Exercise-Induced Cardiac Remodeling
Not a Case of One Size Fits All

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If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we will have found the safest way to health.

-Hippocrates of Kos c.460–c.370 BC

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xercise is the most effective therapy one can prescribe for good health and longevity. In relatively modest doses, regular exercise reduces cardiovascular mortality by 35% and all-cause mortality by 33%.1 However, the effect of high-intensity and high-volume exercise prolonged over decades has been the subject of close scrutiny in recent years. Although some studies suggest that beyond an optimal dose, exercise follows a law of diminishing returns with a plateau of survival despite increasing investment,2,3 other studies suggest a U-shaped relationship with harm at both ends of the spectrum.4,5

See Article by Weiner et al

In health, the resting cardiac output is ≈5 L/min and capable of increasing to 25 to 35 L/min during strenuous aerobic exercise. This increase in cardiac output and muscle performance is facilitated by a symphony of changes in cellular respiration, ventilatory gas exchange, vascular resistance, neurohumoral transmission, and adrenergic stimulation, supporting and enhancing the necessary energy transformations. Repeated bouts of high-intensity and high-volume exercise demand that the myocardium and cardiovascular system remodel and adapt to meet the performance requirements placed on them. Cross-sectional studies of endurance athletes demonstrate that left ventricular wall thickness is 15% to 20% greater than in sedentary controls, and left ventricular cavity dimensions are 10% larger.6 The right ventricle is also enlarged, with elite athletes demonstrating 10% increases in right ventricular dimensions.7 These structural changes are beneficial and serve to equip the athlete with the necessary biological endowments to compete.

However, the precise effects of long-term exercise on the heart and cardiovascular system remain incompletely elucidated. One of the most cited studies on the effect of sporting discipline on exercise-induced cardiac remodeling (EICR) comes from a seminal echocardiography article by Morganroth et al,8 now 40 years old. In this study, endurance-trained long-distance runners and swimmers were shown to have a pattern of eccentric left ventricular hypertrophy, with large left ventricular end-diastolic volumes and minimal or no increase in left ventricular wall thickness, compared with sedentary controls. Resistance-trained wrestlers and shot-putters, by comparison, demonstrated concentric left ventricular hypertrophy with increased left ventricular wall thickness and normal left ventricular end-diastolic volumes. Concentric hypertrophy was presumed to result from Valsalva maneuvers, generating rises in systemic vascular resistance and subsequent pressure overloaded conditions for the left ventricle.

Although numerous and largely cross-sectional studies support eccentric remodeling changes in endurance athletes, few have been able to replicate findings of concentric hypertrophy with normal left ventricular end-diastolic volumes in any athletic population. Through the proliferation of imaging studies performed in athletic populations, our understanding of EICR has improved, highlighting the influences of age, sex, ethnicity, sporting discipline, and exercise dose on the remodeling process. Although cross-sectional studies provide valuable insights into the physiological limits of cardiac enlargement attributable to athleticism, the time course of the development of these changes remains relatively unexplored, and longitudinal studies are welcome.

In this issue of Circulation: Cardiovascular Imaging, Weiner et al9 addressed the subject of left ventricular remodeling in 12 healthy white male rowers with a mean age of 18±0.5 years over a follow-up period of 39 months. It is important to note that these subjects, before enrolment, exercised on average for 8.5 hours per week. As first-year university students joining the men’s varsity rowing program, the stage was set for a natural experiment whereby the subjects increased their training exposure to an average of 13.6 hours per week, in a sport that has both high dynamic and static components.10 The investigators demonstrated that over the initial 90-day period, termed the acute augmentation phase, indexed left ventricular mass increased by 14%, which was attributed to an 11% increase in indexed left ventricular end diastolic volume, culminating in eccentric left ventricular remodeling as determined by echocardiography. Left ventricular early diastolic function improved in this period with an 18% increase in early diastolic relaxation tissue velocity (Ea) but no significant changes in late relaxation tissue velocity (Ae) or transmitral flow velocities. At 36 months of training, a further 9% increase in indexed left ventricular mass was attributed to an 11% increase in left ventricular wall thickness and 5.8% increase in left ventricular

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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length. These observations suggest that a chronic maintenance phase of over 3 years of rowing training is accompanied by eccentric left ventricular hypertrophy. Left ventricular late diastolic function was enhanced in this chronic maintenance phase with stable elevation of early diastolic relaxation tissue velocity ($E_a$) and a significant 64% increase in late relaxation tissue velocity ($A_n$) with concomitant increase in the transmission A-wave flow velocity.

The investigators juxtaposed their study findings with another prospective, longitudinal study by Arbab-Zadeh et al., who studied a distinct population of previously sedentary men and women with a mean age of 29±6 years. At study enrollment, these subjects exercised for ≤30 minutes, 3 times per week, and through a supervised, incremental exercise training program achieved a peak exercise regimen of 7 to 9 hours per week at the end of 1 year, in preparation for a marathon race. Therefore, it is noteworthy that these subjects were, on average, over 10 years older than the subjects of Weiner et al. and reached an exercise dose at the end of the study that reflected the baseline exercise dose of the subjects in the current cohort.

Arbab-Zadeh et al. investigated changes in left ventricular and right ventricular morphology with cardiac magnetic resonance imaging, using invasive pulmonary artery catheterization to examine pressure–volume relationships and maximal exercise testing to demonstrate a 21% increase in maximal oxygen consumption after 12 months of training. Although also reporting a phasic response to EICR, in contrast to Weiner et al., Arbab-Zadeh et al. observed that in their population, the initial increase in left ventricular mass resulted from increased left ventricular wall thickness in a pattern of concentric hypertrophy in the first 6 to 9 months, with subsequent left ventricular dilatation at 9 to 12 months, producing the final picture of eccentric hypertrophy.

Here it is important to highlight the methodological differences in left ventricular wall thickness measurements between the 2 studies. Weiner et al calculated left ventricular wall thickness in accord with the American Society of Echocardiography recommendations on a portable Vivid-I (GE Healthcare) system. This method measures the mean left ventricular wall thickness on a single short axis slice at the level of the papillary muscle and excludes the papillary muscle mass. Arbab-Zadeh et al. calculated mean left ventricular wall thickness by cardiac magnetic resonance imaging using a method that included the papillary muscles (and presumably also left ventricular trabeculation) with averaging over all short-axis images. This is important because increased left ventricular trabeculation is likely to be a feature of EICR, and therefore, the potential inclusion of left ventricular trabeculation and the papillary muscles may result in overestimation of left ventricular wall thickness by this method. Whether the papillary muscles and left ventricular trabeculation should be included in the cavity volume or the myocardial mass is a subject of debate in the cardiac magnetic resonance imaging community. In repeated measures studies of small cohorts such as these, consistency in validated measurements is critical for the correct interpretation of EICR, particularly when comparing small differences in mean left ventricular wall thickness and left ventricular cavity size across different imaging modalities.

This work adds significantly to the field by describing changes in left ventricular twist mechanics that augment both systolic and diastolic function in a population of individuals who undertake frequent exercise. Intriguingly, in the acute augmentation phase where rowing training was intensified, at 90 days, left ventricular apical rotation increased, whereas basal rotation did not change significantly and diastolic untwisting rate also increased by 58%. During the same period, there was an increase in left ventricular systolic peak tissue velocity ($S_n$) but, interestingly, no significant change in left ventricular longitudinal strain. After 39 months of the rowing program, in the chronic maintenance phase, left ventricular apical rotation reverted to baseline values with maintenance of the increased diastolic untwisting rate normalized for left ventricular length. In the chronic maintenance phase, both left ventricular longitudinal strain and systolic peak tissue velocity ($S_n$) increased concurrently with left ventricular length. This phasic relationship of enhanced left ventricular systolic twist mechanics acutely may be alleviated by an increase in chamber size with enhanced longitudinal function with more chronic exercise and advances our current understanding of EICR. Moreover, it may explain why reduced left ventricular twist has been described in more seasoned athletes.

The authors should be commended on conducting a prospective study with such a long period of observation. However, there are some limitations of the study that are worthy of mention. The study cohort was small and consisted only of young, male, white rowers. Therefore, there is limited generalizability to the wider exercising community. Second, EICR changes of the right ventricle were not addressed in this study. In comparison to the left ventricle, the right ventricle suffers a disproportionately high afterload during intense exercise because of the relative pressure increase in the pulmonary circulation exceeding that of the systemic circulation. In this regard, one might expect the right ventricle to be the seat of the most profound EICR changes and, therefore, should not be neglected. Arbab-Zadeh et al. demonstrated that with increasing exercise load, there was eccentric hypertrophy of the right ventricle with a relatively constant right ventricular mass to volume ratio throughout training.

Future studies in the field of EICR would benefit from the use of multimodality imaging with well-validated measurement techniques, taking into consideration changes in left ventricular trabeculation, which may influence left ventricular mass estimation and deserve specific characterization as feature of EICR. Attention should also be paid to the right ventricle and additional instruments evaluating changes in preload and afterload during exercise that may potentially illuminate physiological mechanisms underpinning EICR. Larger studies recruiting a heterogeneous population are needed to compare the effects of age, sex, and ethnicity on EICR, which will resolve the limits of normal physiological remodeling. In doing so, this will create opportunities for testing algorithms to differentiate pathological changes from normal EICR. This is dually important both to guide the clinical assessment of athletes with equivocal features suggestive of potential cardiomyopathy and also to investigate whether prolonged, high-intensity exercise could directly result in maladaptive pathology, such as myocardial fibrosis and arrhythmias.
It remains unclear whether an optimal exercise dose for health and longevity exists and if indeed it is possible to have too much of a good thing. We hope that larger, long-term studies in this field will be able to address these unresolved questions. Until then we are left with ancient wisdom, which instructs us, as with nutrition, to practice moderation—not too little and not too much.

Disclosures
None.

References

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