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UK Biobank Contributes to Aerobic and Muscle Fitness Research

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Considerable evidence indicates a substantial lack of physical activity (PA) and exercise training (ET) and a very high prevalence of sedentary behavior throughout most of the world.[1-5] This often leads to low levels of cardiorespiratory fitness (CRF), which is perhaps one of the strongest predictors of cardiovascular disease (CVD) as well as CVD and all-cause mortality.[1,3,4,6,7] In addition, recent evidence suggests that resistance exercise and muscular fitness also contribute to CVD risk factors,[8,9] including diabetes mellitus risk,[10] and to CVD and all-cause mortality.[11,12] Indeed, many recent articles in *Mayo Clinic Proceedings* have emphasized the importance of PA/ET, CRF, and resistance exercise/muscular fitness for preventing CVD and improving survival.[8-10,13-27]

In this Issue of *Mayo Clinic Proceedings*, two major studies from the UK Biobank contribute significantly to the evidence regarding the importance of PA, CRF, and muscular fitness. Laukkanen et al[28] assessed CRF using 6-minute submaximal cycle tests in nearly 59,000 participants aged 40 to 69 years who were followed for a median of 5.8 years, and they analyzed 936 deaths. Not only was CRF, estimated as metabolic equivalents, strongly associated with survival, as is typically the case in almost all studies, but the data also demonstrated that the addition of CRF to established CVD risk factors strongly augmented the prediction of 5-year survival, with an even more pronounced effect in older individuals, smokers, and men.

Certainly, numerous studies, including many referenced previously herein, show the powerful impact of CRF in predicting risk. Although the gold standard assessment of CRF is cardiopulmonary exercise testing and using gas exchange to measure peak oxygen consumption,[8,22,25] many clinicians do not have easy access to such testing, and neither do they have the equipment and personnel to monitor these tests, not to mention the moderate expense of this testing. Less expensive yet reliable and readily available tests for CRF include modalities such as the 6-Minute Walk Test, walking distance, and shuttle tests. The unique aspect of the present UK Biobank study was using a submaximal 6-minute bicycle test in a very large cohort to assess CRF and mortality combined with established CVD risk factors.[28] We recently reported the potential for submaximal CRF assessed by a 5-minute treadmill test to measure estimated metabolic equivalents and to predict mortality in 6106 men and women from the Aerobics Center Longitudinal Study and the ability of changes in submaximal CRF to predict survival.[17]

Also in this Issue of *Mayo Clinic Proceedings*, Welsh et al[29] assessed more than 400,000 UK Biobank participants without baseline CVD and assessed the associations of grip strength and self-reported walking pace and CVD risk factors on major CVD outcomes during median follow-up of 8.9 years. Assessing 7274 major CVD events and 1955 fatal events, both grip strength and self-reported walking pace were associated with major CVD outcomes even after adjusting for major baseline CVD risk factors. In addition, grip strength and self-reported walking pace added to the baseline risk factors for predicting prognosis. A previous study from the UK Biobank by Yates et al[30] also showed the value of walking pace and handgrip strength on CVD mortality. However, the present study adds to this knowledge about the improved CVD risk prediction by adding these parameters to the existing risk score.

Certainly, usual walking pace is considered as a health risk factor, but probably

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more so in older adults than younger ones. For example, gait speed is often used as one of the diagnostic criteria for sarcopenia in older adults, which is strongly associated with physical function and various health outcomes, including CVD mortality. In the current UK Biobank study,[29] the age range was quite wide (37-73 years), and it seems likely that the effect could be much higher in the older than in the younger cohort. Although the authors adjusted for age in their models, it is still possible that age group–stratified analyses would not completely remove the strong possible influence of age on walking pace. Also, they estimated walking pace as opposed to precisely measuring it, and they assessed self-reported walking pace and not walking volume. A recent study by Lee et al[31] of more than 18,000 women in the Women's Health Study found that the association of walking intensities or cadence with all-cause mortality were largely attenuated or no longer significant after further adjustment for walking amount measured as steps per day, whereas mortality rate progressively decreases with more steps per day even after adjusting for intensity. Finally, although Welsh et al[29] showed large improvements in the C-index when both grip strength and self-reported walking pace were included in their models, if one looks closely at their Figures 2 and 3, there seems to be little difference when walking pace and grip strength are compared with walking pace alone, suggesting that self-reported walking pace is even more important than grip strength for predicting CVD outcomes. Although their walking pace was estimated and not measured, this very simple parameter was a potent predictor of prognosis.

Based on the constellation of findings, considerable efforts are needed to increase both aerobic PA/ET to increase walking pace and CRF and resistance exercise to increase muscular strength. Quoting the famous Walt Disney, "The way to get started is to quit talking and start doing," as certainly we need to do a better job promoting PA and ET (aerobic and resistance) throughout the health care system, schools, the workplace, and society for the primary and secondary prevention of CVD. The long-term health of our populations will depend on the success of these efforts.

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