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Impact of Cardiorespiratory Fitness on All-Cause and Disease-Specific Mortality: Advances Since 2009

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A B S T R A C T

Cardiorespiratory fitness (CRF) has been one of the most widely examined physiological variables, particularly as it relates to functional capacity and human performance. Over the past three decades, CRF has emerged as a strong, independent predictor of all-cause and disease-specific mortality. The evidence supporting the prognostic use of CRF is so powerful that the American Heart Association recently advocated for the routine assessment of CRF as a clinical vital sign. Interestingly, the continuity of evidence of the inverse relationship between CRF and mortality over the past decade exists despite a wide variation of methods used to assess CRF in these studies, ranging from the gold-standard method of directly measured maximal oxygen uptake (VO_{2max}) during cardiopulmonary exercise testing to estimation from exercise tests and non-exercise prediction equations. This review highlights new knowledge and the primary advances since 2009, with specific reference to the impact variations in CRF have on all-cause and disease-specific mortality.

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Abbreviations and Acronyms

ACLS = Aerobics Center Longitudinal Study

AHA = American Heart Association

BMI = body mass index

CPX = cardiopulmonary exercise testing

CHD = coronary heart disease

CR = cardiac rehabilitation

CRF = cardiorespiratory fitness

CV = cardiovascular

CVD = cardiovascular disease

HFH = Henry Ford Hospital

MET = metabolic equivalent

MI = myocardial infarction

NHANES = National Health and Nutrition Examination Survey

O_2 = oxygen

PA = physical activity

PAD = peripheral arterial disease

T2D = type 2 diabetes

UK = United Kingdom

VA = Veterans Affairs Medical Centers

VO_{2max} = maximal oxygen consumption

Cardiorespiratory fitness (CRF), also known as aerobic capacity (i.e., VO_{2max}), was initially described by Hill and Lupton[1] as the maximum amount of oxygen (O_2) that can be taken in, transported to and utilized by the working tissue during dynamically strenuous exercise involving large muscle mass. Since its characterization, CRF has perhaps been one of the most widely examined physiological variables, particularly as it relates to functional capacity and human performance. Historically, physical activity (PA), in the form of exercise of moderate-to-vigorous intensity, to improve CRF was associated with athletic training, whereas chronic moderate-intensity PA has been primarily related to health.[2–4] Although the health benefits of regular PA have been advocated since antiquity,[5] the connection between CRF and mortality was established in a prospective study of 10,224 men and 3120 women followed for over 8 years as part of the Aerobics Center Longitudinal Study (ACLS).[6] The primary findings were an inverse relation between CRF and all-cause mortality, which was independent of sex and persisted after adjustment for traditional cardiovascular (CV) disease (CVD) risk factors (e.g., age, blood cholesterol, blood pressure, obesity, smoking status, family history, blood glucose and type 2 diabetes/T2D). Another notable finding was that the largest reduction in all-cause mortality occurred between the lowest and next lowest CRF quintiles, suggesting that the least fit cohort could receive the greatest survival benefit by increasing CRF. After more than two decades of additional research, this association was confirmed and extended by Kodama et al.,[7] in a meta-analysis of 33 investigations which included 102,980 healthy men and women indicating that higher CRF was associated with lower all-cause and coronary heart disease (CHD)/CVD mortality. The authors noted that each 1-metabolic equivalent (MET) increment in CRF was associated with a 13% and 15% lower risk of all-cause and CHD/CVD mortality, respectively. Since this meta-analysis, there have been numerous additional studies that have further clarified the relationship between CRF and mortality and morbidity. A recent scientific statement by the American Heart Association (AHA) put forth a compelling case for CRF as a vital sign.[8] Although we are not yet to the point where there is global recognition that PA and exercise are medicine and CRF is a primary means to assess baseline status, future health trajectory, and therapeutic efficacy of a PA prescription, the evidence continues to grow. Therefore, this review highlights new knowledge and the primary advances since 2009, with specific reference to the impact variations in CRF have on all-cause and disease-specific mortality.

Methodological characteristics

One of the most remarkable features of the studies showing an association between lower levels of CRF and increased all-cause and CVD mortality is the robustness of the findings. This section provides a brief overview of the range of methodological characteristics in studies that have demonstrated this association. The majority of epidemiologic studies since 2009 were mortality follow-ups based on a single baseline assessment of CRF. Their participant characteristics, follow-up duration and mortality type are summarized in Table 1.

Participant referral and health status

Participants in these studies were generally individuals who voluntarily underwent health and medical screening services (Cooper Clinic; [ACLS])[9–13] or enrolled in Asian, European and Scandinavian country-specific population-based health studies, which likely represent a wide sampling of health characteristics.[9,14–18] The most common inclusion criterion was that individuals were free from known CVD at baseline, with a few studies also including the absence of malignant neoplasms, when cancer mortality was an outcome measure. However, three large medical systems, the Veterans Affairs Medical Centers (VA), Henry Ford Hospital (HFH), and the Mayo Clinic, studied cohorts derived from populations primarily