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Impact of cardiorespiratory fitness changes in cardiac rehabilitation

Giovanni Grazzi[1,2], Jonathan Myers[3,4] and Giorgio Chiaranda[5,6]

What is known on this subject?

Cardiorespiratory fitness (CRF) is a measure of the body's maximal ability to transport and use oxygen to perform physical work. CRF is directly related to the integration of the central nervous, cardiopulmonary, metabolic, and skeletal muscle systems. As such, it is used in the assessment of functional capacity in patients with cardiovascular disease (CVD), and frequently a primary outcome when comparing clinical interventions among individuals or groups, or when following subjects longitudinally.

A plethora of evidence has accumulated in recent decades supporting an independent, strong, and inverse association between levels of CRF and the risk of cardiovascular and all-cause mortality among individuals with and without CVD.[1] Many recent studies have shown that CRF is a more powerful predictor of mortality risk than traditional risk factors such as hypertension, smoking, obesity, hyperlipidaemia, and diabetes mellitus.[1] In addition, a growing number of studies has demonstrated that common exercise testing variables including symptoms, ST-segment depression, and some hemodynamic responses are less powerful predictors of risk than CRF.[1]

These observations have contributed support for the inclusion of CRF assessment in current international guidelines on cardiac rehabilitation/secondary prevention programmes (CR/SP).[2] The assessment of a patient's exercise capacity along with medical history and physical examination in CR/SP programmes is recommended after myocardial infarction (MI), percutaneous coronary intervention, coronary artery bypass graft surgery, heart valve surgery, cardiac transplantation, or in the setting of chronic heart failure.[3] Exercise testing includes the assessment of CRF, usually determined by maximal exercise capacity. Directly measured peak oxygen consumption (peak VO_2) determined during maximal cardiopulmonary exercise testing (CPET) is the gold standard objective measure of exercise capacity (i.e. CRF). Even though many recent studies have demonstrated that CRF outperforms traditional CVD risk factors in the prediction of clinical outcomes, the use of directly measured CRF remains limited in clinical practice by the time, effort, and expertise required conducting a CPET.[1]

Because CPET is often not available, other performance tests, including submaximal exercise tests or endurance walking tests, can provide useful information and should be considered when resources are limited.[1] Submaximal assessments that estimate peak VO_2 are useful for population research in which directly measured peak VO_2 is not practical for large samples of subjects. These approaches have been used in the context of transitioning patients from clinically based and supervised programmes to outpatient settings or health/fitness facilities, and when testing large numbers of subjects. Advantages of submaximal testing protocols are their simplicity, safety, negligible cost, and applicability to everyday activities. However, these evaluations are not as precise or reproducible as maximal or symptom-limited CPET in quantitating CRF.[1]

What does this study add?

Mounting evidence suggests that maintaining or improving a certain level of CRF over time leads to a lower incidence of major cardiovascular events and improves survival. Mikkelsen et al. demonstrated that directly measured peak VO_2 as well as a change in peak VO_2 over time were highly predictive of risk for future readmissions for CVD and all-cause mortality in a large cohort of CVD patients undergoing cardiac rehabilitation.[4] Importantly, the prognostic power of the change in peak VO_2 with serial testing was independent of baseline peak VO_2 and clinical history.

[1]Center for Exercise Science and Sport, University of Ferrara, Italy
[2]Public Health Department, AUSL Ferrara, Italy
[3]Division of Cardiology, VA Palo Alto, USA
[4]Stanford University School of Medicine, USA
[5]Public Health Department, AUSL Piacenza, Italy
[6]General Directorship for Public Health and Integration Policy, Italy

Corresponding author:
Giovanni Grazzi, Center for Exercise Science and Sport, University of Ferrara, V. Gramicia, 35, 44123 Ferrara, Italy.
Email: giovanni.grazzi@unife.it

Only a few studies have examined the effect of change in CRF on clinical outcomes using the gold standard method of directly measured CRF by respiratory gas exchange analysis. Although there are methodological differences between studies, the findings of Mikkelsen et al.[4] are consistent with those of Martin et al. in coronary artery disease patients,[5] Bakker et al. in chronic heart failure patients,[6] and population-based studies in apparently healthy adult men and women.[7–9] Similarly, many studies have demonstrated the importance of maintaining or improving CRF in reducing the risk of adverse clinical outcomes using indirect estimates of CRF.[1] While these observations do not prove cause and effect, such a link is plausible since a great deal of research has documented that biological mechanisms for disease are favourably influenced by CRF, and that higher levels of CRF improve overall cardiovascular health profiles by improving established CVD risk factors.[10]

The results from Mikkelsen et al. suggest that each 1 mL/kg/min higher peak VO_2 was associated with reduced risks of all-cause mortality of 11% and 13% for baseline and change in peak VO_2, respectively. Such survival benefits appear greater than that observed in more than 100,000 subjects included in 13 studies, mostly determined by peak VO_2 estimation.[11,12] Interestingly, the results of Mikkelsen et al. are similar to those obtained by Kavanagh et al., who observed a 10% reduced risk of mortality per each 1 mL/kg/min in 2300 women with CVD referred to CR and evaluated by maximal CPET.[13] This is not surprising since it is well accepted that measured peak VO_2 is more objective and precise, but because it is easier to obtain, estimated CRF derived from peak work rate is the more common expression of CRF, particularly in epidemiological studies involving large populations.

However, Mikkelsen et al. also demonstrated that during a median follow-up of 2.3 years after the conclusion of an eight-week supervised outpatient exercise intervention consisting of two weekly training sessions, the risk of dying after a hospital readmission as a composite of MI, unstable angina pectoris, heart failure, and stroke was not associated with baseline peak VO_2 or improvement in peak VO_2. Having CHF at baseline was the only significant predictor of mortality, although statistical power was limited. This result may reflect something nuanced regarding the subgroup of patients readmitted for CVD, the limited number of subjects ($n = 25$), or the limited duration of follow-up. Nevertheless, this observation is surprising since it is generally well accepted that an improvement in CRF after CR is associated with reduced risk of all-cause mortality or hospitalisation.[1]

It could be argued that since the risk of all-cause mortality, MI, and stroke is inversely associated with physical activity,[14] some patients may not maintain a recommended physical activity pattern and lose the effect of an early CR intervention. Indeed, it is known that after only one or two weeks of detraining, measurable reductions may occur in physiologic function and exercise capacity including peak VO_2.[15] As stated by the authors, these imply the need for a prolonged follow-up following a CR intervention. In fact, it has been recommended that patients with stable ischemic heart disease should have a follow-up evaluation at least every four months during the first year of therapy,[15,16] as part of medically supervised and physician-directed home-based programs (class IA recommendation).[17]

How might this impact on clinical practice?

Even though impaired CRF is a leading risk factor for CVD, it is currently the only risk factor not routinely assessed in clinical practice.[1] Mounting evidence from large population-based studies and randomised clinical trials suggest that adding CRF to a single or several traditional risk factors for CVD substantially improves the precision of risk prediction models.[18]

Evidence for the prognostic value of CRF has largely been based on a single measure at baseline. However, since personal-, health-, disease-, and exercise-training-related characteristics can change during a given follow-up period, inferences based on a single measure at baseline could lead to erroneous conclusions. Thus, determining CRF on a serial basis is valuable not only to determine an individual's risk of future adverse events, but also to evaluate the effectiveness of treatment strategies, including recommendations for participation in physical activity. The latter is a major factor influencing CRF and it is the cornerstone of current CR/SP programmes. Patients whose CRF increases between examinations have a lower risk of adverse health and clinical outcomes than those whose CRF decreases. This should be communicated to patients,[1] with the same seriousness as quitting smoking or taking cholesterol-lowering drugs.[19]

The findings reported by Mikkelsen et al. are promising. They support the limited body of knowledge regarding the impact of CR/SP on directly measured CRF, with potential significant public health impact, expanding the role of longitudinal changes in CRF. The value of maintaining or improving CRF over time is grossly underappreciated but an important goal to decrease the risk of premature death, not only in patients with CVD, but also in patients with common non-communicable chronic disease such as diabetes mellitus, metabolic syndrome, and breast cancer.[20,21]

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