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BRIEF REPORT

Long-term Change in Cardiorespiratory Fitness and All-Cause Mortality: A Population-Based Follow-up Study

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Abstract

Few studies have investigated long-term changes in cardiorespiratory fitness (CRF), defined by indirect measures of CRF, and all-cause mortality. We aimed to investigate whether long-term change in CRF, as assessed by the gold standard method of respiratory gas exchange during exercise, is associated with all-cause mortality. A population-based sample of 579 men aged 42 to 60 years with no missing data at baseline examination (V1) and at reexamination at 11 years (V2) were included. Maximal oxygen uptake (VO_{2max}) was measured at both visits using respiratory gas exchange during maximal exercise testing, and the difference (ΔVO_{2max}) was calculated as VO_{2max} (V2) − VO_{2max} (V1). Deaths were ascertained annually using national death certificates during 15 years of follow-up after V2. The mean ΔVO_{2max} was −5.2 mL/min*kg. During median follow-up of 13.3 years (interquartile range, 12.5-14.0 years), 123 deaths (21.2%) were recorded. In a multivariate analysis adjusted for baseline age, VO_{2max}, systolic blood pressure, smoking status, low- and high-density lipoprotein cholesterol and triglyceride levels, C-reactive protein level, body mass index, alcohol consumption, physical activity, socioeconomic status, and history of type 2 diabetes mellitus and ischemic heart disease, a 1 mL/min*kg higher ΔVO_{2max} was associated with a 9% relative risk reduction of all-cause mortality (hazard ratio, 0.91; 95% CI, 0.87-0.95). This study suggested that in this population, long-term CRF reduction was associated with an increased risk of mortality, emphasizing the importance of maintaining good CRF over the decades.

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Physical fitness is strongly associated with lower cardiovascular disease (CVD) mortality. Multiple studies have reported a consistent inverse association between cardiorespiratory fitness (CRF) and mortality even after adjustment for traditional risk factors.[1,2] Cardiorespiratory fitness is a measure of cardiac and respiratory functioning. Directly measured maximal oxygen uptake (VO_{2max}), an objective and quantitative measure of CRF, is the gold standard for assessing the amount of oxygen consumption during exercise.[3-5] Individual CRF levels have been found to be a stronger predictor of mortality than traditional risk factors, including smoking, hypertension, high cholesterol level, and type 2 diabetes mellitus,[6,7] as well as other exercise test variables, such as ST-segment depression and hemodynamic responses.[1]

The association between CRF and mortality has been proposed to persist across the lifespan, with a single measurement of CRF in midlife strongly associated with the lifetime risk decades later. On the other hand, few studies have assessed the relationship between changes over time in CRF and risk of mortality.[8-10] These studies, however, relied on an indirect estimation of CRF (ie, treadmill time)[8,9] or exercise scores.[10] To help clarify the existing evidence, we assessed whether long-term changes in CRF, as assessed by the gold standard method of oxygen consumption during exercise testing, predict all-cause mortality in the general population.

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PATIENTS AND METHODS

Study Population

The study population is a representative sample of men living in Kuopio and its surrounding rural communities in Eastern Finland. The study group comprised participants in the Kuopio

Ischaemic Heart Disease Risk Factor Study, a longitudinal population-based study designed to investigate risk factors for CVD and related outcomes.[11] These individuals were 42 to 61 years of age during baseline examinations performed between March 20, 1984, and December 5, 1989. Of 3235 potentially randomly selected eligible men, 2682 (82.9%) volunteered to participate in this study.The present analysis is based on 579 men participating in the follow-up study with no missing data on exercise testing and covariates and who had assessment of CRF at baseline (visit 1 [V1]) and at 11-year examination (visit 2 [V2]; mean ± SD interval, 11.1±0.37 years); the repeated assessment was performed without a prespecified clinical indication for exercise testing. The study was approved by the Research Ethics Committee of the University of Eastern Finland, and each participant gave written informed consent.

Assessment of CRF

Maximal oxygen uptake was used as a measure of CRF, which was assessed using a respiratory gas exchange analyzer during maximal symptom-limited cycle ergometer exercise tolerance testing. The standardized testing protocol comprised a 3-minute warm-up at 50 W followed by a step-by-step increase in the workload by 20 W/min, with direct analyses of respiratory gases by the breath-by-breath method using an MGC analyzer (Medical Graphics Corp). The MCG analyzer expresses VO_{2max} as mean values recorded over 8 seconds, and the VO_{2max} was defined as the highest value for or the plateau of oxygen uptake.[11,12] All men with the assessed highest VO_{2max} during the repeated exercise tests were included in the study.[11,12] Although the plateau in oxygen uptake could not have been reached despite an increase in the workload of exercise, the highest (ie, peak) value of oxygen uptake was always defined. The assessment of CRF was performed at V1 and repeated at the 11-year examination (V2). We also tested nonexercise test–based CRF derived from age, body mass index (BMI), heart rate at rest, and physical activity as previously reported.[13]

Assessment of Baseline and 11-Year Risk Factors

A participant was defined as a smoker if he had ever smoked cigarettes, cigars, or a pipe on a regular basis within the past 30 days. Resting blood pressure was measured between 8 and 10 AM using a random-zero sphygmomanometer. Alcohol consumption was assessed using the Nordic Alcohol Consumption Inventory.[12] The BMI was calculated as the weight in kilograms divided by the height in meters squared. Diabetes was defined as a fasting blood glucose level of at least 126 mg/dL (to convert to mmol/L, multiply by 0.0555) or a clinical diagnosis of diabetes with dietary, oral, or insulin treatment. The collection of blood specimens and the measurement of serum lipid, lipoprotein, creatinine, and glucose levels have been described elsewhere.[14] Serum C-reactive protein levels were measured using an immunometric assay (Immulite high-sensitivity C-reactive protein assay, Siemens Medical Solutions Diagnostics). Medication use, baseline diseases, physical activity level, and socioeconomic status were assessed by self-administered questionnaires. Prevalent ischemic heart disease was defined as a previous myocardial infarction, angina pectoris, or the use of nitroglycerin for chest pain at least once a week. The detailed assessment of physical activity and socioeconomic status has been described in previous studies.[15,16] The assessments of risk factors were repeated similarly at V1 and V2.

Ascertainment of Outcomes

All-cause deaths that occurred from V2 (March 1, 2000, through December 31, 2001) through December 31, 2012, were included as an outcome. There were no losses to follow-up. All the study participants were under continuous surveillance for the development of new outcome events. The sources of information were the national death certificates, followed for up to 15 years after V2.[11,15]

Statistical Analyses

For all the analyses, natural logarithm ($\log_e$)–transformed values of nonnormal distributed variables (C-reactive protein levels, BMI, serum triglyceride levels, alcohol consumption, and physical activity) were used. Descriptive data are presented as mean ± SD or median (interquartile range) for continuous variables and as numbers (percentages) for categorical variables. Differences between V1 and V2 values were estimated using the paired