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Change in Maximal Exercise Capacity Is Associated With Survival in Men and Women

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Abstract

Objective: To describe the relationship between change in maximal exercise capacity (MEC) over time and risk of all-cause mortality separately in men and women.

Patients and Methods: Consecutive patients (n=10,854; mean ± SD age, 54±11 years; 43% women; 30% nonwhite) who completed 2 physician-referred exercise tests between January 2, 1991, and May 28, 2009, were identified from the Henry Ford Exercise Testing (FIT) Project. The MEC was quantified in metabolic equivalents of task (METs) calculated from peak workload on a treadmill and adjusted to the equivalent for a 50-year-old man. Multivariable Cox proportional hazards regression was performed to assess risk of all-cause mortality associated with change in MEC based on (1) change from age-/sex-adjusted low fitness (<8 METs) to intermediate or high fitness and (2) an absolute change in METs.

Results: Relative to patients with low fitness at both tests, increasing from low to intermediate or high fitness was associated with lower risk of all-cause mortality (adjusted hazard ratio [aHR] = 0.63 [95% CI, 0.45-0.87] in men and 0.56 [95% CI, 0.34-0.91] in women). Each 1-MET increase in age-/sex-adjusted MEC between baseline and follow-up was associated with an aHR of 0.87 (95% CI, 0.84-0.91) in men and 0.84 (95% CI, 0.79-0.89) in women, with no significant interaction by sex (*P*=.995). Similar aHRs were observed in a subgroup with intermediate fitness at baseline.

Conclusion: In men and women referred for an exercise stress test, change in MEC over time is inversely related to risk of all-cause mortality.

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Scientists first reported an inverse relationship between cardiorespiratory fitness and risk of cardiac-related morbidity in 1975.[1] Since that time, several large observational studies have shown that cardiorespiratory fitness is inversely associated with incident hypertension,[2] diabetes,[3] atrial fibrillation,[4] metabolic syndrome,[5,6] chronic kidney disease,[7] progression of coronary atherosclerosis,[8] and risk of all-cause mortality[9-12] and cardiovascular-related morbidity and mortality.[11,13] Although up to 50% of the variability in fitness may be attributed to genetics,[14] change in fitness is a result of changes in health and physical activity habits. There are limited data describing the relationship between survival and change in fitness, which may improve risk stratification beyond an isolated or single measure of fitness. Compared with individuals who remain in a low fitness category, increasing fitness is independently associated with a lower risk of all-cause mortality in men.[12,15,16] However, the generalizability of these observations to patients typically referred for an exercise stress test may be limited, and similar data have not been reported for women. The purpose of this study was to assess the risk of all-cause mortality associated with individual changes in maximal exercise capacity (MEC) over time separately in men and women who completed 2 physician-referred exercise stress tests.

METHODS

Study Design

The Henry Ford Exercise Testing (FIT) Project is a retrospective observational study based on administrative and electronic medical record data. Design details of the FIT Project have been published previously.[17] The FIT Project comprises consecutive patients 18 years and older who performed a physician-referred exercise stress test between January 2, 1991,

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and May 28, 2009, at Henry Ford Hospital and affiliated medical centers in Detroit, Michigan, and the metropolitan area. In the present analysis, we identified a subset of patients from this cohort who performed 2 physician-referred exercise tests (≥12 months apart) during this period. For patients with more than 1 follow-up test, data from the first test after the baseline test were used. Patients with diagnosed heart disease or heart failure at baseline were excluded. No other exclusion criteria were applied. The resultant cohort for the present analysis included 10,854 patients (43% women, 30% nonwhite). The FIT Project was approved by the Henry Ford Health System institutional review board.

Cardiovascular risk factors, medical history, and medication data were collected at the time of the exercise test by test administrators (ie, clinical exercise physiologists, nurses) based on the patient's medical record and patient interview. Definitions for each of these have been published previously.[17] These data, as well as data from preexercise rest and peak exercise, were entered by the same clinicians into a common clinical reporting tool that directly populated the electronic medical record.[17]

Exercise Tests

All exercise tests were performed on a treadmill using the Bruce protocol.[18] Tests were sign/symptom limited or maximal based on procedures outlined by the American Heart Association.[19] The MEC was quantified using metabolic equivalents of task (METs) calculated from peak speed and grade by an electrocardiography/treadmill controller (Quinton Q-Stress; Cardiac Science) based on published equations for walking and running.[20] Although the Quinton controller calculates METs at 50 seconds into a new stage (workload), our standard practice was to require that a patient complete at least 90 seconds of a workload to be assigned the MET level for a given 3-minute stage. Consistent with methods used by Kodama et al,[11] METs reported for the baseline and follow-up tests were adjusted to the equivalent for a 50-year-old man using the following equation: adjusted METs = METs + 0.1 × (age − 50) + 2 [if female]. For this equation, we assume a 1-MET decline in MEC per decade (0.1 MET per year)[21,22] and a 2-MET difference between men and women.[23,24] Using these adjusted METs, patients were categorized into (1) low fitness (<8 METs), (2) intermediate fitness (8 to <11 METs), and (3) high fitness (≥11 METs). These fitness categories are consistent with important mortality risk thresholds that we have observed for men in the FIT Project.[23]

All-cause mortality was identified through April 2013 via linkage with the Social Security Death Index Master File. Myocardial infarctions and coronary revascularization procedures occurring after the baseline test were identified from administrative and clinical databases using *International Classification of Diseases, Ninth Revision, Clinical Modification* codes (410.xx) and *Current Procedure Terminology* codes (334xx, 335xx, 92973-92996), respectively.

Statistical Analyses

Characteristics at baseline for men and women were compared using *t* and χ^2 tests for continuous and categorical data, respectively. Patients were grouped based on the change in their age-/sex-adjusted fitness category between baseline and follow-up tests: (1) low fitness at both tests, (2) low to intermediate or high fitness, (3) intermediate or high to low fitness, and (4) intermediate or high fitness at both tests. Cumulative survival was calculated from life tables. Multivariable Cox regression analyses stratified by sex were performed to determine the adjusted hazard ratio (aHR) and 95% CI associated with the relationship between changes in fitness category (eg, low fitness to intermediate or high fitness) from baseline to follow-up and time to all-cause mortality. Covariates included baseline age; sex; race; hypertension; diabetes; dyslipidemia; smoking; obesity; sedentary; reason for test; test year (<1996, 1996-2000, 2001-2005, >2005); medications for hypertension, diabetes, and lipid management; and atrial fibrillation; as well as incident myocardial infarction and time (years) between tests. Proportional hazards assumption was assessed using partial residual and log-log plots. As a result, age was categorized in quartiles. Cox regression analyses were repeated with delta METs (follow-up minus baseline) as a continuous variable (using reported and age-/sex-adjusted METs)