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Editorial

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Physical Fitness and Development of High Non-High-Density Lipoprotein Cholesterol

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Elevation of total cholesterol (T-C), low-density lipoprotein cholesterol (LDL-C), non-high-density lipoprotein cholesterol (non-HDL-C), and triglyceride levels and decreases in HDL-C levels can predict the incidence and mortality rates due to coronary heart disease (CHD) in the future even in the Japanese population[1]. Non-HDL-C includes all lipid biomarkers except HDL-C and has been reported to be more associated with highly atherogenic lipids or lipoproteins (e.g., remnant lipoproteins, small dense LDL, Lp(a), and triglyceride) compared with LDL-C[2, 3]. The Japan Atherosclerosis Society Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases 2017 defined hyper-non-HDL cholesterolemia as non-HDL-C levels ≥170 mg/dL[1].

The physical activity (PA) and cardiorespiratory fitness (CRF) levels have been found to be negatively correlated with mortality due to cardiovascular disease (CVD) and cancer as well as all-cause mortality in studies conducted worldwide[1]. Although many randomized controlled trials (RCT) and meta-analyses of these RCTs have reported the beneficial effects of exercise on serum lipid profiles, limited studies have investigated non-HDL-C as targets. Among cross-sectional studies, CRF is positively associated with HDL-C levels and inversely associated with non-HDL-C, LDL-C, and triglyceride levels. However, there are few prospective studies investigating that high CRF levels prevent the incidence of dyslipidemia[4]. Watanabe *et al.*[5] investigated CRF levels measured by cycle ergometer and health habits in 4,067 Japanese healthy men aged 19−60 years without dyslipidemia at baseline. The mean CRF levels, body mass index (BMI), systolic blood pressure (BP), non-HDL-C levels, LDL-C levels, HDL-C levels, triglyceride levels, and glucose levels at baseline were 40.7 ml/min/kg (11.6 metabolic equivalents: METs), 22.5 kg/m^2, 127.0 mmHg, 119.7 mg/dL, 102.3 mg/dL, 58.6 mg/dL, 87.2 mg/dL, and 93.4 mg/dL, respectively, which showed very healthy characteristics of the study population. They observed that 1,482 participants exhibited high non-HDL-C levels during the follow-up period (median 13 years). They reported that multivariate hazard ratio and 95% confidence interval (CI) for the incidence of high non-HDL-C levels was 0.79 (95% CI: 0.67−0.92) in the top quartile of CRF when the lowest quartile was the reference, after adjustment for age, BMI, systolic BP, smoking status, alcohol intake, and family history of dyslipidemia. They concluded that high CRF levels were less likely to have hyper-non-HDL cholesterolemia and that habitual aerobic exercise might prevent high non-HDL-C levels in Japanese healthy men. To the best of our knowledge, this is the first study to demonstrate the inverse association between CRF levels and incidence of high non-HDL-C levels. A recent report from the Aerobics Center Longitudinal study, a prospective study of adults at the Cooper Clinic in Dallas, US, showed an association between CRF levels evaluated by treadmill exercise test duration and aging trajectory of lipids and lipoproteins for the life course from data of health examinations between 1970 and 2006, in 11,408 men, 20−90 years of age, without high cholesterol, high triglyceride, CVD, and cancer at baseline[6]. The serum levels of T-C, LDL-C, non-HDL-C, and triglyceride increased gradually until 50 years of age, with subsequent declines. Compared with men with higher CRF, those with lower CRF developed high non-HDL-C earlier in life. They reported that men with higher CRF levels had more favorable lipid profiles than those with lower CRF levels.

The landmark study by Blair *et al.*, in 1989, demonstrated that low CRF levels were a strong predictor for all-cause mortality independent of traditional CHD risk factors[7]. Similarly, many prospective cohort stud-

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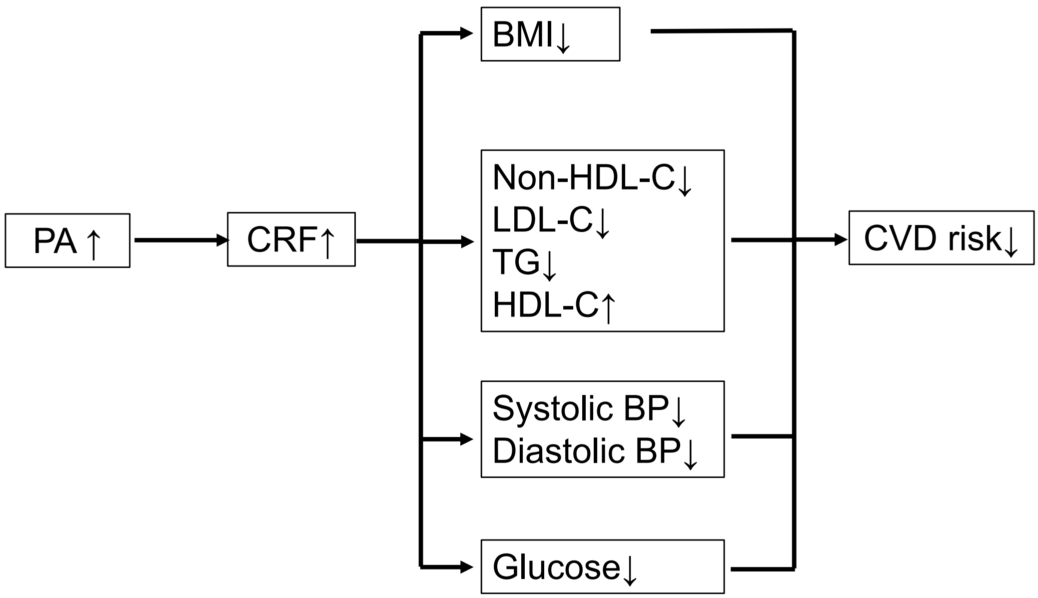

Fig. 1. Effects of PA and CRF on cardiovascular risk. Abbreviations, see text.

ies showed that CRF was important for modifying the effect of risk factors for CVD[8]. A meta-analysis of 23 cohorts of PA or CRF reported that CRF was a stronger predictor of CVD events than PA[9]. A prospective cohort study from Veterans Affairs Medical Centers in US reported that CRF over 5 METs achieved similar or even greater reduction in mortality risk than that achieved by statin therapy alone and that combination of statin therapy and higher CRF resulted in substantially lower mortality risk than either alone in dyslipidemic individuals[10]. Therefore, a high CRF level is very important to prevent CVD events and CVD risk factors. However, the measurement of CRF level is not routinely assessed in general clinical settings. **Fig. 1** shows effects of PA and CRF on cardiovascular risk. In general, PA appears to be the most powerful contributor to CRF, and CRF is recognized as an objective marker for habitual PA. Efforts to increase PA will maintain or increase CRF, resulting in the maintenance or decreases of BMI, non-HDL-C levels, LDL-C levels, triglyceride levels, systolic and diastolic BPs, and glucose levels; maintenance or increases of HDL-C levels; and subsequently decrease CVD risk. The present study confirms that a high CRF level is a significant contributor to maintaining favorable lipid profiles in the future. Physicians should pay attention to the significance of CRF for the prevention of CVD risk factors and incorporate CRF into clinical practice.

Disclosures

The authors have no conflicts to declare.

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