The Relation of Body Mass Index, Cardiorespiratory Fitness, and All-Cause Mortality in Women

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Abstract

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Objective: To examine the relation of body mass index (BMI), cardiorespiratory fitness (CRF), and all-cause mortality in women.

Research Methods and Procedures: A cohort of women (42.9 ± 10.4 years) was assessed for CRF, height, and weight. Participants were divided into three BMI categories (normal, overweight, and obese) and three CRF categories (low, moderate, and high). After adjustment for age, smoking, and baseline health status, the relative risk (RR) of all-cause mortality was determined for each group. Further multivariate analyses were performed to examine the contribution of each predictor (e.g., age, BMI, CRF, smoking status, and baseline health status) on all-cause mortality while controlling for all other predictors.

Results: During follow-up (113,145 woman-years), 195 deaths from all causes occurred. Compared with normal weight (RR = 1.0), overweight (RR = 0.92) and obesity (RR = 1.58) did not significantly increase all-cause mortality risk. Compared with low CRF (RR = 1.0), moderate (RR = 0.48) and high (RR = 0.57) CRF were associated significantly with lower mortality risk ($p = 0.002$). In multivariate analyses, moderate (RR = 0.49) and high (RR = 0.57) CRF were strongly associated with decreased mortality relative to low CRF ($p = 0.003$). Compared with normal weight (RR = 1.0), overweight (RR = 0.84) and obesity (RR = 1.21) were not significantly associated with all-cause mortality.

Discussion: Low CRF in women was an important predictor of all-cause mortality. BMI, as a predictor of all-cause mortality risk in women, may be misleading unless CRF is also considered.

Key words: cardiovascular fitness, women's health, exercise testing, aerobic power, metabolic equivalent

Introduction

Overweight is a common disorder in the United States and other industrialized countries. According to body mass index (BMI) data from the third National Health and Nutrition Examination Survey, the prevalence of overweight (BMI, >25 kg/m^2) for adults in the United States is now estimated to be 55% (1,2).

Using the criteria of BMI, waist-to-hip ratio, or waist circumference, overweight has been associated with increases in both all-cause (3,4) and cardiovascular (5,6) mortality for women in several prospective studies. Whereas this association persists after adjusting for potential confounding variables such as cigarette smoking, these studies did not measure cardiorespiratory fitness (CRF) level. A low CRF level is an important independent predictor of all-cause mortality in both men and women (7,8). Failure to measure and consider CRF may confound the relationship between BMI and mortality. The failure to measure CRF in studies examining the relationship of BMI and mortality may be attributable to logistical constraints, but may also be attributable, in part, to an underlying assumption that all overweight and obese individuals are sedentary and unfit, an assumption that is not valid. Our group has shown that moderately to highly fit overweight or obese men have significantly lower rates of all-cause mortality than normal-weight or overweight men with low levels of CRF (9,10). Additionally, the health benefits of normal weight in men are limited to those who have moderate

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or high levels of CRF (11). Our primary goal in the current study was to extend these observations to women. Thus, the purpose of our study was to quantify the association between BMI, CRF, and all-cause mortality in adult women.

Research Methods and Procedures

Study Participants and Measurements

The Aerobics Center Longitudinal Study (ACLS) is a prospective epidemiological follow-up of patients who underwent an examination at the Cooper Clinic (Dallas, TX). Participants for this study included 9925 female patients (mean age, 42.9 ± 10.4 years) who completed a comprehensive medical examination during the interval between December 6, 1970 and December 31, 1996. All participants were United States citizens, and nearly all (98%) were white.

After receiving written informed consent from each participant, a clinical evaluation was performed. Examinations included fasting blood chemistry, personal and family health history, anthropometry, resting blood pressure, electrocardiogram, and a maximal graded exercise test on a motor-driven treadmill. Height and weight were measured by a stadiometer and a standard physician's scale. BMI was calculated as weight in kilograms per square meter. On the basis of NIH guidelines, three categories of BMI were used in this study: normal weight (BMI, 18.5 to 24.99), overweight (BMI, 25 to 29.99), and obese (BMI, ≥30). All procedures were administered by trained technicians who followed standardized protocols.

CRF was measured on a treadmill with the modified Balke protocol. The treadmill test began at a speed of 88 m/min and 0% elevation. At the end of the first minute, elevation was increased to 2%, then by 1% each minute thereafter. After 25 minutes, elevation remained at 25%, whereas speed was increased by 5.4 m after each minute until volitional fatigue. Treadmill time has been shown to correlate highly ($r = 0.94$) with directly measured maximal oxygen uptake in women (12). Patients were encouraged to give a maximal effort during the test, and those who did not achieve at least 85% of age-predicted maximal heart rate were excluded from the analyses.

Treadmill time was used to group study participants into CRF categories on the basis of age-specific cutoffs. The age groups were as follows: 20 to 29, 30 to 39, 40 to 49, 50 to 59, 60 to 69, and 70 to 79 years. Because there are several different treadmill protocols used in laboratories, and METs are a standard measure well understood in the field, we then calculated maximal MET levels of participants from treadmill time using the following formula (13): maximal MET level = (treadmill time in minutes × 1.750) + 10.5/3.5. Based on previous mortality findings in this population (7), three categories of CRF were created. The least fit 20% in each age group were classified as low fit, the next 40% as moderately fit, and the top 40% as highly fit.

Participants were classified as apparently healthy unless they reported chronic illnesses (e.g., myocardial infarction, stroke, hypertension, diabetes, cancer) at the time of their baseline examination or had an abnormal resting or exercise electrocardiogram. Women with at least one of these conditions were classified as unhealthy.

Mortality Surveillance

We followed study participants for mortality from the date of their initial examination to either the date of death or, for survivors, to December 31, 1996. The National Death Index was used to identify possible deaths, and official death certificates were retrieved for these individuals. Information on the death certificate was compared with the participant's clinical record to confirm a match. The mean length of follow-up was 11.4 ± 6.2 years.

Statistical Analyses

Our initial analysis compared the relative risk (RR) with 95% CIs of all-cause mortality among normal-weight (n = 7801), overweight (n = 1527), and obese (n = 597) women after adjusting for age, smoking status, and baseline health status. After adjustment for age, smoking status, and baseline health status, RR with 95% CIs was determined for low-fit, moderately fit, and highly fit women. We then performed a multivariate analysis using BMI, CRF, age, smoking status, and baseline health status to determine the independent contribution of each to all-cause mortality. We also performed a separate multivariate analysis using these variables to determine whether there was a significant interaction between CRF and BMI.

Results

Demographic characteristics of subjects are shown in Tables 1 and 2. Overall, the CRF level and risk profile of the normal-weight group was more favorable than that of the overweight and obese groups (Table 1). Similarly, the risk profile of the highly fit group was more favorable than the moderately and low-fit groups (Table 2). There were 195 deaths during follow-up (during 113,145 woman-years of follow-up). Cancer (118 deaths) and cardiovascular disease (44 deaths) were the leading causes of mortality in the cohort, accounting for 83% of all deaths. RR of all-cause mortality across different levels of BMI adjusted for age, smoking status, and baseline health status are presented in Figure 1. There were no significant differences in all-cause mortality among the normal-weight (RR = 1.0), overweight (RR = 0.92; 95% CI, 0.61 to 1.37), or obese (RR = 1.58; 95% CI, 0.95 to 2.63) groups. However, the RR of the obese group did approach statistical significance ($p = 0.08$).

Figure 2 shows a comparison of all-cause mortality among low-fit, moderately fit, and highly fit women after adjustment for age, smoking status, and baseline health

Table 1. Descriptive characteristics for 9925 women by BMI category (Aerobics Center Longitudinal Study, 1970 to 1996)

	Normal (n = 7801), BMI 18.5 to 24.99	**Overweight (n = 1527), BMI 25 to 29.99**	**Obese (n = 597), BMI ≥ 30**	***p* value for trend**
Age (years)	42.2 ± 10.4	46.0 ± 10.6	44.2 ± 10.5	0.0001
Height (cm)	164.6 ± 5.9	163.8 ± 6.7	163.4 ± 8.5	0.0001
Weight (kg)	58.2 ± 6.0	72.3 ± 7.0	91.0 ± 13.6	0.0001
BMI (kg/m^2)	21.5 ± 1.7	26.9 ± 1.4	34.1 ± 4.9	0.0001
Cholesterol (mM)	5.1 ± 1.1	5.5 ± 1.1	5.5 ± 1.1	0.0001
Glucose (mM)	5.2 ± 6.1	5.4 ± 1.0	5.7 ± 1.4	0.0486
Triglycerides (mM)	0.9 ± 0.8	1.3 ± 0.9	1.6 ± 1.1	0.0001
Treadmill performance (maximal METs)	9.9 ± 2.3	8.4 ± 1.9	7.1 ± 1.6	0.0001
Resting SBP (mm Hg)	110.7 ± 13.8	115.8 ± 13.8	121.8 ± 15.2	0.0001
Resting DBP (mm Hg)	74.3 ± 9.2	77.4 ± 9.0	82.0 ± 9.6	0.0001
Present smoker (%)	928 (11.9)	141 (9.2)	62 (10.4)	0.0117
Apparently healthy (%)	6629 (85.0)	1150 (75.3)	407 (68.2)	0.0001
Number of deaths (%)	149 (1.9)	29 (1.9)	17 (2.9)	0.2221

With the exception of the last three variables, all data are means ± SD.
BMI, body mass index; MET, metabolic equivalent; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 2. Descriptive characteristics for 9925 women by CRF category (Aerobics Center Longitudinal Study, 1970 to 1996)

	Low CRF (n = 1657)	**Moderate CRF (n = 3747)**	**High CRF (n = 4521)**	***p* for trend**
Age (years)	43.2 ± 10.1	43.0 ± 10.3	42.7 ± 10.8	0.0001
Height (cm)	163.7 ± 6.0	164.2 ± 6.2	164.8 ± 6.3	0.0001
Weight (kg)	69.3 ± 16.1	62.8 ± 10.4	59.5 ± 8.0	0.0001
BMI (kg/m^2)	25.9 ± 5.8	23.3 ± 3.7	21.9 ± 2.5	0.0001
Cholesterol (mM)	5.3 ± 1.0	5.3 ± 1.1	5.1 ± 1.2	0.0001
Glucose (mM)	5.4 ± 1.1	5.2 ± 0.7	5.3 ± 8.0	0.0982
Triglycerides (mM)	1.3 ± 0.9	1.1 ± 0.8	0.9 ± 1.0	0.0001
Treadmill performance (maximal METs)	6.5 ± 1.0	8.6 ± 1.1	11.4 ± 1.9	0.0001
Resting SBP (mm Hg)	116.0 ± 15.7	112.1 ± 14.0	110.8 ± 13.6	0.0001
Resting DBP (mm Hg)	77.6 ± 10.3	75.4 ± 9.4	74.3 ± 9.0	0.0001
Smoker (%)	299 (18.0)	495 (13.2)	337 (7.5)	0.0001
Apparently healthy (%)	1225 (73.9)	3113 (83.1)	3848 (85.1)	0.0001
Number of deaths (%)	75 (4.5)	63 (1.7)	57 (1.3)	0.0001

With the exception of the final three variables, data are means ± SD.
CRF, cardiorespiratory fitness; BMI, body mass index; MET, metabolic equivalent; SBP, systolic blood pressure; DBP, diastolic blood pressure.

status. Compared with low-fit women (RR = 1.0), moderately fit (RR = 0.48; 95% CI 0.34 to 0.68) and highly fit women (RR = 0.57; 95% CI, 0.40 to 0.82) had a significantly lower risk of mortality (p = 0.002).

Figure 3 shows the proportion of women who were classified as having moderate or high CRF within several different strata of BMI. With increasing BMI, the proportion of fit women decreased linearly. For example, 90.5% of women with a BMI between 18.5 and 21 kg/m^2 were classified as having moderate or high CRF, compared with 20.5% of women with a BMI >37.1 kg/m^2.

Table 3 summarizes a multivariate analysis using CRF, BMI, smoking status, and baseline health status as categorical independent variables and age as a continuous independent variable. The RR of each variable was adjusted for all other variables in the model to examine the independent contribution of each on all-cause mortality. We determined that there was no significant interaction between CRF and BMI; therefore, no interaction terms were included in the model. Compared with women with low CRF (RR = 1.0), women with moderate (RR = 0.49; 95% CI, 0.35 to 0.69) and high (RR = 0.57; 95% CI, 0.40 to 0.83) CRF were significantly less likely to die during follow-up (p = 0.003). Overweight (RR = 0.84; 95% CI, 0.56 to 1.26) and obese (RR = 1.21; 95% CI, 0.71 to 2.05) women were no more likely to die than normal-weight women in this model.

Discussion

The purpose of the current study was to examine the relation of BMI, CRF, and all-cause mortality in women. To the best of our knowledge, ours is the first study to explore this topic in women. We have demonstrated in this study that low CRF is a stronger predictor than BMI of all-cause mortality in women.

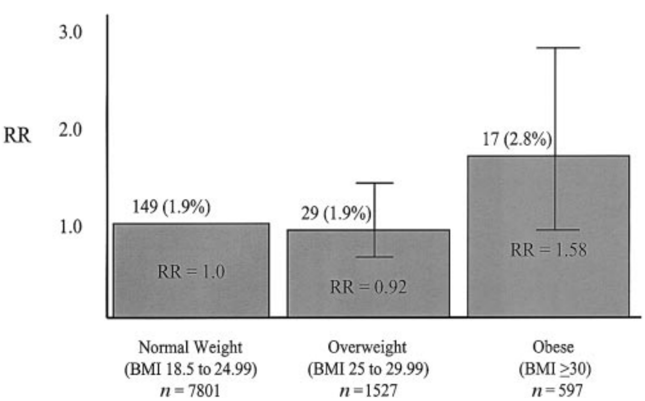

Figure 1: Relative risk (RR) of all-cause mortality by body mass index (BMI) category. RRs have been adjusted for age, smoking, and baseline health status. ACLS women from 1970 to 1996. Numbers on top of bars represent number of deaths and percentage of group members who died.

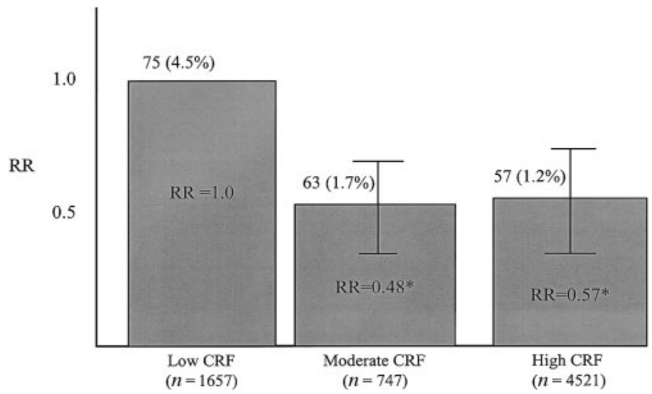

Figure 2: Relative risk (RR) of all-cause mortality by cardiorespiratory fitness (CRF) category. RRs have been adjusted for age, smoking, and baseline health status. ACLS women from 1970 to 1996. Numbers on top of bars represent number of deaths and percentage of group members who died. *, significantly different than low CRF group (p = 0.002).

In the current study, obese women had a RR of 1.58 compared with normal-weight women (Figure 1), and this value approached statistical significance (p = 0.08). One possible reason we did not see a greater RR for obese women is that we adjusted for baseline health status as well as age and smoking in our model. Because conditions such as hypertension and Type 2 diabetes are to some extent a consequence of obesity, adjusting for baseline health status lessens the effect of obesity on mortality because some of its consequences are removed. In a separate analysis where we adjusted for only age and smoking status, the RR of the obese group (RR = 1.70) was significantly different (p = 0.04) from the normal-weight group.

Obesity is an important public health problem; prevalence of obesity and overweight in the United States are currently estimated to be 22% and 55%, respectively. This study was not intended to minimize or trivialize the importance of these conditions. However, we strongly believe it is important to consider CRF levels when examining the impact of overweight status and obesity on mortality. It is also important not to make the assumption that all overweight and obese individuals are sedentary and unfit. Our group has shown previously that some overweight and obese men possess moderate or even high levels of CRF (9,10). Furthermore, fit overweight and obese men have significantly lower rates of all-cause mortality than normal-weight men who are unfit, even after controlling for confounding variables such as cigarette smoking (9).

Whereas most health professionals assume that intentional weight loss in overweight and obese individuals is beneficial, it is interesting to note that the scientific evidence that intentional weight loss decreases all-cause mortality is limited to one study (14). Virtually all other studies on weight loss and mortality failed to differentiate between

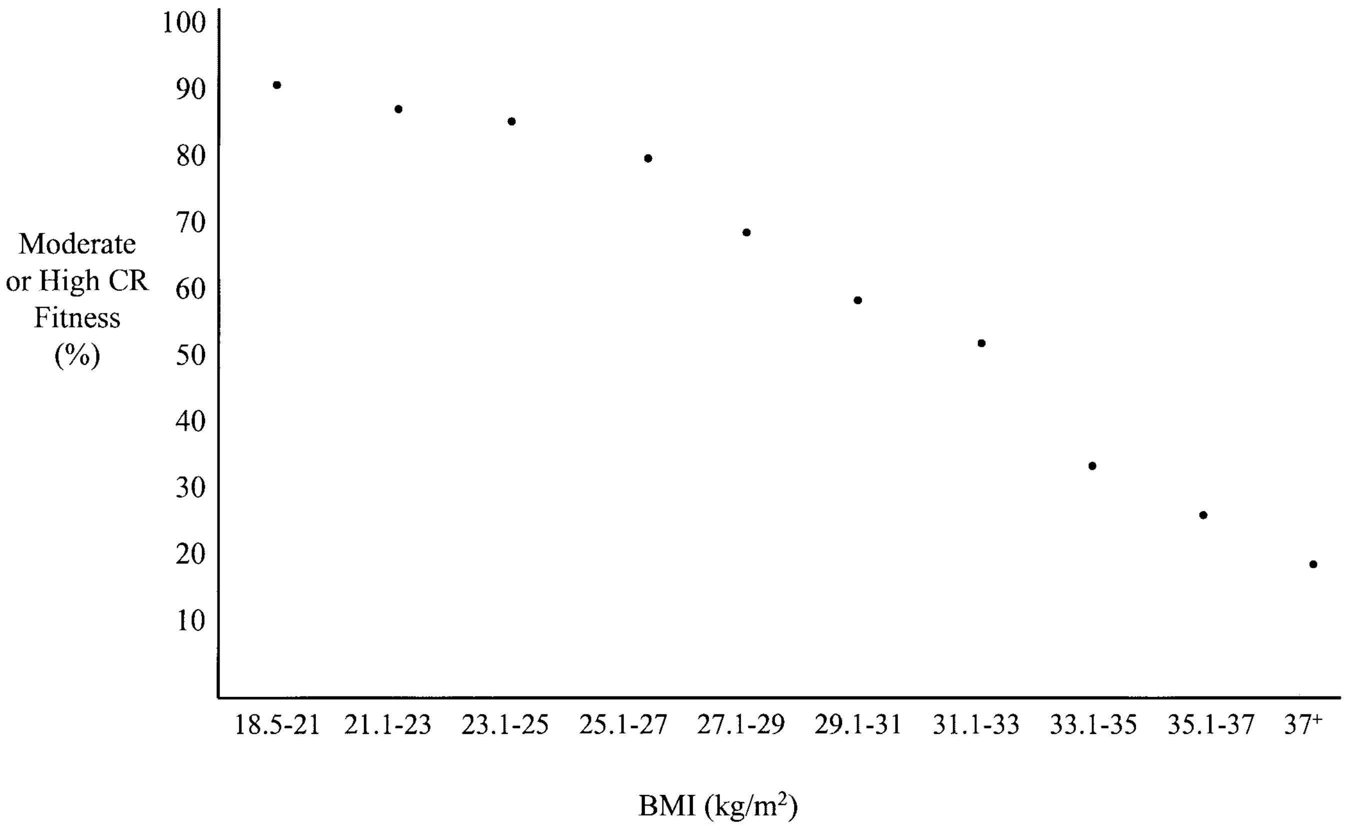

Figure 3: Percentage of women with moderate or high cardiorespiratory fitness (CRF) by body mass index (BMI). ACLS women from 1970 to 1996.

intentional and unintentional weight loss (15), making the results largely noninterpretable. Until we know for certain that intentional weight loss significantly decreases all-cause mortality, it is worth considering that perhaps our time as health professionals would be better spent striving to help sedentary and unfit individuals increase levels of CRF, and encouraging healthy diets and smoking cessation in the population, rather than focusing specifically on weight loss. For example, Project Active (16) compared the effects of a lifestyle physical activity program with a traditional structured exercise program in previously sedentary men and women over a 24-month period. Although body weight did not change in either group, significant improvement in physical activity levels, CRF, systolic and diastolic blood pressure, and percentage of body fat was achieved by both groups. Project Active also demonstrated that exercise prescription and programs need not necessarily be structured, nor is a state-of-the-art fitness center needed for individuals to improve activity levels, CRF levels, and risk factors. In an early study, Tremblay et al. (17) showed that the metabolic profile of obese women could be normalized by exercise and a low-fat diet, even when significant weight loss did not occur.

CRF is primarily a function of the heart's maximal ability to pump blood (maximal cardiac output) and the ability of skeletal muscle to extract and use oxygen (maximal arteriovenous O_2 difference). These two variables have both genetic and environmental influences. For example, the contribution of genetics to heart size, structure, and cardiac function variance in the population is estimated to be between 30% to 70% (18). Similarly, a genetic component is thought to account for 40% to 50% of the population variation in the proportion of type 1 (slow-twitch) skeletal muscle fibers in humans (18). Thus, it is clear there are genetic factors that limit the extent to which CRF can be developed. However, environment (the frequency, intensity, and duration of aerobic training) has a significant effect on CRF as well and appears to account for more of the variation in CRF than do genetic factors.

It should be emphasized that the criterion for the fit category in this study was any value above the 20th percentile for each age group. For example, a 40- to 49-year old woman would require a maximal oxygen uptake of at least 28.0 mL/kg per minute (8 METs) to be classified as fit. This modest goal is attainable for most women, as has been shown by aerobic-training studies where as much as a mean

Table 3. Multivariate analysis using CRF, BMI, age, baseline health status, and smoking status of 9925 women (Aerobics Center Longitudinal Study, 1970 to 1996)

Variable	RR (95% CI)	*p* value
CRF (Maximal METs)		
Low	1.0 (Referent)	
Moderate	0.49 (0.35, 0.69)	0.0001
High	0.57 (0.40, 0.83)	0.003
BMI (kg/m^2)		
Normal	1.0 (Referent)	
Overweight	0.84 (0.56, 1.26)	0.39
Obese	1.21 (0.71, 2.05)	0.48
Age (years)	1.08 (1.07, 1.09)	0.0001
Baseline health status		
Healthy	1.0 (Referent)	
Unhealthy	0.76 (0.55, 1.05)	0.10
Smoking status		
Never	1.0 (Referent)	
Quitter	1.12 (0.81, 1.56)	0.49
Current	1.83 (1.26, 2.67)	0.002

Each variable has been adjusted for all other variables in the model.

CRF, cardiorespiratory fitness; BMI, body mass index; RR, relative risk; CI, confidence interval; MET, metabolic equivalent.

25% increase in maximal oxygen uptake was seen in sedentary women (19). It should also be noted that moderate CRF is attainable even for obese women, as evidenced by the fact that 50.5% of women with BMIs between 31.1 and 33 kg/m^2 were classified as having at least a moderate level of CRF (Figure 3).

The current study has certain limitations. Women in the ACLS do not represent a random sample of the population; rather they are primarily white and college educated. We cannot say for certain that our observations extend to nonwhite women and/or women with lower levels of education. At the present time, there are no national norms in the United States for CRF that are based on a random sample of the population. However, median estimated maximal oxygen consumption for women in the ACLS is remarkably similar to a random sample of women in the Canada Fitness Survey (20). Thus, it would seem that women in the ACLS are not a select group of fitness enthusiasts and are similar to other groups of North American women.

In this study, we used treadmill time to estimate maximum VO_2 (and METs) rather than a direct measurement of oxygen uptake. Whereas our group has previously shown that the correlation between treadmill time and directly measured maximum VO_2 in women is 0.94 (12), most of the women in that particular study were in the normal BMI category. Although currently we have no evidence to the contrary, we cannot say for certain that the correlation between treadmill time and maximum VO_2 is as high in overweight and obese women. Therefore, it is possible that some overweight and obese women might have been misclassified with regard to CRF category.

We used baseline measurements to determine CRF and BMI categories. It is possible that some women may have changed their CRF or BMI category during the study, and we did not measure changes in these variables in the present study.

It is also important to note that there are various classes of obesity. Our observations extend primarily to women who are normal weight, overweight, Class 1 obese (BMI, 30 to 34.9 kg/m^2), and Class 2 obese (BMI, 35.0 to 39.9 kg/m^2). We do not have sufficient data to make any observations on women who are Class 3 obese (BMI, $\geq$40 kg/m^2). It is likely from the trend observed in Figure 3 that the vast majority of women who are Class 3 obese are sedentary and unfit, and thus are at significantly increased risk for all-cause mortality.

Because of the limited number of deaths in this cohort, we were not able to examine the effects of CRF and BMI on specific causes of mortality. We await additional mortality data for this purpose.

In summary, a low level of CRF as measured by a maximal treadmill exercise test was a more important predictor of all-cause mortality in ACLS women than was baseline BMI. Because previous work by our group has shown that unfit men who become fit enjoy a substantial reduction in mortality (21), it seems reasonable to suggest that a much stronger emphasis should be placed on increasing the CRF level of all unfit women as well. From an all-cause mortality perspective, we strongly suggest that clinicians and other health professionals spend at least as much time encouraging sedentary women to become more physically active as encouraging overweight and obese women to lose weight.

Acknowledgments

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