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Extreme Physical Activity May Increase Coronary Calcification, But Fitness Still Prevails

Considerable data have emphasized the powerful impact of sedentary behavior, physical inactivity, and low levels of physical activity (PA) that result in poor levels of cardiorespiratory fitness (CRF) on overall and cardiovascular health.[1-5] In fact, low PA and CRF may be the greatest threat to health in the 21st century. Therefore, greater efforts are needed throughout the health care system and at the government level to promote PA that improves CRF and contributes to reduced cardiovascular disease (CVD) and total mortality worldwide.[1-7]

Nevertheless, there is also considerable data and attention directed at the possible adverse effects of extreme endurance exercise (EEE) on CVD end points, pointing out potential U-shaped relationships with some CVD end points.[1-3,8] For instance, regular EEE increases cardiac troponin and brain natriuretic peptide release and normally leads to transient right ventricular dilation that sometimes is linked to right ventricular dysfunction and dysfunction of the ventricular septum. Furthermore, strenuous PA and EEE have also been reported to promote coronary artery calcification (CAC), leading to coining of the phrase "hearts of stone" among heavy endurance athletes.[9-11] This issue has raised concerns about the safety of such exercise in athletes with very high CAC.

In this issue of *Mayo Clinic Proceedings: Innovations, Quality & Outcomes*, 2 landmark studies address the association of EEE in marathon runners and patients with high levels of CRF with levels of CAC.[12,13] Jafar et al[12] studied 85 runners and compared those who had performed many EEE events during the past 10 years compared with those who had completed only shorter races during this time and compared CAC levels between these groups. They found that those with a constant high participation in EEE had higher percentages of CAC scores greater than 0 (73.3% vs 23.1%), rankings above the 50th percentile per age and sex (70% vs 19.2%), and more CAC scores greater than 100 (33% vs 11.5%) compared with those who had completed only shorter races. Although the risk of having a CAC score greater than 100 among the EEE group was not significantly different than that for the short distance runners after controlling for age, sex, and years running (P=.12), the EEE athletes were 10 times and 9 times more likely to have CAC at the 50th percentile or greater and scores greater than 0 compared with the lower distance runners after controlling for the covariates.

In the second study, Kermott et al[13] analyzed almost 3000 participants from the Mayo Clinic Executive Health Program who had assessment of CAC and CVD risk factors from January 1, 1995, through December 31, 2008, although they did not quantify levels of PA or exercise training in this cohort. Not surprisingly, known CVD risk factor profiles

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and high-risk calculations tended to uniformly improve with higher levels of CRF. Surprisingly, however, a U-shaped relationship occurred with CRF and CAC. Those with above average CRF levels had lower levels of CAC, whereas CAC scores were increased with highest levels of CRF despite the fact that this group had better levels of CVD risk factors.

These 2 studies certainly add to the current literature regarding the potential for EEE and now high levels of CRF to be associated with high levels of CAC.[9-13] However, one of these studies assessed EEE but did not measure CRF,[12] whereas the Mayo study assessed CRF but not PA.[13] A recent study found that very high CRF levels (approaching 20 estimated metabolic equivalents on treadmill testing) continued to be associated with lower mortality, and they made the case that this vindicated high levels of PA and exercise for increasing CVD risk.[14] However, Arena and Lavie[15] pointed out that their study only assessed CRF and not PA, which are different, and although the main determinant of CRF is PA, there is a genetic or nonexercise component of CRF. Clearly, high CRF is associated with low risk of CVD-associated and all-cause mortality in large studies, and even in patients with chronic conditions such as diabetes, dyslipidemia, and obesity, those with high CRF generally have a better prognosis than their counterparts with low levels of CRF.[1-5] Another issue is that all of these studies are retrospective with implicit bias, and none are true outcome studies. The number of participants in the ultramarathon study was quite small,[12] causing the authors to combine this group with the marathon group. Finally, an issue with the entire exercise CAC literature is that PA, exercise, and now CRF classifications differ considerably from study to study. If the hypothesis exists that PA/EEE/CRF above a certain level promote acceleration of atherogenesis, these levels should be relatively consistent between studies, rather than at the highest level in each particular study.

A major issue is how clinicians should interpret the emerging data on EEE and CRF and CAC. Does high PA and EEE increase the risk of having CAC and "hearts of stone" and how should clinicians react to this evidence? First, the constellation of data supports the fact that high PA/EEE, and now possibly high CRF, is associated with higher levels of CAC. A recent large study found that those with the highest level of PA from marathon running often have CAC levels greater than 100 and even averages over 800.[10] However, despite this finding, the highest levels of PA/exercise were associated with low rates of CVD-associated and all-cause mortality and show that exercise is safe even at high levels of CAC.[10,11] Quite possibly, as with high-intensity statin therapy,[16] high-intensity PA/EEE may promote more calcific coronary atherosclerosis that may be more stable than soft, noncalcified plaque, which is less likely to rupture and cause acute, morbid CVD events.[9-11,16] Certainly, considerable evidence supports that high levels of CRF are associated with low all-cause and CVD mortality[1-5,8] even if CAC presumably is present.

Finally, does this mean that CAC levels are worthless in those patients with high PA/EEE? In fact, Defina et al[10] recently reported that high CAC retained its ability to predict risk with high volumes of PA, as high CAC scores were still associated with higher risk at any given PA level. Clearly, CAC scores are useful to predict risk and potential need for greater prevention and lipid treatment for the primary and secondary prevention of CVD.[17-19] We would still advocate consideration of CAC testing in those with high PA/EEE who have intermediate coronary risk profiles, with plans to intensify risk factor modification and statin therapy in those with high CAC scores and consideration for stress testing in those with very high CAC scores, at least to assess for severe ischemia and malignant arrhythmias.[11] However, as Lavie et al[11,20] recently explained, high levels of PA and CRF are extremely protective against CVD events and mortality, making it possible for individuals to perform high doses of running and exercise safely even with high CAC and "hearts of stone."

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