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Cardiorespiratory Fitness and All-cause Mortality in Men With Emotional Distress

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Abstract

Objective—Mental health and emotional disorders are often associated with higher mortality risk. Whether higher cardiorespiratory fitness (CRF) reduces the risk for all-cause mortality in individuals with emotional distress is not well known.

Patients and Methods—Participants were 5,240 men (mean age 46.5±9.5 years) with emotional distress (including depression, anxiety, thoughts of suicide, or a history of psychiatric or psychological counseling), completed an extensive medical examination between 1987 and 2002, and were followed for all-cause mortality through December 31, 2003. CRF was quantified as maximal treadmill exercise test duration and was grouped for analysis as low, moderate, and high. Cox proportional hazards regression was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs).

Results—During a median (range) 8.7 (1.0–16.9) years and 46, 217 person years of follow-up, there were 128 deaths from any cause. Age- and examination year- adjusted all-cause mortality rates (95% CIs) per 10,000 person years according to low, moderate, and high CRF groups were

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CONFLICT OF INTEREST DISCLOSURES

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64.7 (44.9, 89.3), 28.0 (23.8, 31.5), and 19.6 (17.1, 21.6) (trend $P < .001$) in men who reported any emotional distress. Overall, the multivariable-adjusted HRs and 95% CIs across incremental CRF categories were 1.00 (referent), 0.54 (0.32–0.90), and 0.47 (0.26–0.85), linear trend $P = .03$.

Conclusions—Among men with emotional distress, higher CRF is associated with lower risk of dying, independent of other clinical mortality predictors. Our findings underscore the importance of promoting physical activity to maintain a healthful level of CRF in individuals with emotional distress.

Introduction

Mental health conditions represent the fifth greatest contributor to the global burden of disease, with an estimated economic cost of US \$2.5 trillion in 2010 and an expected \$6.0 trillion by 2030¹. The association between mental health issues and all-cause mortality has been explored in populations around the world. For example, in Norway, depression has been shown to be a risk factor for all-cause mortality at a similar level to smoking². In Canada, major depressive episodes have been shown to be a strong predictor of all-cause mortality³. In a clinic-based study from England, depression was associated with higher all-cause mortality decades after patients received treatment, even excluding factors such as suicide, accidents, and other non-natural causes of death⁴. In the US, having both cancer and depression together has been associated with higher all-cause mortality, as opposed to having just one⁵. Depression is also associated with all-cause mortality among patients with cardiovascular disease (CVD)⁶. Finally, meta-analyses have demonstrated that even some forms of subclinical levels of depression are associated with higher risk of all-cause mortality⁷.

These findings suggest that people with poor mental health have a shorter life expectancy. Physical inactivity⁸ or low cardiorespiratory fitness (CRF)⁹ has been linked to higher risk of all-cause and CVD-mortality in healthy populations of men and women. This is significant in light of the evidence that negative emotions may play a role in all-cause mortality and CVD risk¹⁰. The connection between CRF and negative emotions has been investigated in previous research¹¹. Increasing fitness has been shown to ease depressive symptoms^{10, 12–14} and help symptoms of anxiety¹⁵. Therefore, a better understanding of the inter-correlations among CRF, emotions, and mortality can help us formulate a more specific strategy to promote longevity. The current study seeks to examine whether CRF could protect against premature all-cause mortality among men with emotional distress.

Methods

Study Population

Participants were from the Aerobics Center Longitudinal Study (ACLS) at the Cooper Clinic in Dallas, Texas. Between January 27, 1987 and December 30, 2002, 43,459 men came to the clinic for a thorough preventive health examination and for counseling regarding diet, exercise, and other lifestyle factors associated with increased risk of chronic disease. Participants thus were volunteers (i.e., were not paid for participation). Many were sent by their employers for the examination, some were referred by their doctors, and others were

self-referred. Informed consent was obtained from each participant before beginning the study. The study was reviewed and approved by the Institutional Review Board at the Cooper Institute.

Only participants with a history of emotional distress were included in the current study (n=6,660, 15.3%). The exclusion criteria included: at baseline participants did not achieve at least 85% of aged-predicted maximal heart rate (220-age) during the treadmill test (n=230); those who reported history of myocardial infarction (n=71), stroke (n=30), or cancer (n=376); who were underweight (body mass index (BMI) < 18.5 kg/m²) (n=318); or were followed less than one year (n=395). These criteria resulted in 5,240 men with emotional distress, aged 20–86 years, who were followed from the date of their baseline examination until their date of death, or December 31st, 2003. Women were excluded due to the small number of deaths across CRF groups (3, 5, and 8 deaths across low, moderate, and high CRF, respectively).

Emotional distress was self-report from the medical history questionnaire that asked participants whether they had ever experienced depression, anxiety, or thoughts of suicide, or received psychological or psychiatric counseling. Participants were instructed to answer “yes,” “no,” or “don’t know.” If participants responded “yes” to any of the above questions, they were defined as having emotional distress. One person can report multiple types of distress, therefore, these categories were not mutually exclusive. There were 2,229 (43%) men who reported more than one emotional distress item.

Clinical Examination

After an overnight fast of 12 hours, participants were given a baseline examination consisting of individual and family health history, a physical examination, a questionnaire to record demographics and health habits, anthropometry, blood chemistry tests, blood pressures, and, of particular note for this current study, a maximal treadmill exercise test. Details on the ACLS study have been described in previous literature⁹. Smoking habits (current smokers or not), alcohol intake habits (heavy drinkers or not), physical inactivity (no leisure-time activities during the past three months), and parental history of CVD were assessed with a standardized questionnaire. Drinks per week were computed with one drink standardized to 12 ounces of beer (3.41 dl) 5 ounces of wine (1.421 dl) or 1.5 ounces of liquor (0.4262 dl). Heavy drinking (in men) was defined as more than 14 drinks per week. Hypertension was defined as a physician diagnosis or measured blood pressure ≥ 140/90 mm Hg. Diabetes was defined as a physician diagnosis, insulin usage, or fasting glucose ≥ 126 mg/dL (7.0 mmol/L). Body mass index was calculated from the measured height and body weight. Hypercholesterolemia was defined as a physician diagnosis or fasting blood cholesterol measured at ≥ 240 mg/dL (6.20 mmol/L)¹⁶.

Cardiorespiratory Fitness

Cardiorespiratory fitness was the primary exposure of interest and was determined by measuring the maximal amount of time participants ran on the treadmill until volitional exhaustion or physician intervention. Participants were divided into three categories. To determine physical fitness, the treadmill speed was first set at 88 m/min. The first minute the

grade was 0%, the second minute 2%, and increased 1% each minute until 25 minutes passed. At that point, the grade no longer changed and each minute the speed increased 5.4 m/min until the end of the test. Encouragement was given for patients to give the maximal amount of effort. The variable used in analysis was treadmill test time in seconds. CRF was classified as low, moderate, and high based on the cutpoints developed from the ACLS¹⁷. These cutpoints were derived from age- and sex-specific distributions of treadmill time duration among the ACLS population, as we published previously¹⁷. Because there are no current standard cut points to categorize low, moderate, or high CRF, to maintain consistency in our study methods, we used this approach in the ACLS.

All-Cause Mortality Surveillance

Time to all-cause mortality was the outcome of interest. Participants were followed from the date of the baseline examination until death, lost to follow-up, or 12/31/2003. Mortality surveillance was primarily conducted through the National Death Index (NDI). The NDI is an accurate method of ascertaining deaths in observational studies, with high sensitivity (96%) and specificity (100%)¹⁸. Death certificates were collected from states in which participants deaths occurred. The NDI data have similar accuracy to the mortality data determined by an Endpoints Review Committee, which reviews death certificates and also medical records relevant to the event and study to make their decision¹⁹.

Statistical analysis

Baseline characteristics are presented across levels of CRF (low, moderate, and high). Continuous variables were summarized using mean $\pm$ SD and categorical variables were summarized using frequency (%). Linear regression models were used to determine trends in continuous variables across levels of CRF. The Cochran-Armitage test for trend was used to determine trends in categorical variables across levels of CRF. Age and examination year adjusted all-cause mortality rates per 10,000 person years were calculated across levels of CRF together with corresponding 95% CIs. Unadjusted and adjusted Cox proportional hazards regression models were used to assess the association between levels of CRF and all-cause mortality. Hazards ratios (HRs) and 95% confidence intervals (CIs) are presented. Schoenfeld residuals were used to assess the proportional hazards assumption and no violation was found. Multivariable analyses were adjusted for age (years), examination year, smoking status (current smoker vs. non-smoker), alcohol intake (≤ 14 drinks/week vs. >14 drinks/week), abnormal resting or exercise electrocardiogram (ECG) responses (present vs. not present), physically inactive (yes vs. no), number of emotional distress, and parental history of CVD (yes vs. no). Further adjustments were made for hypertension (yes vs. no), diabetes (yes vs. no), hypercholesterolemia (yes vs. no), and BMI (kg/m^2). An interaction term between number of emotional distress (1 and >1) and CRF groups was also assessed to further explore the effect modification of emotional distress. Adjusted – Cox proportional hazards regressions were performed separately among men with 1 type of emotional distress and those with at least 2 types of emotional distress to assess whether the associations between CRF and all-cause mortality were different among particular subgroups. All *P* values are two-sided and *P* $< .05$ was regarded as statistically significant. All analyses were performed using SAS statistical software, version 9.4 (SAS Institute, Inc., Cary, NC).

Results

Among men who experienced emotional distress, 46% reported depression, 58% reported anxiety, 51% reported mental counseling, and only a small portion of participants reported ever having suicide thoughts (8%). During a median (range) 8.7 (1.0–16.9) years and 46,217 person years of follow-up, there were 128 deaths from any cause. Table 1 shows the baseline characteristics of the study population based on CRF categories. As expected, exercise duration and maximal METs were higher in the higher CRF groups, whereas BMI, blood pressure, total cholesterol, fasting glucose, physical inactivity, current smoking, and chronic diseases were greater in the lower CRF groups. In addition, the percentage of men who reported more than 1 type of emotional distress was greater in those with low CRF comparing with those with higher level of CRF.

Age- and examination year-adjusted all-cause mortality rates (95% CIs) per 10,000 person years are shown in Table 2, and were as follows: 64.7 (44.9, 89.3) for low CRF, 28.0 (23.8, 31.5) for moderate, and 19.6 (17.1, 21.6) for high ($P<.001$). After additional controlling for number of emotional distress, BMI, alcohol consumption, smoking, physical inactivity, abnormal resting or exercise ECG responses, diabetes, hypertension and hypercholesterolemia, and family history of CVD, the inverse association between CRF and all-cause mortality attenuated, but remained significant ($P=.03$). As also shown in Table 2, HRs and 95% CIs among incremental CRF groups were 1.00 (Low CRF as referent), 0.54 (0.32–0.90), and 0.47 (0.26–0.85).

Whether the number of emotional distress modified the association between CRF and all-cause mortality was examined in Figure 1. Figure 1 showed the stratified analyses among number of emotional distress (1 vs. >1), although the interaction term was not significant ($P=.15$). High CRF was associated with lower risk of all-cause mortality than those with low CRF, regardless of number of emotional distress reported (HR (95% CI): 0.47 (0.22,0.99) for those with 1 emotional distress and 0.27 (0.12, 0.57) for those with 2 or more emotional distress). No significant linear trend was observed between CRF and all-cause mortality among men with 1 type of emotional distress ($P=.09$), however, a dose-response gradient was present among those who reported more than 1 type of emotional distress ($P=.001$).

Discussion

In this study, higher CRF was associated with a lower risk of all-cause mortality, independent of other all-cause mortality predictors, among men with emotional distress. The inverse association remained significant even after adjustment for intermediate factors including BMI, hypertension, diabetes, and hypercholesterolemia. In addition, the number of emotional distress modified the association between CRF and all-cause mortality. The inverse association was observed in men who reported more than 1 type of emotional distress, but not in those with only 1 type of emotional distress. However, the statistical power is likely inadequate to address this issue (P for interaction = .15). These findings suggest that men affected by emotional distress could reduce their risk of all-cause mortality by increasing their level of CRF. However, more research is required to both confirm and better understand the pathways of this possible association.

Emotional distress is a global health issue. Associations between negative emotions and poor physical health are not limited to western nations²⁻⁵, and have been reported in other regions such as South Korea²⁰, Japan²¹, Tanzania²², Hong Kong²³. The relationship between negative emotions and health has been demonstrated in low-gross domestic product (GDP) countries, such as Haiti, Nigeria, and Sierra Leone, as well as moderate-GDP countries, such as Brazil, Russia, and China²⁴. Therefore, finding modifiable factors among people with emotional distress can provide us a pathway for increasing longevity.

Our study suggests that CRF may offer a protective effect against premature mortality among individuals with emotional distress. The findings of the current study are in line with previous research in the general population which demonstrated that higher levels of CRF are associated with a lower risk of all-cause mortality²⁵. Investigating how CRF affects all-cause mortality risk among people with mental health issues or emotional distress is of substantial clinical interest given the debilitating nature of these conditions. Further, people with depression may have reduced levels of CRF¹¹. Importantly, previous research has demonstrated beneficial effects of increasing CRF with exercise training among people with mental disorders^{26, 27} and there is an increasing focus on lifestyle behavior interventions for mental or psychological problems.^{26, 28-30} These data underscore that interventions that aim to decrease cardiometabolic risk among people with mental health or emotional problems should aim to increase CRF.

In addition to reducing all-cause mortality risk, physical activity and exercise may also benefit men with emotional problems for psychological reasons. Increasing fitness has been shown to ease depressive symptoms as well as decrease all-cause mortality^{10, 12-14, 31}. In a Grade A, Level 1 meta-analysis, researchers have demonstrated that exercise may be useful for treating depressive symptoms³². Aerobic exercise and resistance training have also been shown to help symptoms of anxiety¹⁵. Exercise has been shown to be at least equally as effective as antidepressants^{33, 34} and, in a 10-month follow-up study, was determined to be even more effective than sertraline³⁵. Both social³⁶ and biological³⁷ mechanisms have been proposed linking exercise and an improved emotional state.

The association between emotion and all-cause mortality appears to be due to various factors, although the underlying mechanisms are the subject of debate and discussion³⁸. Behavioral explanations include the influence of negative emotions on health behaviors. For example, poorer CVD outcomes in depressed persons are due, in part, to poor health choices, particularly physical inactivity³⁹. After a myocardial infarction, patients with depression are less likely to adhere to recommended lifestyle changes which can reduce all-cause mortality^{10, 40}. On the other hand, regular physical activity had a protective effect on the development of depressive symptoms after first myocardial infarction⁴¹. These studies in fact support a bidirectional relationship between physical activity and negative emotions.

Several potential caveats should be considered in the current study. One limitation is the primarily well-educated non-Hispanic white samples from middle-to-upper socioeconomic strata. Women were also excluded from the current analysis due to the small number of deaths across CRF groups. This may limit the generalizability of the results to other populations, therefore, future study in women is warranted to clarify the association between

CRF and all-cause mortality in those with emotional distress. However, homogeneity in ethnicities and social economic status reduces potential confounding by these factors. Another limitation of this study is the method used for measuring negative emotions. The large-scale nature of the ACLS precluded us from using a more thorough means of testing emotional distress, such as validated questionnaires^{42, 43} or structured clinical interviews performed by clinicians or trained mental health professionals. Finally, the non-mutually exclusive emotional distress and the small number of participants with more than 2 types of emotional distress limited our ability to clarify the modification effect related to these factors. Future research may also benefit from examining specific mental issues separately, rather than having a population based on a broad inclusion of depression, anxiety, suicidal ideation, and a history of psychological/psychiatric counseling.

Conclusion

Our research suggests that higher CRF is associated with a lower risk of all-cause mortality, independent of other all-cause mortality predictors, among men who self-reported depression, anxiety, suicidal ideation, or psychological/psychiatric counseling. Healthcare professionals should focus on improving CRF among men with emotional distress not only to potentially reduce the distress but to also reduce all-cause mortality risk. Although CRF is also partly determined by inherited factors, by far the leading determinant of CRF is physical activity and exercise training^{10, 44}, which should be promoted to achieve a healthful category of CRF.

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LIST OF ABBREVIATIONS

ACLS	Aerobics Center Longitudinal Study
BMI	body mass index
CI	confidence interval
CRF	cardiorespiratory fitness
CVD	cardiovascular disease
GDP	gross domestic product
HR	hazard ratio

MET	metabolic equivalent
NDI	National Death Index
SD	standard deviation

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Figure 1.

Multivariable*-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) of all-cause mortality by cardiorespiratory fitness (CRF) groups across number of emotional distress (1 and >1). * Adjusted for age (years), examination year, smoking status (current smoker vs. non-smoker), alcohol intake (≤ 14 drinks/wk vs. >14 drinks/week), abnormal resting or exercise electrocardiogram responses (present vs. not present), physically inactive (yes vs. no), and parental history of cardiovascular disease (yes vs. no). Low CRF is the referent.

Baseline Characteristics of Study Participants Across Cardiorespiratory Fitness (CRF) Levels, Aerobics Center Longitudinal Study, Dallas, Texas, 1987–2002

Characteristic	All	CRF			P for linear trend
		Low	Moderate	High	
N	5240	652	1942	2646	
Age, years	46.5 ±9.5	44.4 ±9.1	46.3 ±9.6	47.2 ±9.5	<.001
Body mass index, kg/m ²	27.0 ±4.0	31.5 ±5.7	27.8 ±3.5	25.4 ±2.7	<.001
Maximal METs	11.7 ±2.4	8.5 ±1.1	10.5 ±1.1	13.4 ±1.8	<.001
Treadmill time duration, minutes	18.1 ±4.9	11.1 ±2.5	15.7 ±2.5	21.6 ±3.5	<.001
Total cholesterol, mmol/L	5.4 ±1.1	5.6 ±1.1	5.4 ±1.1	5.2 ±1.0	<.001
Fasting blood glucose, mmol/L	5.6 ±1.0	6.1 ±1.9	5.6 ±0.9	5.4 ±0.7	<.001
Blood pressure, mmHg					
Systolic	123 ±14	126 ±14	124 ±14	121 ±13	<.001
Diastolic	82 ±10	86 ±10	83 ±10	81 ±9	<.001
Current smokers (%)	842 (16.1)	168 (25.8)	375 (19.3)	299 (11.3)	<.001
Heavy drinkers (>14 drinks/week) (%)	662 (12.6)	76 (11.7)	277 (14.3)	309 (11.7)	.27
Physically inactive ^a (%)	1289 (24.6)	349 (53.5)	629 (32.4)	311 (11.8)	<.001
Abnormal resting or exercise ECG (%)	489 (9.3)	73 (11.2)	203 (10.5)	213 (8.1)	.002
Hypertension (%)	1897 (36.2)	355 (54.5)	813 (41.9)	729 (27.6)	<.001
Diabetes (%)	313 (6.0)	103 (15.8)	134 (6.9)	76 (2.9)	<.001
Hypercholesterolemia (%)	1787 (34.1)	297 (45.6)	718 (37.0)	772 (29.2)	<.001
Parental history of CVD (%)	1334 (25.5)	192 (29.5)	484 (24.9)	658 (24.9)	.06
Emotional distress (%)					
Depression	2398 (45.8)	347 (53.2)	924 (47.6)	1127 (42.6)	<.001
Anxiety	3029 (57.8)	407 (62.4)	1182 (60.9)	1440 (54.4)	<.001
Thoughts of suicide	429 (8.2)	66 (10.1)	170 (8.8)	193 (7.3)	.01
Psychological counseling	2655 (50.7)	299 (45.9)	933 (48.0)	1423 (53.8)	<.001
Number of emotional distress >1 (%)	2229 (42.5)	318 (48.8)	865 (44.5)	1046 (39.5)	<.001

Abbreviations: METs, maximal metabolic equivalents achieved during the treadmill test; ECG, electrocardiogram; CVD, cardiovascular disease.

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Data shown as Means $\pm$ SD unless specified otherwise.
Defined as no leisure-time physical activity during the past three months.
^b

Rates and Hazard Ratios for All-cause Mortality by Cardiorespiratory Fitness (CRF) Groups, Aerobics Center Longitudinal Study, Dallas, Texas, 1987–2002

Table 2

	Death	Rate (95% CI) ^a	HR ^b	95% CI ^b	HR ^c	95% CI ^c
Low CRF	27	64.7 (44.9, 89.3)	1.00	Referent	1.00	Referent
Moderate CRF	43	28.0 (23.8, 31.5)	0.48	0.29, 0.80	0.54	0.32, 0.90
High CRF	58	19.6 (17.1, 21.6)	0.37	0.22, 0.62	0.47	0.26, 0.85
<i>P</i> linear trend		<.001		<.001		.03

Abbreviations: CVD, cardiovascular disease; HR, Hazard ratio; CI, Confidence interval.

^aRate per 10,000 person years adjusted for age and examination year.

^bAdjusted for age (years), examination year, smoking status (current smoker vs. non-smoker), alcohol intake (< 14 drinks/wk vs. >14 drinks/week), abnormal resting or exercise electrocardiogram responses (present vs. not present), physically inactive (yes vs. no), number of emotional distress, and parental history of CVD (yes vs. no).

^cAdjusted for the above plus body mass index (kg/m²), hypertension (yes vs. no), diabetes (yes vs. no), and hypercholesterolemia (yes vs. no).