied as a function of the defining criteria,¹³ but it has been reported to exist in one-fourth to one-third of adults in the United States.¹³⁻¹⁶ Moreover, the prevalence appears to be on the rise,¹⁴⁻¹⁶ particularly in women,¹⁴⁻¹⁶ and with advancing age, with the greatest prevalence seen in adults 60 years

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or older.¹⁴ When combining the adverse consequences associated with MetSyn with its continuing rise in prevalence, it seems clear that MetSyn will continue to represent a serious public health issue well into the future.

Low cardiorespiratory fitness (CRF) has been associated with the presence of metabolic risk factor clustering and MetSyn in numerous published studies.¹⁷⁻³¹ However, the defining criteria for MetSyn, the assessment of CRF, and the specific cohort characteristics have varied considerably among these studies. Variations in any one or all the above parameters could influence the overall study findings and the generalizability of the results. Early reports used higher thresholds for impaired fasting blood glucose (≥110 mg/dL [to convert to mmol/L, multiply by 0.0555]),^{18,21,23,26-28,31} hypertension (blood pressure >140/90 mm Hg),^{18,27,31} and/or varying measures/thresholds for abdominal obesity, 17,18,27,31 which were more consistent with the defining criteria for MetSyn at the time. Other studies used population- and/or country-specific definitions for abdominal obesity.^{17,24,28,30} Only 3 recent reports incorporated the current MetSyn risk factor criteria for each of the 5 common markers-including drug treatment for hypertension, dyslipidemia, and/or elevated fasting glucose as a qualifying factor.^{25,29,30} Of these, 2 of the studies included only older³⁰ or only younger²⁹ adults, and only 1 study included women.30

In light of the recent public health recommendation to include assessment of CRF in medical examinations³² and the advocacy for inclusion of cardiopulmonary exercise testing (CPX),^{33,34} more information from studies in which CRF was directly measured may aid clinicians in the evaluation and treatment of multiple chronic diseases (eg, cardiovascular disease and heart failure). Most of the published studies on MetSyn incorporated a CRF level estimated from a maximal exercise test,^{17,19,21-23,26-31} which has been associated with an estimation error of between 1 and 2 metabolic equivalents. Only 5 of the published studies on MetSyn used CPX-derived maximal oxygen uptake $(VO_{2max})^{23,27-30}$ to define CRF. Two of these studies used leg cycling as the mode of exercise, which is associated with 10% to 20% lower measured oxygen uptake as compared with treadmill testing. 23,27,35 Four of the 5 studies incorporated solely older 23,30 or younger 28,29 adults, which would not be as generalizable across a wide age spectrum. Furthermore, only 2 of the studies in which CRF was defined using measured VO_{2max} included women, and these 2 cohorts collectively represented approximately 1171 older women.^{23,30} When combining the limited number of participants within these studies with the sex and/or age delimitations, the VO_{2max} thresholds associated with increased risk for MetSyn in middle-aged adults are less clear. Therefore, additional information from studies that include (1) contemporary risk factor thresholds, (2) a large sample and broad age range of men and women, and (3) VO_{2max} determined with CPX is needed to refine the understanding of the association between CRF and MetSyn.

The purpose of the present investigation was to assess the association between directly measured CRF (VO_{2max}) and metabolic risk factor clustering in a broad age range of men and women using current MetSyn risk factor criteria.

PARTICIPANTS AND METHODS

Study Population and Design

Participants completed laboratory assessments through the Ball State Adult Fitness Program Longitudinal Lifestyle STudy (BALL ST), which is an ongoing population-based program initiated in 1970 to promote healthy lifestyles and physical fitness. This retrospective crosssectional analysis included 3636 self-referred adult males and females (aged 19-95 years) who completed a physical examination including maximal exercise testing with respiratory gas analysis (CPX) within the BALL ST between the years January 1, 1971, and November 1, 2016. Deidentified data were exported from the BALL ST longitudinal database. Inclusion criteria consisted of being 18 years or older, having complete data for all MetSyn risk markers (see below), and attainment of greater than or equal to 1.0 respiratory exchange ratio during the maximal exercise test. For individuals with multiple test records, the first test with complete data for all relevant MetSyn risk markers was used. All data were deidentified, and participants provided written informed consent for their

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