Implementing Cardiorespiratory Fitness as a Routine Measure in Health Care Settings

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ABSTRACT

It is well established that cardiorespiratory fitness (CRF) is inversely associated with numerous morbidities independent of age, biological sex, race or ethnicity, and commonly obtained risk factors. More recent evidence also demonstrates that the addition of CRF to multivariable risk prediction algorithms used to estimate cardiovascular disease risk improves risk stratification. However, it is neither feasible nor appropriate to perform an exercise test to quantify CRF during most routine clinical encounters. A growing number of studies have suggested that CRF can be assessed pragmatically and reasonably accurately without performing a maximal exercise test. The concept that CRF can be substantially improved in response to regular exercise consistent with consensus recommendations underscores the recommendation that CRF should be a routine measure—a vital sign—across health care settings. Herein, we provide a brief, narrative overview of the evidence in support of this recommendation. *Journal of Clinical Exercise Physiology*. 2021;10(2):62–69.

Keywords: review, vital sign, CRF

INTRODUCTION

For a new biomarker to become a routine measure in clinical practice, at least 4 questions should be addressed (1). The first considers whether the biomarker is associated with morbidity and mortality independent of the biomarkers commonly obtained in clinical settings. The second seeks to determine whether the addition of the biomarker improves risk stratification. In the current context, the question is, "does the addition of cardiorespiratory fitness (CRF) to established risk prediction algorithms (risk engines) enhance risk prediction?" Third, can the biomarker be measured pragmatically in health care settings, and fourth, can it be improved in response to treatment consistent with consensus recommendations? In this brief, narrative review, our response to these questions provides the structure used to support the recommendation that the routine incorporation of CRF into health care settings reflects best evidence and, consequently, will improve patient or client management. For further details in support of this recommendation, the reader is referred to references 2–8.

WHAT IS CARDIORESPIRATORY FITNESS?

CRF is a human trait that refers to the ability of the circulatory and respiratory systems to supply oxygen to skeletal muscles during all forms of physical activity. Specifically:

> CRF quantifies the functional capacity of an individual and is dependent on a linked chain of processes that include pulmonary ventilation and diffusion, right and left ventricular function (both systole and diastole), ventricular-arterial coupling, the ability of the vasculature to accommodate and efficiently transport blood from the heart to precisely match oxygen requirements, and the ability of the muscle cells to receive and use the oxygen and nutrients delivered by the blood, as well as to communicate these metabolic demands to the cardiovascular control center. (2)

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The implication is that CRF is a unique trait that reflects the integrated function of numerous systems and, thus, is a good representation of total body health. The fact that CRF reflects the integrity of numerous systems at least partially explains why CRF predicts morbidity and mortality risk beyond commonly obtained risk factors.

ARE MEASURES OF CRF ASSOCIATED WITH MORBIDITY AND MORTALITY INDEPENDENT OF COMMONLY OBTAINED RISK FACTORS?

There is now indisputable evidence that CRF is inversely associated with mortality and numerous morbidities independent of age, biological sex, race or ethnicity, and commonly obtained risk factors (2–11). The association between CRF and mortality was underscored in a meta-analysis by Kodama et al. (9) and updated more recently in a meta-analysis by Harber et al. (10). Data from 33 studies, including nearly 103,000 participants, revealed that, in comparison with subjects in the high CRF tertile, those with low CRF had 70% and 56% higher risks for all-cause and cardiovascular mortality, respectively. The authors observed that for every 1 metabolic equivalent of task (MET) higher CRF, cardiovascular and all-cause mortality were reduced by 13% and 15%, respectively. These meta-analyses also confirmed the previous finding that the greatest mortality benefits occur when progressing from the least fit and the next least fit group; lesser improvements in health outcomes were noted when individuals in the moderate- to high-fit groups were compared, suggesting that the association between CRF and health outcomes may plateau at higher CRF values. Recently, Mandsager et al. (11) assessed the association between CRF and all-cause mortality in a cohort of 122,007 subjects stratified into 5 age- and sex-matched CRF groups: low (<25th percentile), below average (25th–49th percentile), above average (50th–74th percentile), high (75th–98th percentile), and elite (≥98th percentile). The increases in all-cause mortality associated with reduced CRF (low versus elite: adjusted heart rate [HR] = 5.04; 95% confidence interval [CI] = 4.10–6.20; below average versus above average: adjusted HR = 1.41; 95% CI = 1.34–1.49) was comparable with or greater than traditional clinical risk factors. While these findings confirm that CRF is inversely associated with mortality, they also suggest that the association between CRF and all-cause mortality may not have an upper limit of benefit.

Many of the studies that first considered the associations between CRF and health outcomes were based on the observation of a single baseline measure of CRF. A growing number of more recent studies have examined the association between changes in CRF across 3–6 years and mortality in both asymptomatic and diseased populations. These studies have confirmed earlier observations based on a single measure (7). In a seminal study, Blair et al. (12) demonstrated that men who remained fit over 5 years between measures of CRF had a relative risk of 0.33 (95% CI = 0.23–0.47) for all-cause mortality and a relative risk of 0.22 (95% CI = 0.12–0.39) for cardiovascular disease (CVD) mortality compared with those who were unfit, after adjusting for all known confounders. These seminal observations were subsequently confirmed in numerous studies (2,7).

DOES CRF IMPROVE RISK ESTIMATES FOR MORBIDITY AND MORTALITY?

Despite considerable evidence demonstrating that CRF is independently associated with CVD and/or all-cause mortality, resistance to its routine incorporation into clinical practice remains. One plausible explanation is the lack of appreciation among clinicians of the fact that the addition of CRF improves risk prediction models. For CRF to truly be a novel risk marker, it must improve risk prediction beyond traditional markers. A growing body of evidence now indicates that the addition of CRF to risk engines designed to determine absolute risk of CVD (e.g., the Framingham coronary heart disease risk assessment algorithm) enhances risk stratification (2). Recent studies have applied a statistical technique termed *net reclassification improvement* (NRI) to address this issue. NRI quantifies the extent to which a given risk marker adds to existing markers to predict adverse outcomes. It indicates whether the addition of a biomarker correctly and significantly alters risk classification and is defined as the net change in risk among those who do and do not experience an event (13). Using traditional risk factors as a standard for comparison (e.g., age, sex, hypertension, diabetes, hyperlipidemia, smoking), these studies have reported NRI values in the range of 10% to 30% by adding CRF to traditional risk models (14–18). Both directly measured CRF and CRF estimated from nonexercise test models have been applied for this purpose. These findings demonstrate that the addition of CRF to traditional models markedly improves the ability to estimate risk for mortality and cardiovascular events.

The observation that the addition of CRF to traditional risk factors results in significant improvement in risk prediction is important and may help convince those in clinical practice that CRF should be a vital sign routinely measured in clinical settings. Regardless, the fact that improvements in CRF are strongly associated with corresponding reductions in CVD risk is of equal if not greater importance. In short, CRF remains a simple evidence-based target within all clinical settings and provides practitioners with an opportunity to counsel patients or clients on the health benefits of lifestyle-based strategies designed to reduce health risk. In addition to improving risk prediction modeling, CRF serves as an important modifiable treatment target for risk reduction.

NONEXERCISE APPROACHES TO ESTIMATING CRF

If CRF is to be used as a risk factor routinely measured in clinical practice and considered of equal importance to traditional risk factors, it needs to be simple, rapid, and inexpensive to obtain. While the most accurate metric for CRF requires a maximal exercise test, it is neither feasible nor appropriate to perform an exercise test during routine clinical encounters. In addition to time and cost factors,

performing an exercise test in most individuals does not meet appropriate use criteria (19). A 2018 update of the US Preventive Services Task Force (USPSTF) Recommendations on Resting or Exercise Electrocardiography (20) did not recommend routine exercise testing for asymptomatic individuals. This is in accordance with earlier recommendations from the USPSTF (21) and other guidelines on exercise testing (22,23). This recommendation is based in part on the tests' limited predictive accuracy for detecting CVD (the percentage of times the test provides a correct result) in asymptomatic individuals and its low cost effectiveness. These guidelines are consistent in recommending that an exercise test should generally be performed only in patients with known or suspected CVD. How then should CRF be routinely incorporated into clinical practice?

There have been a growing number of efforts in recent years to estimate CRF without exercise testing. These studies have applied easily available information such as age, body mass index (BMI), physical activity patterns, symptom questionnaires, smoking history, and other factors that have a potential impact on CRF. A synopsis of key studies that have developed multivariable models to estimate CRF from nonexercise data is shown in Table 1 (24–39). Several observations are notable from the table. First, the associations between estimated and measured CRF range in the order of 0.60 to 0.85 (using the coefficient of determination, or R^2). This degree of association appears to be generally adequate in terms of classifying individuals into CRF categories (e.g., quartiles or quintiles). In real terms, the error between estimated and measured CRF is generally in the range of 5%–15% (24–26,32,36,39,40). Nes et al. (36), for example, studied >4,000 men and women using a nonexercise test model to estimate CRF and reported that >90% of subjects were correctly classified into the lowest and highest quartiles of CRF. The available equations have tended to underestimate CRF among higher fit individuals and overestimate CRF among lower fit individuals (24,26,27,29,32,36,39). This is generally not an issue among highly fit individuals who would still be correctly classified into the higher CRF categories but is a potential concern for low fit individuals because correct classification is much more likely to influence their estimation of risk. Variation in results of the studies can be attributed to differences in the populations studied, the fact that accessible nonexercise variables differed in the different samples, and differences in the methods of expressing the association between estimated and measured exercise capacity. The error and variation in estimated CRF are similar to that for day-to-day variation in other risk factors such as blood pressure or lipids (41–43). There are several clinical situations in which the measurement of CRF requires precision and therefore a maximal exercise test, but this degree of variation suggests that the available nonexercise estimates are acceptable for the purposes of applying CRF as a risk factor, for physical activity counseling, or for many research purposes.

There are several notable differences between the various nonexercise methods to estimate CRF. Approaches to estimating CRF have ranged from submaximal cycle or treadmill tests, walking tests, field tests, and the application of clinical and demographic data that is readily available from clinical records or questionnaires at the time of an encounter. Many early studies in this area relied on field tests, and while these studies reported reasonable associations with measured peak VO_2 from an exercise test (44–51), they are impractical to apply in large populations or as widely used public health tools. Moreover, field or submaximal tests are generally not more accurate than the use of nonexercise data available at the time of an encounter (2,26,28,39,46). The most appropriate method to estimate CRF from nonexercise data will undoubtedly differ depending upon the context in which CRF is applied and the sample being studied. For example, applying a symptom questionnaire (such as the Veterans Specific Activity Questionnaire (24) or Duke Activity Status Index (52)) is suitable for clinically referred samples (the group for which they were developed), but most of the models have been derived from relatively healthy, asymptomatic subjects for whom these tools would not apply. Not all samples had physical activity patterns available, which is the key behavioral factor influencing CRF. Indeed, in many studies, physical activity patterns explained a significant proportion of variance in exercise capacity (24,32–36,39,53). The addition of variables such as gender, age, height, weight, and/or BMI to models has generally improved the accuracy of the equations; these variables are particularly appropriate when there is significant variation in the population characteristics. In clinical settings, an optimal approach might be to automatically provide estimations of CRF as part of electronic medical records so that they are available at the time of a clinical encounter, as has been advocated for physical activity behavior (54).

Role of Nonexercise CRF in Epidemiologic Studies

A rapid and reasonably accurate nonexercise estimate of CRF would be particularly useful when testing large populations or performing epidemiologic research, in which exercise testing of large numbers of participants is impractical. A growing number of studies have applied estimates of CRF derived from a nonexercise prediction model to estimate future risk of mortality, CVD events, or cancer (16,55–58). Notably, the risk reductions per each 1 MET higher nonexercise estimate of CRF have been demonstrated to be similar to those using measured exercise capacity from a treadmill or cycle ergometer (10%–20%). Artero et al. (57) studied 43,356 adults from the Aerobics Center Longitudinal Study and estimated CRF based on sex, age, BMI, waist circumference, resting heart rate, physical activity level, and smoking status. After adjustment for potential confounders, both measured and estimated CRF were inversely associated with risk of all-cause mortality, CVD mortality, and nonfatal CVD incidence in men, and with all-cause mortality and nonfatal CVD in women. Importantly, measured CRF had superior discriminative ability than estimated CRF (c-statistic 0.70 versus 0.64 for all-cause mortality and 0.74 versus

TABLE 1. Selected nonexercise equations to estimate cardiorespiratory fitness.

Authors	Population	Gender	No.	Age	Equation	R^2	SEE*
Jackson et al. (1990)[24]	Employees of NASA	M/F	1,393/150	20–70	50.513 + 1.589 (PAR 0–7) – 0.289 (age in years) + 5.863 (sex, male = 1 and female = 0) – 0.552 (% fat)	0.66	5.35
Myers (1994)[25]	Veterans referred for an exercise test	M	212	62 ± 8	4.7 + 0.97 (VSAQ) – 0.06 (age).	0.67	1.43
Heil et al. (1995)[26]	Healthy	M/F	210/229	20–79	36.580 + 1.347 (activity 0–7) + 0.558 (age in years) – 0.00781 (age^2) + 3.706 (sex, male = 1 and female = 0) – 0.541 (% fat)	0.77	4.90
Whaley et al. (1995)[27]	Active adults	M/F	702/473	41.8 ± 11	61.66 + 1.832 (PAS 1–6) – 0.328 (age in years) + 5.45 (sex, male = 1 and female = 0) – 0.446 (smoking 1–8) – 0.436 (% fat) – 0.143 (RHR)	0.73	5.38
George et al. (1997)[28]	Active college students	M/F	50/50	18–29	44.895 + 0.688 (PAR 0–10) + 7.042 (sex, male = 1 and female = 0) – 0.823 (self-reported BMI) + 0.738 (PFA 1–13)	0.71	3.60
Matthews et al. (1999)[29]	Healthy	M/F	390/409	19–79	34.142 + 1.463 (PAS 0–7) + 0.133 (age in years) – 0.005 (age^2) + 11.403 (sex, male = 1 and female = 0) – 0.254 (WT in kg) + 9.170 (HT in m)	0.74	5.64
Malek et al. (2004)[30]	Aerobically trained	F	80	38 ± 9.5	22.931 + 0.392 (h/week training) + 1.035 (RPE 6–20) + 4.368 (natural log of years of training) – 0.287 (age in years) + 0.309 (WT in kg) + 0.200 (HT in cm)	0.67	4.32
Malek et al. (2004)[31]	Aerobically trained	M	112	40.2 ± 11.7	57.912 + 0.329 (h/week training) + 1.444 (RPE 6–20) + 6.366 (natural log of years of training) – 0.346 (age in years) + 0.344 (WT in kg) + 0.335 (HT in cm)	0.65	4.75
Jurca et al. (2005)[32]	ACLS	M/F	35,826/10,364	20–70	65.835 + 2.838 (activity1) + 4.095 (activity2) + 7.56 (activity3) + 10.675 (activity4) – 0.28 (age in years) + 8.715 (sex, male = 1 and female = 0) – 0.595 (BMI) – 0.175 (RHR)	0.60	5.25
Bradshaw et al. (2005)[33]	Healthy	M/F	50/50	18–65	48.073 + 0.671 (PAR 0–10) – 0.246 (age in years) + 6.178 (sex, male = 1 and female = 0) – 0.619 (BMI) + 0.712 (PFA 1–13)	0.86	3.44
Cao et al. (2010)[34]	Healthy	F	148	20–69	51.853 + 0.408 (SC, 10^3 steps/d) + 0.060 (MVPA in min) – 0.175 (age in years) – 0.244 (WC in cm)	0.72	3.14
Cao et al. (2010)[35]	Healthy	M	127	20–69	61.925 + 0.577 (SC, 10^3 steps/d) + 0.305 (VPA in min) – 0.338 (age in years) – 0.698 (BMI)	0.71	4.15
Nes et al. (2011)[36]	Healthy	M/F	2,067/2,193	48.4 ± 13.6	100.27 + 0.226 (PA index 0–8.3) – 0.296 (age) – 0.369 (WC in cm) – 0.155 (RHR) for men 74.74 + 0.198 (PA index 0–8.3) – 0.247 (age) – 0.259 (WC in cm) – 0.114 (RHR) for women	0.61 0.56	5.70 5.14
Jang et al. (2012)[37]	Healthy	M/F	113/104	34.2 ± 8.4	43.98–0.12 × age + 11.64 × gender (0 = female; 1 = male) – 0.271 × BMI – 1.36 × smoking (0 = never or quit; 1 = current) + 0.70 × LTPA + 1.05 × ATC + 0.03 × ATD + 0.035 × BMR + 0.72 × heavy physical work	0.79	3.36
Maranhao Neto (2012)[38]	Cardiovascular or metabolic disease	M/F	109	69.1 ± 7.4	6.095 – 0.096 (age) + 8.84 (handgrip strength/WT) + 0.67 (RPC)	0.79	1.1 (METs)

ACLS = Aerobics Center Longitudinal Study; ATC = ambulation time during commute; ATD = ambulation time on duty; BMI = body mass index; BMR = body motion rate; HT = height; LTPA = leisure time physical activity; MET = metabolic equivalent of task; MVPA = moderate to vigorous physical activity; NASA = National Aeronautics and Space Administration; PAR = physical activity rating; PAS = physical activity status; PFA = perceived functional ability; RHR = resting heart rate; RPC = rating of perceived capacity; RPE = rate of perceived exertion; SEE = standard error of estimate (in $mL \cdot kg^{-1} \cdot min^{-1}$); VPA = vigorous physical activity; VSAQ = Veterans Specific Activity Questionnaire; WC = waist circumference; WT = weight.

0.73 for CVD mortality). Using similar nonexercise test variables, Stamatakis et al. (16) followed 32,319 subjects for a mean of 9 years and observed that a higher nonexercise CRF score was associated with a lower risk of mortality from all-causes (hazard ratios per standard deviation [SD] increase; 0.85 in men and 0.88 in women) and CVD (hazard ratios 0.75 in men and 0.73 in women). Both studies reported that the discriminative utility of estimated CRF was higher than that from any of its individual components, separately or together, for all-cause mortality and CVD events. In fact, by adding nonexercise CRF, Stamatakis et al. (16) reported NRIs for CVD mortality (compared with a standardized aggregate score of modifiable risk factors) of 27.2% and 21.0% for men and women, respectively. Thus, for large population-based observational studies, nonexercise estimates generally appear to provide adequate reflections of CRF, although they are somewhat less powerful than directly measured CRF. Nevertheless, these and other studies applying nonexercise estimates of CRF (16,55–58) provide further confirmation of the power of CRF in predicting risk for adverse outcomes.

Mechanisms

While the mechanisms by which nonexercise test estimates of CRF mediate health outcomes are not fully understood, they are likely similar to those for directly measured CRF. As described above, CRF is related to the integrated function of numerous physiological systems, is considered a reflection of overall health, and is a stronger predictor of risk for adverse outcomes than traditional risk factors. Fitter individuals tend to have more cardioprotective cardiovascular risk profiles (mediated in part through higher activity levels), more favorable autonomic tone (potentially reducing arrhythmogenic risk), lower risk for thrombotic events, reduced inflammation, and improved indices of endothelial function (43–45). It follows that impaired CRF relative to a normal age- and gender-related standard is associated with higher incidence of numerous chronic conditions such as CVD, stroke, kidney disease, metabolic syndrome, and cancer (3–6).

CAN CRF BE IMPROVED IN RESPONSE TO CONSENSUS RECOMMENDATIONS FOR PHYSICAL ACTIVITY?

A detailed review of the literature with respect to the dose-response associations between physical activity and CRF are beyond the scope of this report. The interested reader is referred to references 2, 23, and 60, which provide more extensive reviews of the pertinent literature.

Current physical activity guidelines recommend that adults accumulate 150 min per week of moderate to vigorous physical activity (MVPA) to achieve health benefits (22,23,59). Meeting these minimal guidelines has been demonstrated to have numerous health benefits independent of changes in CRF (4,5,59). Given that physical activity is the primary modifiable determinant of CRF regardless of age, biological sex, or race (60), it follows that 150 min of weekly MVPA would result in an increase in CRF. However, for improving CRF, whether performing moderate-intensity exercise (3–5.9 METs) for 150 min/week at a fixed amount of exercise is the same as 75 min/week of vigorous intensity exercise (6 METs or greater) at a fixed amount remains to be firmly established. Determining the effects of exercise intensity and amount or volume on changes in CRF has been the objective of several carefully controlled randomized trials (61–64). Church et al. (61) performed a groundbreaking study in which they randomized 464 sedentary, postmenopausal overweight or obese women to 1 of 4 groups to determine the effects of exercise amount on CRF. The primary objective was to determine whether exercise levels at 50% below (about 75 min/week) and 50% above (about 200 min/week) the consensus recommendation (150 min/week) were associated with differences in the CRF response after 9 months. Importantly, all participants regardless of group exercised at 50% of their CRF (VO_2peak). The principal finding was that CRF increased across the 3 exercise amounts in a graded dose-response manner.

This observation was extended by Ross et al. (63), who assessed the separate effects of exercise amount and intensity in a sample of 300 abdominally obese adults. Participants were randomized to 1 of 4 groups: control, or 5 weekly sessions of low-amount, low-intensity exercise at 50% of maximum CRF; high-amount, low-intensity exercise at 50% of maximal CRF; or high-amount, high-intensity exercise at 75% of maximal CRF. The results shown in Figure 1 illustrate that, like the observations by Church et al. (61), for a given exercise intensity (50% of maximal CRF), the observed increase in CRF is proportional to the increase in exercise amount. In addition, for a given exercise amount, a higher exercise intensity was associated with a corresponding increase in CRF; a finding consistent with others (62). A novel finding was that the greatest increase in CRF was observed in the high-amount, high-intensity group (Figure 1). That exercise intensity is a strong driver of improvements in CRF is consistent with studies showing that improvements in CRF are generally greater in response to high-intensity interval training than continuous, moderate-intensity exercise (64). In summary, substantial improvements in CRF are observed in response to physical activity consistent with consensus recommendations. The fact that an increasing amount and/or intensity of exercise is associated with further improvements in CRF provides practitioners with treatment options to match individual variability (ability or willingness) of their clients or patients to adopt physical activity to improve CRF.

SUMMARY

There is now overwhelming evidence demonstrating that CRF provides information to the practitioner that improves patient management independent of age, biological sex, and race or ethnicity. Substantial improvements in CRF can be achieved by following the consensus recommendations for physical activity, and consequently, practitioners who assess CRF have opportunities to counsel patients or clients on the

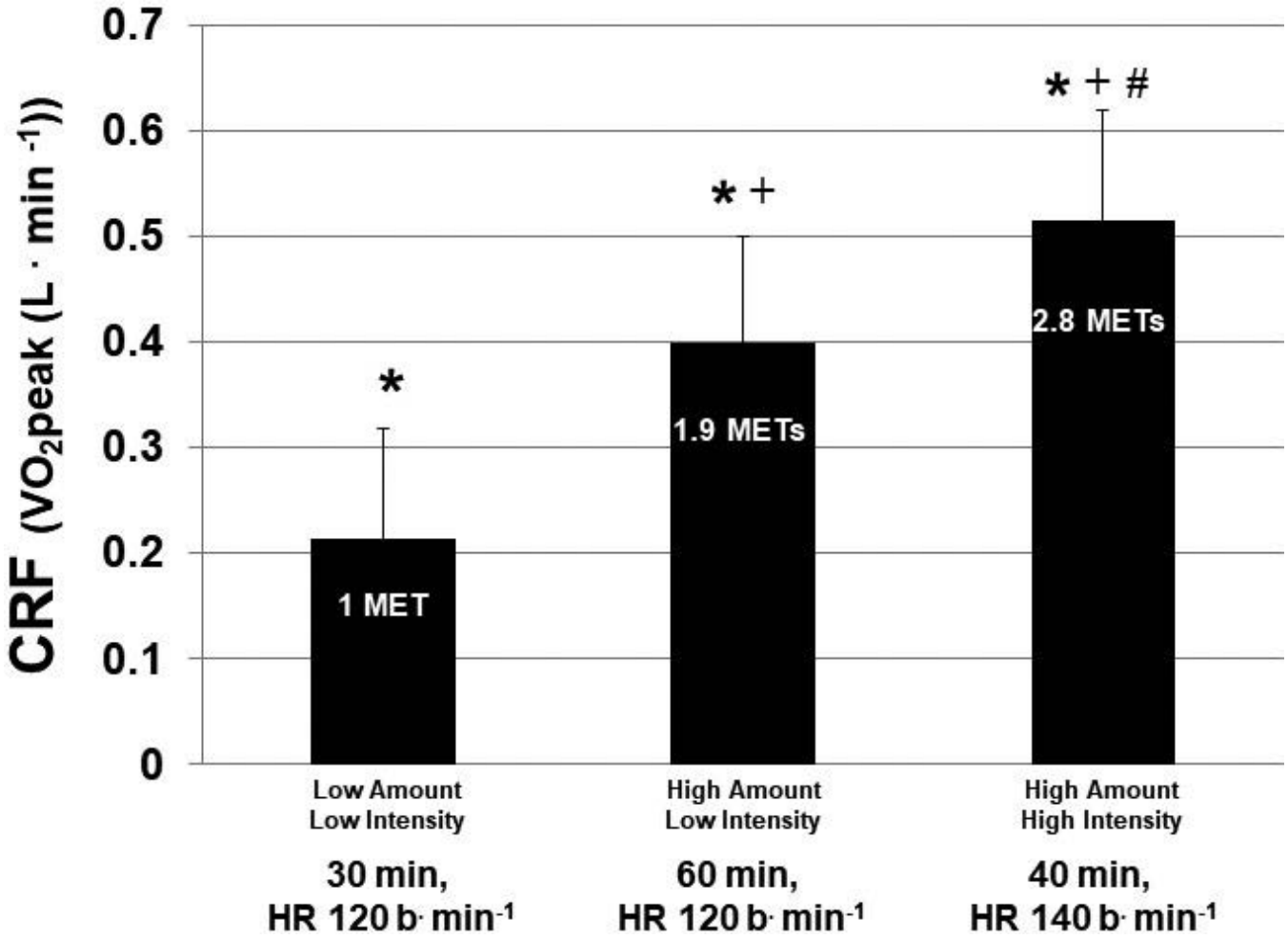

FIGURE 1. Corresponding improvements in cardiorespiratory fitness (CRF) expressed in metabolic equivalents (METs) are shown within the horizontal bars for each group. *, different from control, +, different from low amount-low intensity, #, different from high amount-low intensity. Adapted from (62).

importance of physical activity. This is particularly important given the fact that most adults do not meet the minimal guidelines for physical activity (58), and CRF has been decreasing worldwide in recent decades (65). Simple and rapid estimates of CRF using nonexercise models can be critical for the purposes of educating patients and the public regarding their CRF level and its implications for a given individual's risk level. The availability of a rapid estimate of CRF also provides an impetus for the practitioner to provide physical activity counseling and to motivate individuals to incorporate physical activity in their daily lives. Nonexercise estimates of CRF have also been demonstrated to be useful for stratifying risk in large populations of subjects for the purposes of conducting epidemiologic research (16,55–58). Taken together, it is hard to imagine why CRF is not a vital sign. Indeed, CRF measurement or its estimation affords all practitioners with a vitally important opportunity to improve patient management and, consequently, patient health.

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