Preventive Medicine 150 (2021) 106720

Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

Short Communication

Body mass, cardiorespiratory fitness, and cardiometabolic risk over time: Findings from the Cooper Center Longitudinal Study

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ARTICLE INFO

Keywords:
Fitness
Body mass
Metabolic syndrome
Longitudinal analysis

ABSTRACT

Few studies have adequately assessed the simultaneous effects of changes in cardiorespiratory fitness (fitness) and body mass on cardiometabolic risk. Hence, the current study's aims were twofold: (1) To determine whether increases in body mass result in higher cardiometabolic risk after controlling for fitness changes; and (2) To assess whether increases in fitness result in lower cardiometabolic risk after controlling for weight changes. The study consisted of 3534 patients who came for preventive medicine visits ≥4 times over any 10-year period (1979–2019). The primary independent variables were body mass and fitness, and the dependent variable was metabolic syndrome (MetS) and its components. Mixed-effects regression was used to model the relationship between changes in body mass, fitness, and MetS. Results indicate that increasing body mass up to a 10-year period was significantly related to increasing risk of MetS while controlling for changes in fitness. Specifically, a 1-kg increase in body mass was associated with a 17% (OR = 1.17; 95% CI 1.15–1.19) increased odds for MetS, while adjusting for fitness changes. A 1-MET increase in fitness was related to a 23% (OR = 0.77; 95% CI 0.70–0.84) decrease in odds for MetS, while adjusting for body mass changes up to 10 years. Moreover, body mass change was significantly related to changes in all cardiometabolic components of MetS. Fitness change was significantly associated with changes in MetS components. Future interventions should focus concurrently on increasing fitness and on body mass loss (or maintenance) to improve cardiometabolic health.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death among Americans, with 859,125 men and women dying from CVD in the United States (US) in 2017(Virani et al., 2020). Risk factors for CVD include elevated resting blood pressure (BP), dyslipidemia, elevated blood glucose, and excess abdominal obesity (The National Health Service, 2017). Metabolic syndrome (MetS) is a clustering of at least three of these risk factors, and has been linked to increased risk for type 2 diabetes and CVD (Ginsberg and MacCallum, 2009; Grundy, 2016). Control of these risk factors through a healthy lifestyle such as maintaining appropriate weight and achieving adequate cardiorespiratory fitness (henceforth "fitness") results in improvements in overall cardiovascular health and a reduction in CVD mortality (Al-Mallah et al., 2018; Fontana and Hu, 2014; Imboden et al., 2018).

More specifically, excess weight and weight gain is associated with increased risk of hypertension, hypercholesterolemia, type 2 diabetes, and multiple chronic conditions, whereas weight loss and maintenance results in improvements in these outcomes (Al-Mallah et al., 2018; Fontana and Hu, 2014). Low fitness is an established risk factor for these same morbid conditions (Farrell et al., 2004; Imboden et al., 2018), and detrimental changes in body mass and fitness each contribute to their

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https://doi.org/10.1016/j.ypmed.2021.106720
Received 22 February 2021; Received in revised form 19 May 2021; Accepted 6 July 2021
Available online 10 July 2021

development. Unfortunately, most studies that examine body mass changes and CVD risk factors do not account for changes in fitness.

While the cross-sectional associations between body mass or fitness and cardiovascular health are well established (Choi et al., 2018; Shuval et al., 2012), it is not sufficiently clear what effect changes in body mass and fitness measured together during an extended follow up period have on cardiometabolic risk factors. The Cooper Center Longitudinal Study (CCLS) is a robust resource available for assessing the simultaneous associations between changes in body mass and fitness on cardiometabolic risk since it includes objectively measured fitness data and clinical measurements over an extended period (DeFina et al., 2015; Farrell et al., 2020). Therefore, we used the CCLS to evaluate the cross-sectional and longitudinal relationships between body mass, fitness, and clustering of cardiometabolic risk factors (i.e., MetS and components) while controlling for covariates. Specifically, the purpose of this study was to determine whether variations in body mass up to 10 years are associated with changes in MetS status (and components), while controlling for changes in fitness; and if variations in fitness over time are associated with changes in MetS status (and components), while controlling for changes in body mass.

2. Methods

2.1. Study population

The CCLS is a prospective cohort study aimed at determining the effects of lifestyle behaviors and fitness on health-related outcomes (Shuval et al., 2012). Individuals receiving preventive medical examinations at the Cooper Clinic in Dallas, TX, are invited to enroll in the CCLS and sign an informed consent (DeFina et al., 2019). This study is reviewed and approved annually by The Cooper Institute Institutional Review Board. The CCLS cohort consists predominantly of non-Hispanic whites who are generally self-referred or referred by their employer to the clinic (Pavlovic et al., 2018).

For the current study, a total of 4092 participants with complete information on the primary exposures (body mass and fitness), outcomes (MetS and components) and covariates, and who met the following criteria were considered for inclusion: 4 or more preventive medicine visits during any 10-year period from 1979 to 2019; aged 21–89 years; not underweight (BMI $\geq$18.5 kg/m^2); not pregnant; and without unexplained weight loss or gain. Of these, 335 were excluded due to reporting a personal history of cancer, stroke, or myocardial infarction, and 223 additional participants were excluded due to missing smoking status. This resulted in an analytic sample of 3534 participants who had an average of 5.3 (SD = 1.5) visits during any 10-year period during 1979–2019. The median time between first and last visits was 7.0 years.

2.2. Medical examination

Clinical staff measured patients' anthropometrics (e.g., height, body mass, waist circumference). Height and body mass were assessed via a stadiometer and a standard physician's scale (Farrell et al., 2017). Waist circumference was measured at the umbilicus level with a cloth tape measure. Moreover, seated resting BP was measured with a mercury sphygmomanometer using the American Heart Association protocol (Perloff et al., 1993). Additionally, glucose, HDL-C, and triglyceride levels were determined from fasting venous blood at the clinic laboratory following standard procedures. A medical history questionnaire captured demographic information and lifestyle behaviors (Willis et al., 2011). Additionally, participants completed a maximal treadmill exercise test using a modified-Balke protocol. Details regarding the specific protocol including speed and grade of each exercise stage have been previously described (Willis et al., 2011). Duration of the treadmill test strongly correlate with measured maximal oxygen uptake in men (r = 0.92) and women (r = 0.94) (Pollock et al., 1982; Pollock et al., 1976). We estimated VO_2max in mL/kg/min from the final speed and grade of the modified Balke treadmill test using the equation VO_2max = (speed in meters/min x 0.1) + (speed in meters/min x 1.8 x %grade expressed as a decimal) + 3.5 (American College of Sports Medicine, 2013). We then converted to metabolic equivalents (METs) using 1 MET = 3.5 mL O_2 uptake·kg^{-1} body weight·min^{-1} (Farrell et al., 2020).

The outcome variables were MetS and its components. MetS was defined as meeting at least 3 of the following 5 criteria: elevated waist circumference ($\geq$102 cm in men, $\geq$88 cm in women); elevated triglycerides ($\geq$150 mg/dL) or drug treatment; low HDL-C ($<$40 mg/dL in men, $<$50 mg/dL in women) or drug treatment; elevated BP ($\geq$130 mmHg systolic and/or $\geq$ 85 mmHg diastolic) or treatment; or elevated fasting glucose ($\geq$100 mg/dL) or drug treatment (Grundy, 2016). For analysis, models were estimated with MetS (yes/no) as the outcome, and separate models were computed with each MetS component as a dichotomous or continuous measure. The main exposures, body mass in kg and fitness in METs (Jakicic et al., 2019; Kodama et al., 2009), measured at baseline and all follow-up visits, were entered as continuous variables adjusted for each other in multiple regression models. Other covariates were age, sex, current smoking, and year of exam (included in all models), whereas medication use was adjusted for in models where systolic BP, diastolic BP, glucose, triglycerides, and HDL were the outcome measures.

2.3. Statistical analyses

Metabolic syndrome and components (dichotomous outcomes) were modeled using mixed-effects multiple logistic regression, and continuous outcomes were modeled using mixed-effects multiple linear regression (Fitzmaurice et al., 2012). These models accommodate unbalanced data, support both continuous and discrete covariates, and are robust to missing data (Fitzmaurice and Ravichandran, 2008; Gibbons et al., 2010). All models were fit using the same set of fixed and random effects with no selection. Longitudinal variables included in the models were body mass, fitness, age, and current smoking. Baseline values of these same variables were also included in the models to provide simultaneous estimation of cross-sectional (between-person) and longitudinal (within-person) effects. Sex and year of exam were included as additional cross-sectional effects. Random intercept and slope (aging) effects were included to model correlation among repeated measures and changes over time within individuals. Body mass and fitness change modification by baseline factors was tested by including interaction terms constructed from the corresponding longitudinal and baseline variables. All analyses were performed using SAS/STAT®, version 9.4 (SAS Institute, Cary, NC).

3. Results

At baseline, 19.6% of participants were women, and 10.4% were current smokers. Their mean age was 46.8 years (SD = 8.0), mean waist circumference 89.2 cm (SD = 11.6), mean body mass 83.6 kg (SD = 15.3), and mean fitness 11.6 METs (SD = 2.1). Between first and last visits, the median net change in body mass was 0.3 kg with interquartile interval (−2.6, 3.1), and the median net change in fitness was −0.1 MET with interquartile interval (−0.9, 0.5). In terms of cardiometabolic risk factors, 17.1% had MetS, 14.9% elevated waist circumference, 27.6% elevated fasting glucose, 22.7% elevated triglycerides, 44.9% elevated BP, and 19.8% low HDL-C. In addition, baseline mean glucose was 95.6 mg/dL (SD = 10.7), mean triglycerides 117.0 mg/dL (SD = 77.4), mean systolic BP 119.7 mmHg (SD = 12.8), mean diastolic BP 80.7 mmHg (SD = 9.2), and mean HDL-C 53.5 mg/dL (SD = 15.2). It should be noted that compared to women, men had a higher prevalence of metabolic syndrome and all components, all $p < 0.001$. For example, the prevalence of MetS in men was 2.5 times higher than women (17.4% and 7.1%, respectively), and the prevalence of elevated BP was 1.5 times higher (men: 45.7%; women: 30.4%).

Table 1 presents the longitudinal and cross-sectional relationships

Table 1
Cross-sectional and longitudinal associations of body mass and cardiorespiratory fitness with metabolic syndrome (and components) over 10 years: Mixed effects logistic regression[a].

	Metabolic syndrome		Components of the metabolic syndrome									
			Elevated waist circumference		Elevated blood pressure		Elevated glucose		Elevated triglycerides		Low HDL-C	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Cross-sectional												
Body mass (per 1 kg)	1.08**	1.07, 1.08	1.28**	1.27, 1.30	1.03**	1.03, 1.04	1.03**	1.02, 1.03	1.02**	1.01, 1.03	1.03**	1.02, 1.04
Fitness (per 1 MET)	0.65**	0.61, 0.69	0.55**	0.51, 0.59	0.86**	0.82, 0.90	0.88**	0.84, 0.91	0.71**	0.67, 0.74	0.73**	0.69, 0.77
Longitudinal												
Body mass (per 1 kg)	1.17**	1.15, 1.19	1.40**	1.36, 1.44	1.07**	1.05, 1.09	1.06**	1.04, 1.07	1.14**	1.12, 1.16	1.07**	1.05, 1.09
Fitness (per 1 MET)	0.77**	0.70, 0.84	0.72*	0.62, 0.84	0.90**	0.85, 0.96	0.94*	0.88, 0.99	0.85**	0.79, 0.92	0.81**	0.74, 0.88

METs- metabolic equivalent of task; OR- odds ratio; CI- confidence interval.
*$p < 0.05$; ** $p < 0.01$.
[a] Models are adjusted for sex, age, current smoking, and year of exam. Both exposures (body mass and fitness) are adjusted for each other.

between the exposures (body mass and fitness), and the main outcome (MetS). Longitudinally, increases in body mass were related to significantly increased odds of MetS (OR = 1.17 per kg; 95%CI 1.15–1.19), and increases in fitness were related to significantly reduced odds of MetS (OR = 0.77 per MET; 95% CI 0.70–0.84). The effects of body mass and fitness change were estimated simultaneously, each account for the effect of the other. Moreover, there was no significant interaction between the longitudinal exposures and baseline values. Further, when examining the body mass-MetS relationship longitudinally, the strength of the association was more robust than cross-sectionally, and vice versa for the fitness-MetS association. Specifically, a 1 kg increase in body mass was related to 8% higher MetS odds cross-sectionally (compared to 17% longitudinally), and a 1-MET increase in fitness was associated with 35% lower odds for MetS cross-sectionally versus only 23% reduced odds longitudinally. In addition, increased body mass and fitness were significantly related to each MetS component categorically in cross-sectional and longitudinal analysis (Table 1). Increased body mass was significantly associated with each continuous cardiometabolic risk factor cross-sectionally and longitudinally, whereas fitness was significantly related to all risk factors except for diastolic BP, which did not reach significance (Table 2).

4. Discussion

The current study's analytic approach enabled isolating the effects of changes in body mass and fitness on MetS within individuals through a longitudinal prism, while controlling for differences between people (e.g., genetics differences) via the cross-sectional design. Moreover, the longitudinal design brings forth a more accurate representation of cardiometabolic risk associated with weight gain and increased fitness within individuals over time. While this robust approach is evidence-based (Fitzmaurice et al., 2012), few have made such an attempt in this research vein. Specifically, present longitudinal findings reveal that a 1 kg within individual increase in body mass leads to 17% higher risk for MetS, and 1-MET within person increase in fitness corresponds to 23% lower risk. When relying on cross-sectional analysis, the risk associated with body mass gain appears lower (8%), whereas the benefits of fitness appear larger (35%) than those from the longitudinal analysis, which is more clinically relevant. Thus, particular focus should be put on preventing body mass gain over time and on improving fitness levels through habitually engaging in physical activity and adhering to a healthful diet, which are both paramount to cardiometabolic health (Piercy et al., 2018; U.S. Department of Agriculture, 2020).

An additional unique feature of this study is that we examined participants with at least 4 clinic visits that included an objective measure of body mass and fitness, as well as measured clinical outcomes at all visits within a ten-year period. A study by Knell et al. (2018), in comparison, observed that higher levels of body mass loss were significantly related to a lower likelihood of MetS. However, these findings did not take fitness into account, and were based on a cross-sectional design, which inhibits estimating risk within individuals. Previous studies of fitness and metabolic syndrome have often measured fitness at one time point and do not account for changes in this exposure (Farrell et al., 2004; LaMonte et al., 2005; Shuval et al., 2012). In other studies that did

Table 2
Regression coefficients for cross-sectional and longitudinal associations of body mass and cardiorespiratory fitness with cardiometabolic risk factors over 10 years: Mixed effects linear regression[a].

	Waist circumference (cm)		Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)		Glucose (mg/dL)		Triglycerides (mg/dL)		HDL-C (mg/dL)	
	Estimate	95%CI	Estimate	95%CI	Estimate	95%CI	Estimate	95%CI	Estimate	95%CI	Estimate	95%CI
Cross-sectional												
Body mass (per 1 kg)	0.58**	0.57, 0.59	0.16**	0.13, 0.19	0.11**	0.09, 0.13	0.12**	0.09, 0.14	0.70**	0.54, 0.86	−0.22**	−0.25, −0.19
Fitness (per 1 MET)	−1.01**	−1.08, −0.93	−0.15	−0.35, 0.04	−0.29**	−0.42, −0.16	−0.46**	−0.62, −0.30	−8.30**	−9.39, −7.20	1.84	1.61, 2.08
Longitudinal												
Body mass (per 1 kg)	0.74**	0.72, 0.76	0.41**	0.36, 0.46	0.32**	0.28, 0.35	0.25**	0.21, 0.29	3.05**	2.76, 3.34	−0.48**	−0.52, −0.44
Fitness (per 1 MET)	−0.42**	−0.50, −0.34	0.22*	0.02, 0.42	−0.12	−0.28, 0.03	−0.26**	−0.42, −0.09	−3.41**	−4.55, −2.28	0.76**	0.60, 0.93

METs- metabolic equivalent of task; CI- confidence interval.
*p < 0.05; ** p < 0.01.
[a] All models are adjusted for sex, age, current smoking, and year of exam. Models for systolic and diastolic blood pressure, glucose, triglycerides, and HDL-C are additionally adjusted for pertinent medication. Both exposures (body mass and fitness) are adjusted for each other.

assess changes in fitness, participants were described as losing, maintaining, or gaining fitness (Blair et al., 1995; Lee et al., 2012), rather than the more accurate continuous estimates in the current study.

Further, results from our study suggest that longitudinal changes in body mass predict changes in each of the five cardiometabolic risk components of MetS, even when accounting for simultaneous changes in fitness. These results support previous studies that show body mass gain is detrimental to blood pressure and lipid levels, whereas body mass loss corresponds with improvements in these factors (Bot et al., 2010; Knell et al., 2018; Norman et al., 2003; Williams, 2008). An earlier study reported that individuals who gained a mean body mass of 9.3 kg over ten years had significantly higher levels of triglycerides, LDL-C, BP, and lower HDL-C compared to baseline (Norman et al., 2003). This study, however, only used two visits to assess change in body mass and lacked fitness data. Additionally, present study findings indicate that increased fitness resulted in continued improvement in cardiometabolic components, yet diastolic BP did not reach statistical significance, which warrants further investigation.

Several limitations of the present study should be noted. The CCLS population is comprised of predominantly non-Hispanic white individuals with access to preventive medical care. While the homogenous nature of the population increases the internal validity of the study, it may hinder the generalizability of the results to more ethnically diverse populations. In addition, the frequency of clinical visits was generally annual (or less), thus we are unable to detect changes that occurred over shorter periods. Finally, sufficient dietary information was not available and therefore not included in the analyses.

In conclusion, longitudinal changes in body mass consistently predict changes in risk of MetS and its components, after adjusting for fitness. Changes in fitness over time predicted changes in risk of MetS and components, after adjustment for body mass. Therefore, striving to improve fitness through habitually engaging in physical activity is recommended for cardiovascular disease prevention. Additionally, clinical and public health recommendations for improving cardiovascular health should continue to include avoiding weight gain and encouraging weight loss for adults who are overweight or obese. Future research examining changes in body mass, fitness, cardiometabolic risk factors, and their effects on CVD morbidity and mortality is warranted using randomized controlled trials.

Credit author statement

DL, CEF and KS conceived the study. DL and KS led all aspects of the study. KS, CEF, and DL meaningfully contributed to the write up. DL performed the statistical analysis. All authors (DL, KS, CEF, CEB, WLH, SWF, AP, LD, MS, and LFD) provided critical insight on the methodology and/or feedback pertaining to study design and participated in critical revisions of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

No external funding was provided for this study. The authors thank Kenneth H. Cooper, MD, MPH for establishing the Cooper Center Longitudinal Study, the Cooper Clinic physicians and staff for collecting clinical data, and The Cooper Institute for maintaining the database. Additionally, we are grateful to the CCLS participants.

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