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Sex Differences in Cardiorespiratory Fitness and All-Cause Mortality: The Henry Ford ExercIse Testing (FIT) Project

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Abstract

Objective: To determine whether sex modifies the relationship between fitness and mortality.

Patients and Methods: We included 57,284 patients without coronary artery disease or heart failure who completed a routine treadmill exercise test between 1991 and 2009. We determined metabolic equivalent tasks (METs) and linked patient records with mortality data via the Social Security Death Index. Multivariable Cox regression was used to determine the association between sex, fitness, and all-cause mortality.

Results: There were 29,470 men (51.4%) and 27,814 women (48.6%) with mean ages of 53 and 54 years, respectively. Overall, men achieved 1.7 METs higher than women ($P<.001$). During median follow-up of 10 years, there were 6402 deaths. The mortality rate for men in each MET group was similar to that for women, who achieved an average of 2.6 METs lower ($P=.004$). Fitness was inversely associated with mortality in both men (hazard ratio [HR], 0.84 per 1 MET; 95% CI, 0.83-0.85) and women (HR, 0.83 per 1 MET; 95% CI, 0.81-0.84). This relationship did not plateau at high or low MET values.

Conclusion: Although men demonstrated 1.7 METs higher than women, their survival was equivalent to that of women demonstrating 2.6 METs lower. Furthermore, higher MET values were associated with lower mortality for both men and women across the range of MET values. These findings are useful for tailoring prognostic information and lifestyle guidance to men and women undergoing stress testing.

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Cardiorespiratory fitness is an important measure of human health[1] that represents both cumulative physical activity and underlying genetic composition.[2,3] However, there are known differences in fitness levels between the sexes.[4] Although some of these differences in fitness are physiologic (eg, skeletal muscle mass, heart and lung size),[5,6] there are also a variety of social and behavioral differences between the sexes.[7] For example, in a 2003-2004 survey of US adults, men reported being more physically active than women.[8,9] Whether these sex-specific differences in fitness translate into a difference in mortality risk is unknown because many of the existing cohort studies on fitness have been limited to either men[10-12] or women[13,14] rather than both sexes.[15] Furthermore, current recommendations to improve individual fitness through physical activity do not account for differences in fitness between men and women.[16]

The purposes of this study were to (1) compare the population distribution of fitness levels between men and women, (2) determine what levels of fitness are associated with the same absolute risk of all-cause mortality in men and women, and (3) assess whether sex modifies the relative association between fitness and mortality. We hypothesized that although men have higher levels of fitness than women, these levels are associated with different absolute risks across the sexes.

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PATIENTS AND METHODS

Study Population

The Henry Ford ExercIse Testing Project (The FIT Project) is a retrospectively defined registry of 69,885 consecutive patients who underwent physician-referred treadmill stress testing in the Henry Ford Health System in metropolitan Detroit, Michigan, between January 1, 1991, and May 28, 2009. Details of the study are published elsewhere.[17] In brief, patients were excluded from the registry if they were younger than 18 years at the time of stress testing or if they underwent pharmacologic stress testing or exercise stress testing using non-Bruce protocols. In this analysis, we further excluded patients with known coronary artery disease (n = 10,190), congestive heart failure (n = 877), and missing relevant variables (n = 1534). The final sample included 57,284 patients. The FIT Project was approved by the institutional review board of Henry Ford Health System.

Treadmill Stress Testing and Cardiorespiratory Fitness

The reason for ordering an exercise stress test was based on physician referrals in the electronic medical record (EMR) and was organized by the most common indications (chest pain, shortness of breath, to rule out ischemia, or other). All the patients underwent routine clinical treadmill stress testing using the standard Bruce protocol for various clinical indications between January 1, 1991, and May 28, 2009. The day the treadmill test was performed was the baseline for this study. Participants were encouraged to exercise as long as possible independent of achieved heart rate. The treadmill test was stopped if the patient had exercise-limiting chest pain, shortness of breath, or other limiting symptoms as assessed by the supervising clinician. In addition, testing could be terminated early at the discretion of the supervising clinician for significant arrhythmias, abnormal hemodynamic responses, diagnostic ST-segment changes, or other clinical reasons, such as patient fatigue.

Resting heart rate and blood pressure were measured in the seated position before exercise testing by trained clinical personnel. In addition to continuous heart rate monitoring, blood pressure was measured every 3 minutes during the test. Cardiorespiratory fitness, expressed in metabolic equivalent tasks (METs), was calculated by the Quinton treadmill controller based on maximal speed and grade achieved. The METs achieved were examined as a continuous variable as well as in 4 groups based on distribution of the data, consistent with previous publications of these data: less than 6, 6-9, 10-11, and 12 or more METs.[18]

Primary Outcome: All-Cause Mortality

Participants were followed from the date of their baseline exercise test through May 28, 2009. Patient information was linked with vital status using the Social Security Death Index Death Master File, a national registry of nearly all deaths that have occurred in the United States. A complete algorithmic search of the Death Master File was completed in 100% of patients. Patients who were not identified as dead in the death registry were administratively censored on the date of their last EMR encounter.

Mortality Risk Factors

Nurses and clinical exercise physiologists collected cardiovascular risk factor data immediately before the stress test. Age at the time of stress testing was derived from participants' date of birth. Sex and race were self-reported. Risk factors were also defined and gathered prospectively by self-report and then were augmented by a retrospective search of the EMR. History of smoking was based on self-reported current cigarette smoking. Diabetes mellitus was defined as a previous diagnosis of diabetes, use of hypoglycemic medications including insulin, or an EMR problem list–based diagnosis of diabetes. Hypertension was defined as a previous diagnosis of hypertension, use of antihypertensive medications, or an EMR problem list–based diagnosis of hypertension. Dyslipidemia was defined as a previous diagnosis of any major lipid abnormality, use of lipid-lowering medications, or an EMR problem list–based diagnosis of hypercholesterolemia or dyslipidemia. Obesity was identified by clinical staff at the time of testing or as a problem listed in the EMR. Family history of coronary artery disease was defined as a compatible history in a first-degree relative. Physical activity status (active vs sedentary) was informally assessed by a nonstandard question asking patients whether they regularly

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