Cardiorespiratory fitness, muscle strength and risk of cardiovascular outcomes

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Physical fitness is associated with lower cardiovascular disease (CVD) mortality, with multiple studies demonstrating a consistent, inverse association between cardiorespiratory fitness (CRF) and mortality even after adjustment for the traditional risk factor burden (1,2). This association has persisted across the lifespan, as a single measurement of CRF in midlife is strongly associated with the lifetime risk for cardiovascular mortality decades later. Cardiorespiratory fitness is associated with a reduced risk of several adverse health outcomes (3-9). Although CRF is recognized as an important marker of both functional ability and cardiovascular health, it is currently one of the most important risk factors that is not routinely and regularly assessed in either the general or specialized clinical setting. The relationship between CRF and other nonfatal cardiovascular outcomes is not well understood, which reflects the limited data on nonfatal cardiovascular events including atrial fibrillation, heart failure (HF) and stroke with objectively measured physical fitness and muscle strength. Much of the focus on the mechanisms of benefit of physical exercise and CRF have focused on prevention of atherosclerosis and its complications, although the specific effects of physical exercise on cardiac and vascular function suggest that low CRF might be an important risk factor for HF and other nonfatal cardiovascular events (10).

Increasing attention is being given to the importance of physical activity and fitness, including both CRF and muscular strength, for decreasing the incidence of chronic diseases, promoting overall cardiovascular and general health, improving quality of life, and delaying CVD and mortality (1,11). The importance of CRF has been neglected in the equation of coronary heart disease and CVD risk, despite the fact that it appears to be one of the most important correlates of overall health status and a predictor of an individual's future risk of CVD (1). Among both asymptomatic subjects and those with previous CVD, the least fit individuals had about 4 times higher risk of all-cause mortality compared with those with the highest level of CRF (12). Importantly, an individual's CRF level was even a stronger predictor of mortality than traditional risk factors such as smoking, hypertension, high cholesterol, and type 2 diabetes mellitus (2,12,13). It has been suggested that the greatest health benefits are observed between the least fit and the next least fit group; whereas lesser improvements in health outcomes occur between individuals who are in the moderate- to high-fit groups. From the public health point of view, the health benefits of CRF are most evident in the low end of the fitness spectrum.

Cardiorespiratory fitness has been shown to be a more powerful predictor of risk than other exercise test variables, including ST-segment depression, symptoms, and hemodynamic responses (1,12,13), a fact not broadly appreciated by the clinical medical community. Commonly used exercise testing parameters consists of electrocardiogram (ECG), blood pressure and heart rate recordings before, during, and after the exercise test. In previous studies, the prognostic importance of ST segment depression, delayed slowing of heart rate and ventricular arrhythmias that appear during recovery from exercise phase are shown to be valuable risk markers for CVD events (14) Studies on ST segment interpretation in ECG and consideration of non-ST segment measures such as CRF and evaluation of the exercise testing as a prognostic rather than a diagnostic test suggest that the prognostic value of fitness may have been underestimated. Secondly, an increasing amount of attention has been directed towards using exercise testing with the assessment of CRF (as measured by maximal oxygen uptake (VO_2max) to measure the therapeutic responses to lifestyle changes or pharmaceutical and invasive interventions. However, there is limited amount of data comparing relative importance of CRF and muscular fitness (strength) as a protective factor for non-fatal and fatal CVD events.

There is growing evidence that objective measures of physical performance such as hand grip strength, walking speed, chair rising and standing balance not only characterize physical capability but also act as markers of general health status (15). A meta-analysis recently demonstrated associations between each of these measures of physical capability and all-cause mortality in community-dwelling populations (15). Another large study found evidence that weaker grip strength in men, assessed in early adulthood, was associated with an increased risk of incident coronary heart disease (CHD) (16). It has also recently been suggested that overall isometric muscle strength in young men is inversely associated with later risk of CVD death, independently of baseline levels of CRF (17). Although grip strength measured at younger ages is related to overall mortality, it is not well known whether walking speed and standing balance performance are associated with HF and all-cause mortality in younger or middle-aged to older populations. Additionally, existing data is limited to show whether gender differences may explain the association between handgrip strength and HF risk. Age-associated loss of muscle mass appears to be inevitable and is likely to be the most significant contributing factor to the decline in muscle strength.

Given that strong data already exist to demonstrate that CRF is a more potent measure of health and prognosis than muscular fitness or physical activity patterns only (18,19), the inclusion of the former measure in future CVD guidelines would be considered a highly valuable benefit. It is shown that, in addition to a genetic component, habitual physical activity is an important determinant for the level of CRF (20).

In a recent published study (21), Lindgren and colleagues evaluated the value of CRF and muscle strength with HF risk. They investigated the associations of CRF and muscle strength at the time of military conscription among young men with the long-term risk of HF events in later life. Linkage of the Swedish registry of conscripts, which contains CRF and muscular strength data for more than one million Swedish men, with the Swedish national inpatient registry (IPR), allowed the analysis of all reported cases of HF over the long follow-up period. A main limitiation of this military conscription registry-based study is that conventional CVD risk factors such as smoking habits were not so extensively studied at the study baseline during the military service. The lack of information regarding weight gain, lipid levels, alcohol consumption, physical activity and lifestyle changes may have caused additional bias on the observed findings. However, in this longitudinal study of young men, the study showed inverse associations of CRF and muscle strength with risk of hospitalization for HF. This recent long-term study suggested that the risk of HF associated with low level of muscle strength was comparable with the risk associated with having low CRF levels (21).

There is limited evidence supporting a protective effect of muscle strength on the cardiovascular system independent of the level of CRF. The authors concluded that these results may emphasize the importance of the promotion of CRF and muscle strength in younger populations (21), although further studies are needed to show if there is a causal relationship to the association. Additionally, another recent study from Norway showed that handgrip strength and chair-rise test performance are associated with the risk of all-cause and CVD mortality independent of the levels of physical exercise (22). This prospective study of apparently healthy older women at baseline suggested that two affordable, quick and clinically feasible tests of skeletal muscle strength in the arms (handgrip strength) and the legs (chair-rise test) predict future all-cause, CVD, and stroke (22).

Cardiorespiratory fitness (CRF), ideally assessed directly by VO_2max from respiratory gases, has been found to be one of the strongest predictor for fatal and non-fatal CVD events (4,7,23-25), although the clinical value of muscle strength seems to be underrated. It is not well known to which extent the incremental information offered by functional capacity in risk stratification beyond that of conventional risk factors, would prompt interventions and ultimately reduce CVD-related events. Previous results may indicate that CRF and muscle strength partly influence the risk of HF through different causal pathways, where metabolic aberrations and their effects on atherosclerotic disease and myocardial function seem to be important (21,22).

Frailty is usually quantified by the degree of impairment in functional reserve across multiple organ systems and is often associated with fatigue, reduced muscle strength, and high susceptibility to chronic disease. Further research is needed to examine the associations between changes in capability with age and HF and mortality, as a decline in physical capability may be a better predictor of mortality than is the absolute level at a single point in time. In addition, associations between these measures of functional capacity (CRF and muscle strength) and cause specific mortality and other health outcomes, including potential effects on mental well-being (26), may help to clarify the pathways underlying the associations with HF and all-cause mortality. Elucidating the underlying biological pathways that link poorer functional capacity such muscle strength to HF and mortality will help in the development of effective interventions.

An unanswered question is still if new epidemiological data on the importance of functional capacity including assessment of CRF and muscle strength can be used to implement a stronger recommendation in favor of routine functional capacity recordings for risk assessment in normal clinical practice. It would be important to know if physical exercise, muscle strength training and other life-style interventions would decrease frailty, which is known to be related to HF and CVD outcomes. There is still need to study the role of preventive measures and exercise-based life-style interventions. Although muscular fitness is considered to be an indicator of general health, further studies are needed to show whether improvement in muscle strength is associated with lower HF and CVD risk independently of CRF level (VO_2max).

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