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Brief Report

Fitness and Fatness as Mortality Predictors in Healthy Older Men: The Veterans Exercise Testing Study

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Background. Low body mass index (BMI) and low cardiorespiratory fitness (CRF) are independently associated with increased mortality in the elderly. However, interactions among BMI, CRF, and mortality in older persons have not been adequately explored.

Methods. Hazard ratios (HRs) were calculated for predetermined strata of BMI and CRF. Independent and joint associations of CRF, BMI, and all-cause mortality were assessed by Cox proportional hazards analyses in a prospective cohort of 981 healthy men aged at least 65 years (mean age [±*SD*], 71 [±5] years; range, 65–88 years) referred for exercise testing during 1987–2003.

Results. During a mean follow-up of 6.9 ± 4.4 years, a total of 208 patients died. Multivariate relative risks (95% confidence interval [CI]) of mortality across BMI groups of <20.0, 20.0–25.0, 25.0–29.9, 30.0–34.9, and ≥35.0 were 2.51 (1.26–4.98), 1.0 (reference), 0.66 (0.48–0.90), 0.50 (0.31–0.78), and 0.44 (0.20–0.97), respectively, and across CRF groups of <5.0, 5.0–8.0, and >8.0 metabolic equivalents were 1.0 (reference), 0.56 (0.40–0.78), and 0.39 (0.26–0.58), respectively. In a separate analysis of within-strata CRF according to BMI grouping, the lowest mortality risk was observed in obese men with high fitness (HR [95% CI] 0.26 [0.10–0.69]; $p = .007$).

Conclusions. In this cohort of elderly male veterans, we observed independent and joint inverse relations of BMI and CRF to mortality. This warrants further investigation of fitness, fatness, and mortality interactions in older persons.

***Key Words*:** Cardiorespiratory fitness—Body mass index—Mortality—Obesity paradox.

OBESITY, as defined by body mass index (BMI), is associated with increased mortality in the general population of U.S. adults (1). However, among older adults, the mortality risk associated with being overweight or obese is controversial (2,3). Some studies show a U-shaped BMI–mortality relationship (4,5), whereas others show an inverse association (6–9) or no association (10). Such disparate findings warrant further investigation of this relationship in the elderly.

Cardiorespiratory fitness (CRF) is a strong independent predictor of mortality in older adults (11–13). However, data on interactions among CRF, BMI, and mortality are sparse (10). Furthermore, the mortality risk of underweight may be confounded by unintentional weight loss stemming from poor health. To avoid this problem, we confined this investigation to healthy persons.

The purpose of this study was to test the hypothesis that high CRF and high BMI are independently and jointly associated with a lower risk for death among healthy elderly men.

Methods

Study Population

The Veterans Exercise Testing Study is an ongoing epidemiological investigation of more than 9,000 veteran patients referred to two university-affiliated Veterans Affairs medical centers (Long Beach, California from 1987 to 1991 and Palo Alto, California from 1992 onward) for clinical exercise testing. From this database, we identified 2,469 consecutive men aged 65 years or older who completed a baseline medical examination and maximal exercise test at least once at either Long Beach, or Palo Alto, during 1987–2003. This comprised approximately one third of all tests referred to our Cardiology Section during this time period. After excluding patients with an abnormal exercise test, documented cardiovascular disease (CVD), or both, we evaluated a total of 981 apparently healthy men aged 65–88 years. CVDs included coronary artery disease, myocardial infarction, heart failure, and stroke. Participants were classified according to five predetermined BMI groups: <20.0, 20.0–24.9, 25.0–29.9, 30.0–34.9, and ≥35.0 kg/m^2, and according to three predetermined CRF groups: <5.0, 5.0–8.0, and >8.0 metabolic equivalents (METs). Low fitness (<5.0 METs) and “normal” weight (BMI 20.0–24.9 kg/m^2) were used as the reference groups. To evaluate the interaction of BMI and CRF, we further classified participants within strata of CRF according to BMI group (for these analyses, BMI 30.0–34.9 and ≥35.0 kg/m^2 were combined). This resulted in nine crossover groups, with normal BMI–low fitness as the reference group (the group with <20.0 BMI had too few participants and was excluded). Hazard ratios (HRs) were calculated using Cox proportional hazards analyses adjusting for age, ethnicity, current smoking, hypertension, and hypercholesterolemia. For the independent analyses of the BMI and CRF groups, we developed a second proportional hazards model that added adjustment for CRF and BMI as continuous variables, respectively. All participants gave written informed consent. Additional information on study methods and participant characteristics of this cohort has been published elsewhere (14).

Mortality Surveillance

Mortality data were gathered from the Social Security Death Index and California Death Registry. Participants in the study were those who completed their baseline examination as of December 31, 2003. Vital status was determined as of December 31, 2004. Therefore, all participants were followed for at least 1 year from baseline.

Clinical Evaluation and Exercise Testing

All participants completed a symptom-limited maximal exercise test using an individualized ramp treadmill protocol (15). Before testing, a self-administered questionnaire was used to predict target maximal METs that would be achieved within a range of 8–12 minutes (16). Immediately prior to the exercise test, height and weight were measured using standard procedures, and BMI was calculated as weight in kilograms divided by the square of height in meters. A microcomputer automatically increased workload after an individualized walking speed was established and predicted values for maximal exercise capacity were entered.

A 12-lead electrocardiogram was recorded each minute, and blood pressure was recorded on alternate minutes throughout the test. Standard clinical criteria for terminating the tests (e.g., fall in systolic blood pressure, ST-segment depression >2.0 mm, dangerous arrhythmias) were followed (17), but no heart rate or time limit was imposed, and a maximal effort was encouraged. Standardized equations were used to determine the calculated peak METs on the basis of treadmill speed and grade (17). Exercise capacity was expressed as the maximal MET value attained during the exercise test.

Statistical Analysis

The statistical software Numbers Crunching Statistical Software (Kaysville, UT) was used for all statistical analyses. The mean and standard deviation of each variable were calculated, with participants categorized as survivors or decedents. The independent effects of BMI and CRF were assessed using two proportional hazards models: first, adjusting for age, ethnicity, and CVD risk factors (hypertension, hypercholesterolemia, and current smoking), and second, by adding CRF (for BMI) and BMI (for CRF) entered as continuous variables. In joint analyses, nine CRF–BMI categories were assessed using a single proportional hazards model adjusting for age, ethnicity, and CVD risk factors. The Shoenfeld residuals were used to assess the proportional hazards assumption and the assumption was met.

Results

During a mean follow-up of 6.9 ± 4.4 years (range, 1.0–17.6 years), 208 deaths were recorded. The general characteristics of the study population, grouped by survival status, are presented in Table 1. The study population consisted of 75% non-Hispanic Whites, 9% Hispanics, 10% African Americans, and 6% Asian Americans, who ranged in age from 65 to 88 years (mean 71.3 ± 5.0). Underweight patients represented 2.1% of the cohort, normal weight 26.3%, overweight 46.6%, and obese 25.0%. In general, surviving patients were more fit, had a significantly higher BMI, and had a higher prevalence of hypercholesterolemia, and included a lower percentage of current smokers.

In the fully adjusted model, each 1-unit increase in BMI and METs was associated with reductions in mortality risks of 9% (HR [95% confidence interval {CI}] of 0.91 [0.88–0.95]; $p < .001$) and 12% (HR [95% CI] of 0.88 [0.83–0.92]; $p < .001$), respectively (Tables 2 and 3). The HRs (95% CI) for mortality associated with underweight, overweight, and obesity were 2.51 (1.26–4.98), 0.66 (0.48–0.90), and 0.48 (0.32–0.74), respectively, compared with the reference group of normal-weight men (Table 2). Compared with the reference group of men with low fitness, HRs (95% CI) for moderate and high fitness were 0.56 (0.40–0.78) and 0.39 (0.26–0.58), respectively (Table 3).

In the fully adjusted multivariate model, the association of the interaction of BMI and METs to all-cause mortality was significant ($p = .005$). Stratified results for CRF according to BMI are shown in Table 4. Among men having low CRF, multivariate risk of mortality did not differ by BMI classification. However, in the moderate CRF group, overweight and obese men were 61% and 63% less likely to die compared with the low CRF–normal BMI reference group of 56 men. Compared with this reference group, men in the high-fitness group with normal weight, overweight, and obesity had reduced mortality risks of 51%, 64%, and 74%, respectively.

Discussion

Our main finding was that both higher BMI and higher CRF reduced the risk of all-cause morality in healthy elderly men who were referred to exercise testing for clinical reasons but determined to be free of CVD. Furthermore, mortality risk was reduced as BMI increased within groups having moderate or high CRF, but BMI was not significantly associated with mortality within the low-CRF group.

Table 1. Baseline Characteristics of 981 Healthy Elderly Men According to Survival Status, Veterans Exercise Testing Study, 1987–2003

Characteristics	Total (*N* = 981)	Survived (*N* = 773)	Died (*N* = 208)	*p*
Demographic and clinical data				
Follow-up (y)	6.9 ± 4.4	6.9 ± 4.5	6.8 ± 3.9	.78
Age (y)	71.3 ± 5.0	71.3 ± 5.0	71.6 ± 4.9	.37
Non-Hispanic White ethnicity (%)	74.9	74.3	77.4	.35
BMI (kg/m^2)	27.5 ± 4.4	27.9 ± 4.4	26.2 ± 4.0	<.001
Resting systolic BP (mm Hg)	138.9 ± 19.9	138.7 ± 19.1	139.9 ± 22.5	.42
Resting diastolic BP (mm Hg)	80.3 ± 10.8	80.4 ± 10.3	79.6 ± 12.5	.31
Resting heart rate (beats/min)	73.6 ± 13.6	73.1 ± 13.0	75.6 ± 15.4	.02
BMI groups (%)				
<20.0	2.1	1.4	4.8	.003
20.0–25.0	26.3	24.2	34.1	.004
25.0–29.9	46.6	47.1	44.7	.54
≥30.0	25.0	27.3	16.3	.001
Currently smoking (%)	14.8	12.8	22.1	<.001
Hypertension (%)	57.0	57.4	55.3	.58
Hypercholesterolemia (%)*	27.9	30.1	19.7	.003
Exercise test responses				
CRF (METs)†	7.1 ± 2.9	7.2 ± 2.9	6.4 ± 2.9	<.001
<5.0 METs (%)†	23.1	21.1	30.8	.004

Notes: Data are means ± standard deviation, unless otherwise indicated. BP = blood pressure; BMI = body mass index; CRF = cardiorespiratory fitness; MET = metabolic equivalents.

* Fasting serum total cholesterol >5.6 mmol/L (>220 mg/dL).

† METs: 1 MET = 3.5 mL/kg/min oxygen uptake; CRF is maximal METs achieved during the exercise test and is calculated from treadmill speed and grade using standard equations.

Our findings on BMI accord with some (6,7,9) but not other (4,5,8) previous reports examining the relationship between BMI and mortality in elderly persons. We offer four possible explanations for our findings: (i) healthy obesity, (ii) the survival effect, (iii) increased coronary artery size, and (iv) veteran population differences. In healthy obese mice, there is preferential storage of triglycerides in adipose tissue and reduced levels in the liver (18). This may result in improved insulin sensitivity, preventing diabetes and heart disease in such animals. A similar mechanism has been proposed for obese humans (19). Furthermore, older individuals who have greater fat stores may be better able to tolerate periods of low caloric intake associated with acute illness. A second possible explanation is the well-known survival effect (3). Participants surviving until inclusion in our study were possibly less susceptible to the negative effects of overweight. Third, greater coronary artery size among patients with higher BMI has been proposed as a possible mechanism for the so-called obesity paradox (20). This may also be a factor in the better survival outcomes we observed among the healthy obese men in the present study. Finally, the possibility of a population-specific veteran effect should not be discounted. Veterans differ from other populations of patients. One of the most prominent differences is the meeting of selection criteria at the time of enlistment. These criteria include, among others, minimum height requirements, maximum weight requirements, and exclusion of recruits having certain preexisting health problems (21). Hence, obesity, when present in our population, must have developed after discharge in later life.

Moderate fitness (5.0–8.0 METs) was independently associated with lower mortality risk, and high fitness (>8.0 METs) the lowest mortality risk relative to the low-fitness group (<5.0 METs). These results are consistent

Table 2. Multivariate HRs of All-Cause Mortality According to BMI for 981 Healthy Elderly Men, Veterans Exercise Testing Study, 1987–2003

			Model 1*		Model 2†	
BMI (kg/m^2)	No. of Men	No. of Deaths (%)	HR (95% CI)	*p*	HR (95% CI)	*p*
Per 1-unit increment	981	208 (21)	0.93 (0.89–0.96)	<.001	0.91 (0.88–0.95)	<.001
<20.0	21	10 (48)	2.01 (1.02–3.98)	.045	2.51 (1.26–4.98)	.009
20.0–24.9	258	71 (28)	1 (reference)	—	1 (reference)	—
25.0–29.9	457	93 (20)	0.66 (0.48–0.90)	.009	0.66 (0.48–0.90)	.008
30.0–34.9	193	27 (14)	0.56 (0.35–0.87)	.01	0.50 (0.31–0.78)	.003
≥35.0	52	7 (14)	0.56 (0.37–0.85)	.15	0.44 (0.20–0.97)	.042

Notes: BMI = body mass index; CI = confidence interval; HR = hazard ratio.

* Adjusted for age, ethnicity, and cardiovascular disease risk factors (hypertension, hypercholesterolemia, and current smoking).

† Model 1 plus cardiorespiratory fitness.

Table 3. Multivariate HRs of All-Cause Mortality According to CRF for 981 Healthy Elderly Men, Veterans Exercise Testing Study, 1987–2003

			Model 1†		Model 2‡	
CRF (METs)*	No. of Men	No. of Deaths (%)	HR (95% CI)	p	HR (95% CI)	p
Per 1-unit increment	981	208 (21)	0.89 (0.85–0.94)	<.001	0.88 (0.83–0.92)	<.001
<5.0	227	64 (28)	1 (reference)	—	1 (reference)	—
5.0–8.0	446	93 (21)	0.59 (0.43–0.83)	<.002	0.56 (0.40–0.78)	<.001
>8.0	308	51 (17)	0.45 (0.30–0.67)	<.001	0.39 (0.26–0.58)	<.001

Notes: CI = confidence interval; CRF = cardiorespiratory fitness; HR = hazard ratio; MET = metabolic equivalents.

* METs: 1 MET = 3.5 mL/kg/min oxygen uptake; CRF is maximal METs achieved during the exercise test and is calculated from treadmill speed and grade using standard equations.

† Adjusted for age, ethnicity, and cardiovascular disease risk factors (hypertension, hypercholesterolemia, and current smoking).

‡ Model 1 plus body mass index.

with the findings from previous studies on fitness and mortality in older adults (11). However, interactions among BMI, CRF, and mortality are less well studied because objective measures of CRF, such as maximal exercise testing on a treadmill, are required. From the Aerobic Center Longitudinal Study (ACLS), Sui and colleagues (10) recently reported that CRF attenuates the mortality risk of obesity. Our results are consistent with their main finding that CRF attenuates the morality risk associated with obesity. But our findings differ in that obesity was independently associated with reduced all-cause mortality and that obese patients having moderate or high fitness survived better than their normal-weight or overweight counterparts. These observed differences may be due in large part to demographics (the ACLS cohort was younger, predominately White, included women and participants not clinically referred, and comprised mainly of civilians).

Table 4. Multivariate HRs of All-Cause Mortality Within Strata of CRF Groups According to BMI for 981 Healthy Elderly Men, Veterans Exercise Testing Study, 1987–2003

Fitness Category	No. of Men	No. of Deaths (%)	HR (95% CI)*	p
Low, <5.0 METs				
BMI <20.0†	3	3 (100)	—	—
BMI 20.0–24.9	56	17 (30)	1 (reference)	—
BMI 25.0–29.9	103	32 (31)	0.96 (0.57–1.63)	.89
BMI ≥30.0	65	12 (19)	0.56 (0.28–1.13)	.11
Moderate, 5.0–8.0 METs				
BMI <20.0†	10	5 (50)	—	—
BMI 20.0–24.9	107	35 (33)	0.85 (0.51–1.42)	.54
BMI 25.0–29.9	205	36 (18)	0.39 (0.23–0.64)	<.001
BMI ≥30.0	124	17 (14)	0.37 (0.20–0.71)	.003
High, >8.0 METs				
BMI <20.0†	8	2 (25)	—	—
BMI 20.0–24.9	95	19 (20)	0.49 (0.27–0.91)	.03
BMI 25.0–29.9	149	25 (17)	0.36 (0.20–0.63)	<.001
BMI ≥30.0	56	5 (9)	0.26 (0.10–0.69)	.007

Notes: BMI = body mass index; CI = confidence interval; CRF = cardiorespiratory fitness; HR = hazard ratio; MET = metabolic equivalents

* Adjusted for age, ethnicity, and cardiovascular disease risk factors (hypertension, hypercholesterolemia, and current smoking); METs: 1 MET = 3.5 mL/kg/min oxygen uptake; CRF is maximal METs achieved during the exercise test and is calculated from treadmill speed and grade using standard equations.

† Too few participants for stratified analysis.

A novel finding of the present investigation was that among healthy older men, the effects of CRF and BMI were multiplicative. Specifically, our obese, highly fit participants had the lowest mortality risk of any group. Thus, among individuals with moderate or high fitness levels, those with higher BMI had better survival. To our knowledge, this has not been previously demonstrated.

Our study has several strengths, including: (i) all participants underwent an extensive physical examination, which provides thorough information on the presence or absence of baseline disease; (ii) all participants had a normal exercise test and were free of CVD, which demonstrates the apparent health of participants; (iii) CRF was determined by maximal exercise testing; and (iv) our sample size consisted of nearly 1,000 elderly patients with an average follow-up of almost 7 years.

Our study has several limitations. First, because waist circumference measures were not obtained, we were not able to evaluate body fat distribution characteristics. Second, we included only men who had prior military service and were referred for exercise testing for clinical reasons. Any effort to predict mortality by using fitness, BMI, clinical, or demographic data should be considered population specific. Though deemed "healthy," all participants were referred to exercise testing for clinical reasons. Third, CRF is a single measure that is influenced by many factors, including age, heredity, and recent and lifelong activity patterns (17). The extent to which CRF may be improved in the elderly, or the influence this may have on mortality, cannot be determined from the present investigation. Finally, because we only have baseline data on weight, exercise capacity, and other exposures, we do not know if changes in any of these variables occurred during follow-up or how this might have influenced the results.

In summary, both higher BMI and higher fitness were protective for all-cause mortality in this cohort of elderly men. Future studies should focus on the influence of fitness and fatness on mortality in diverse populations and whether changes in fitness level and/or body weight improve health outcomes in the elderly.

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