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The U-shaped relationship between exercise and cardiac morbidity

*Ahmed Merghani, MRCP, Aneil Malhotra, MRCP, and Sanjay Sharma, MRCP, FESC**

Department of Cardiovascular Sciences, St George's, University of London, Cranmer Terrace, London, UK

ABSTRACT

Exercise confers a plethora of health benefits that are well documented, whereas physical inactivity is a leading risk factor for cardiovascular morbidity and mortality. The dose of physical activity required to achieve these benefits is relatively modest and equates to jogging at a pace of 15 min per mile for 20–30 min daily. In the current era, most athletes engage in a volume and intensity of exercise that is at least 5–10-fold greater than the general recommendations for physical activity. Such practice is evidenced by the fact that many sportsmen have achieved athletic feats that were considered impossible only 2 decades ago. Numerous studies in retired athletes have consistently shown a reduced incidence of heart disease and an increased longevity of life. Occasionally, however, intense exercise is associated with sudden deaths in athletes harboring quiescent yet potentially sinister cardiac diseases. Despite the visibility afforded by such catastrophes, the reputation of exercise remains unscathed because most deaths can be accounted for by an underlying cardiac abnormality where exercise is a mere trigger for a fatal arrhythmia rather than the actual cause of death. More recently, there have been an emerging number of reports suggesting that intense exercise may have an adverse impact on an otherwise normal heart. This article will review the morbidity and mortality associated with sport and pose the question whether one can have "too much of a good thing."

Keywords: Athlete's Heart, Sports cardiology, Veteran athlete, Atrial fibrillation, Myocardial fibrosis, Sudden cardiac death, Cardiomyopathy.

The benefits of exercise

Exercise may be considered as the safest, cheapest, and most potent therapy that a physician can prescribe to manage, avoid, or curtail an adverse risk profile for cardiovascular disease in any individual. Exercise is associated with better lipid and blood pressure profiles as well as a lower incidence of obesity and diabetes [1,2]. Even marginal occupational exposure to physical activity has substantial benefits. In a seminal study, Morris et al. [3] reported that active London bus conductors from the 1950s had a 50% reduction in coronary heart disease compared to their sedentary driver counterparts. A similar finding was replicated between postmen and less-active post clerks [3]. Since these studies, there has been a deluge of large prospective cohort studies from numerous countries that provide irrefutable evidence that exercise confers at least a 30–50% risk reduction of developing coronary heart disease (CHD) [4]. Data in octogenarians show that those who are physically active have a lower prevalence of atrial fibrillation (AF), and studies in heart failure patients demonstrate that exercise improves functional capacity and well-being [5]. AF is the commonest arrhythmia in the general population and is associated with a 5-fold increase in the risk of cerebrovascular accidents and a 2-fold increase in all-cause mortality. Moderate physical activity is associated with a reduced prevalence of AF especially in older adults, possibly by mitigating the effects of ischemic heart disease and hypertension, which are commonly implicated in the causation of the arrhythmia [6].

There are also compelling data that athletes live longer than their sedentary counterparts. A study of over 15,000 former Olympic athletes from 9 different countries showed a longevity benefit of approximately 3 years when compared to the general

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*Corresponding author. Tel.: +44 208 725 5939; fax +44 208 297 9100.
E-mail address: sasharma@sgul.ac.uk (S. Sharma).

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population [7]. An even more impressive 6-year survival (75.5 vs 69.9 years) was observed in 2600 Finnish athletes who competed in elite competitions between 1920 and 1965 compared to army recruits [8]. Similar findings have been replicated in former *Tour de France* participants [9], Italian track and field athletes [10], major league baseball players [11], and professional tennis players [12]. It is unclear whether this survival benefit is solely attributable to a healthier lifestyle associated with exercise or to a superior genetic constitution that promotes the ability to exercise intensively. In addition, regular physical activity has also been implicated in the prevention of several neoplastic diseases, depression, and dementia [13] (Fig. 1).

The physiological mechanisms underpinning the observed benefits of exercise have been widely documented. Endothelial dysfunction is one of the earliest precursors for atherosclerosis, and exercise improves endothelial function by increasing the bioavailability of nitric oxide and reducing the production of endothelium-derived vasoconstrictors [14]. Several in vivo and in vitro studies have also demonstrated favorable exercise-related effects on fibrinolysis and platelet function and aggregation that may account for the lower prevalence of cardiovascular disease observed with moderate exercise [14]. Exercise also improves age-related decreases in left ventricular and aortic compliance and elasticity, which may predispose to cardiovascular morbidity in late life [15].

Is there a recommended dose of exercise?

The British Association of Sports and Exercise Sciences [16] and the US Department of Health and Human Services [17] recommend that healthy adults should engage in 150 min of moderate-intensity exercise or at least 75 min of vigorous-intensity aerobic activity per week. Moderate-intensity exercise is considered to be any activity causing a raised heart rate and increased breathing but being able to speak comfortably and includes a brisk walk at 4 mph or cycling at 10–12 mph. The intensity of physical exercise is usually expressed in terms of energy expenditure or metabolic equivalents (METs). One MET represents an individual's energy expenditure while sitting quietly for 1 min (equivalent to about 1.2 kcal/min for a person weighing 72 kg). Moderate-intensity exercise is equivalent to 3–6 METS, whereas athletes typically perform in excess of 15 METS.

There are emerging data that suggest a U-shaped relationship between exercise intensity and adverse cardiovascular events; moderate exercise is better than no exercise, but vigorous exercise may be harmful in some individuals (Fig. 2). A recent prospective study from Denmark reported mortality data in over 1000 apparently healthy joggers (aged 20–86 years) and approximately 4000 sedentary healthy controls. The investigators described a U-shaped association between all-cause mortality and dose of jogging, as expressed by pace, quantity, and frequency of jogging. Light joggers who exercised 1–2.4 h per week, divided into 3 sessions, had a lower mortality than sedentary non-joggers, whereas more strenuous joggers had a mortality rate that was not statistically different to that of the sedentary group [18]. It should be noted that the number of individuals engaged in strenuous jogging was small ($n = 36$), and the conclusions were based on 2 deaths in this small cohort. Furthermore, the precise cause of the 2 deaths was not ascertained. Based on this study, it may be concluded that the greatest benefits of exercise on the cardiovascular system are derived from relatively mild

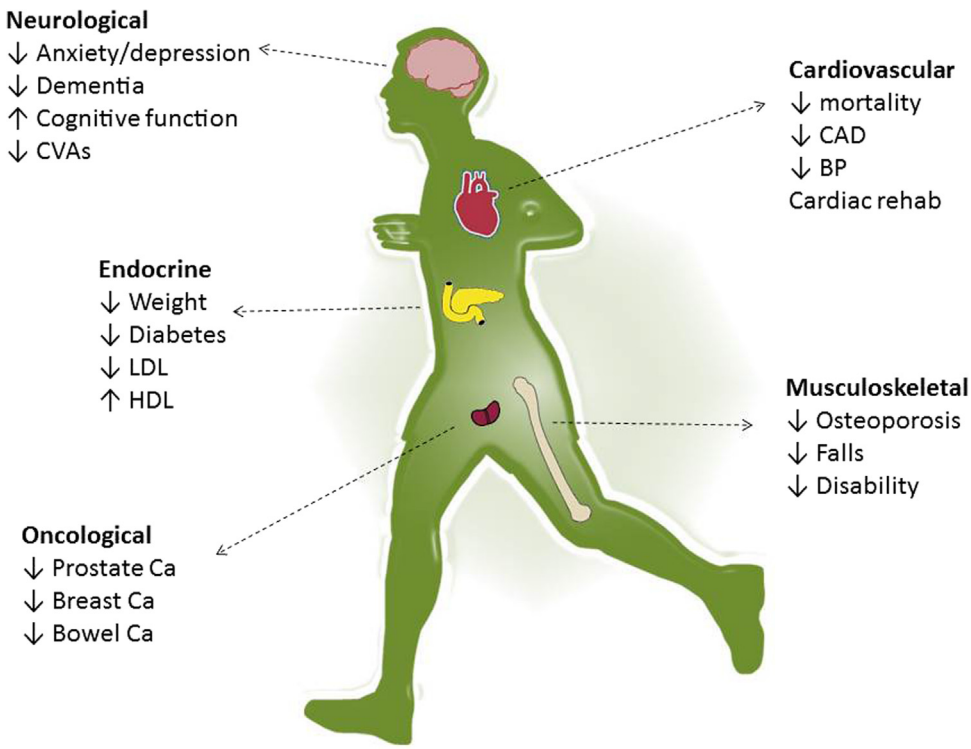

Fig. 1 – The benefits of exercise. BP = blood pressure, Ca = cancer, CAD = coronary artery disease, CVAs = cerebrovascular accidents, HDL = high-density lipoprotein, LDL = low-density lipoprotein.

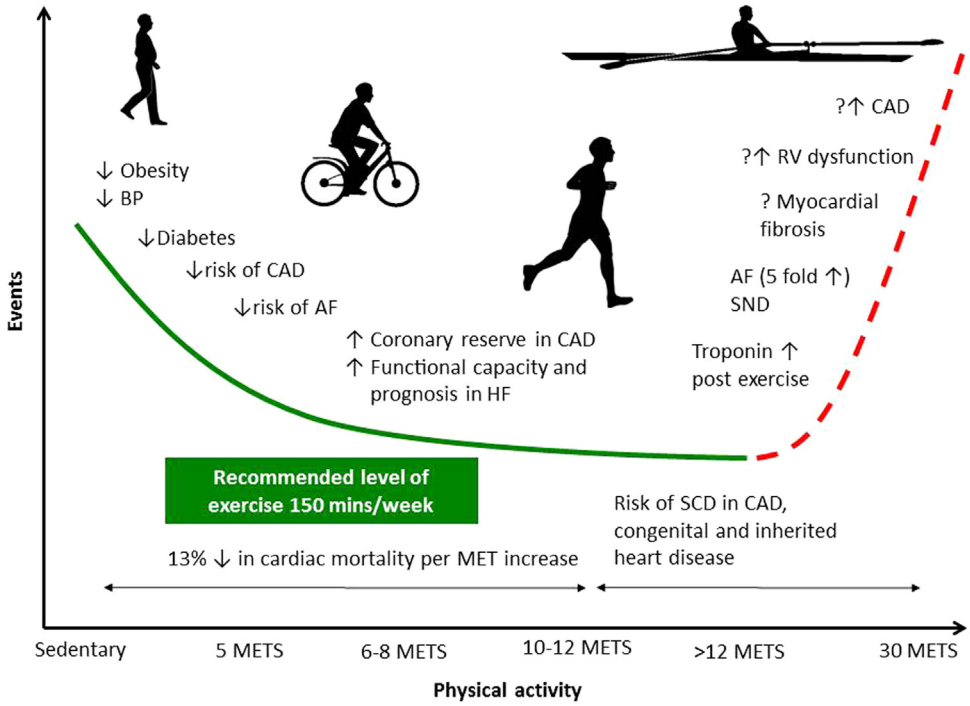

Fig. 2 – The U-shaped curve; moderate exercise is better than no exercise, but extreme exercise may be harmful. CAD = coronary heart disease, BP = blood pressure, AF = atrial fibrillation, SND = sinus node disease, RV = right ventricular.

exercise; however, the dose at which no further benefit is derived is not established. A large study by Kokkinos et al. showed that fitness conferred a 13% reduction in mortality per MET achieved between 4 and 10 METs. However, there did not appear to be any additional benefit beyond 10 METs [19].

An athlete's heart

It is well established that participation in at least 4 h of intensive exercise each week is associated with electrical, structural, and functional alterations within the heart in order to support a large cardiac output for sustained periods (Fig. 3). The magnitude of such adaptations depends upon sporting discipline and a variety of demographic features. In general, Afro-Caribbean male athletes demonstrate greater degrees of left ventricular (LV) hypertrophy and repolarization changes, while endurance athletes generally have the largest LV and right ventricle (RV) cavity sizes.

Electrocardiographic changes in athletes

A combination of high vagal tone and increased cardiac dimensions accounts for a variety of electrocardiogram (ECG) manifestations in athletes. Sinus bradycardia, sinus arrhythmia, and early repolarization changes such as tall

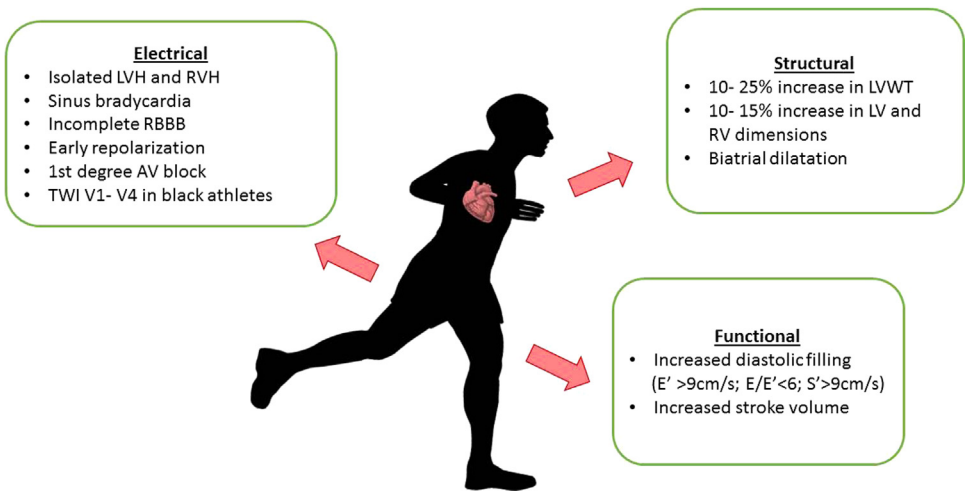

Fig. 3 – Electrical, structural, and functional changes observed in the athlete's heart. AV = atrioventricular, LV = left ventricle, LVH = left ventricular hypertrophy, LVWT = left ventricular wall thickness, RBBB = right bundle branch block, RV = right ventricular, TWI = T wave inversion.

T-waves, J-point elevation, and concave ST segment elevation are common. First-degree heart block and Mobitz type I (Wenckebach) second-degree atrioventricular block are also recognized findings in up to 5% of athletes at rest; the majority will revert to sinus rhythm with mild exertion to help the differentiation between physiological conditioning and cardiac conduction tissue disease [20]. Atrial enlargement and axis deviation are considered normal variants in isolation and do not require further investigation in the absence of symptoms and a positive family history of premature cardiac disease [21].

A variety of demographic factors influence what is considered normal in an athlete's ECG, including sporting discipline, age, sex, and ethnicity. Endurance athletes demonstrate the most marked electrical changes. Male athletes exhibit similar changes to females, though to a greater degree. Adolescent athletes aged ≤14 years often show a "juvenile" ECG pattern of T wave inversion (TWI) in the precordial leads. However, after the age of 16 years, persistence of TWI in Caucasians beyond V2 is uncommon [22,23]. TWIs are more pronounced in Afro-Caribbean male athletes. While TWI in leads other than III, aVR, or V1 are considered abnormal in an adult Caucasian athlete, such repolarization patterns are present in up to 25% of Afro-Caribbean athletes, with the most common being TWI preceded by convex ST segment elevation and confined to leads V1–V4, which is now considered a normal variant [24,25].

Structural changes in the athlete

Athletes demonstrate a 10–20% increase in left ventricular wall thickness (LVWT) compared with age- and sex-matched sedentary controls. Most adult Caucasian athletes reveal a LVWT within the normal range of 7–12 mm [26,27]. Only 2% show a LVWT > 12 mm, and such dimensions are confined to large male athletes participating in endurance events such as rowing, cycling, and long-distance running. However, Afro-Caribbean athletes reveal a greater magnitude of left ventricular hypertrophy [27], and up to 13% males exhibit a LVWT > 12 mm. Despite these ethnic differences, a LVWT > 16 mm is highly suggestive of hypertrophic cardiomyopathy (HCM).

Athletes may also demonstrate an increase in left and right ventricular cavity size by up to 15%. Almost half of male Caucasian athletes had a LV cavity size beyond predicted upper limits [26], while in 14%, this measured >60 mm, which would usually be consistent with a dilated cardiomyopathy (DCM). Similarly, Zaidi et al. [28] revealed that over 40% of male athletes exhibit RV dimensions exceeding the upper limits of normal for the general population, raising the suspicion of arrhythmogenic right ventricular cardiomyopathy (ARVC).

Differentiating physiology from pathology in athletes

While the vast majority of athletes exhibit relatively modest electrical and structural changes, a small proportion may reveal more profound variations that overlap with those observed in individuals who have morphologically mild expressions of inherited cardiac conditions such as HCM, DCM, or ARVC (Fig. 4). A variety of investigative modalities (ECG, echocardiography, ambulatory ECG monitoring, exercise testing, and cardiac MRI) are routinely used to help such differentiation, as an erroneous diagnosis has potentially catastrophic consequences.

Hypertrophic cardiomyopathy

Athletes with a LVWT ranging between 13 and 16 mm, although in the minority, pose the greatest conundrum and comprise a gray zone that overlaps with morphologically mild HCM. ECG anomalies favoring a diagnosis of HCM over physiological adaptations include deep TWIs in the inferior and/or lateral leads, left bundle branch block, pathological Q-waves, and ST segment depression (> −0.2 mV). In a recent study of 155 athletes with pathological TWI, nearly half were

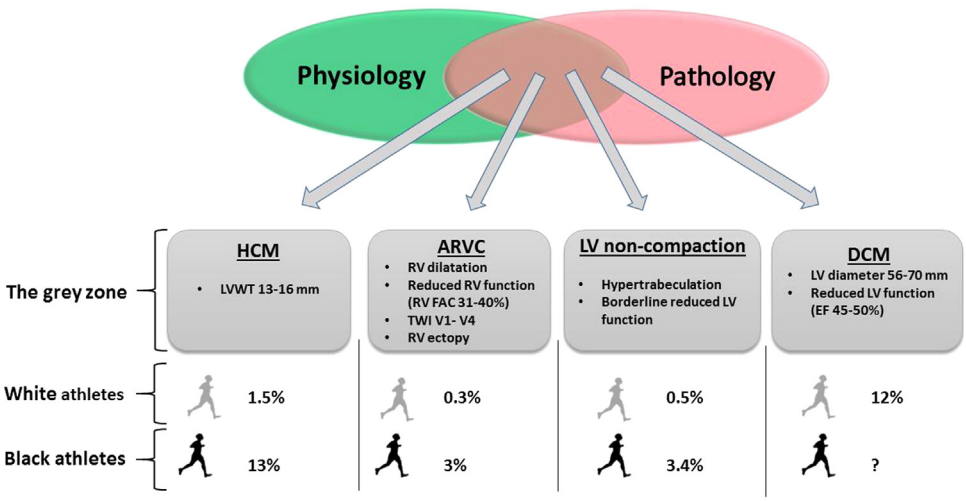

Fig. 4 – Differentiating features between athletes with underlying cardiomyopathy and athletes with physiological adaptations to exercise, with gray zones highlighted below for the respective cardiomyopathy. ECG = electrocardiogram, EF = ejection fraction, LV = left ventricle, LVH = left ventricular hypertrophy, LVWT = left ventricular wall thickness, RV = right ventricular, RVFAC = right ventricular fractional area change.

diagnosed with a cardiac condition, of which HCM accounted for 81% [29]. TWI was mainly confined to the lateral leads, with 80% exhibiting concomitant ST segment depression laterally. The significance of inferior TWI confined to the inferior leads is unknown; however, longitudinal follow-up studies have revealed an association between lateral TWI and sudden death or a subsequent diagnosis of HCM [25,29].

Abnormal structural features suggestive of HCM include asymmetrical, septal, or apical hypertrophy, whereas physiological LVH is homogeneous, and adjacent segments do not vary by >2 mm. Our experience has demonstrated that just over one-third of athletes with HCM exhibit the apical variant compared with only 10% of sedentary HCM patients [30]. In addition, dynamic LV outflow tract obstruction, systolic anterior motion of the mitral valve, or a relative wall thickness (sum of the interventricular septum and posterior wall thickness in end diastole, divided by the LV end-diastolic cavity size) >0.45 are highly suggestive of HCM. In contrast, an enlarged left ventricular cavity supports physiological LVH. A recent study comparing athletes with LVH and HCM controls found that an LV cavity size <54 mm was 100% sensitive and specific for the diagnosis of HCM [31].

Few studies have compared athletes with physiological LVH to athletes with HCM. Our experience of 19 athletes with physiological LVH and 37 athletes with HCM demonstrated that tissue Doppler imaging (TDI) indices of longitudinal systolic and diastolic function had poor sensitivity for the detection of disease in HCM [32]. The sensitivity of pathology for $S' < 9$ cm/s, $E' < 9$ cm/s, and $E/E' > 12$ was 43%, 35%, and 14%, respectively, indicating that their absence does not exclude HCM. However, the specificity of these markers was above 84%, suggesting that in the context of LVH, the presence of any of these parameters is indicative of HCM. Cardiac MRI, exercise stress testing, and Holter monitor are useful investigations for facilitating the differentiation between an athlete's heart and HCM. Late gadolinium enhancement on cardiac MRI, exercise-induced arrhythmias, complex ventricular arrhythmias on Holter monitoring, and a peak oxygen consumption <50 ml/min/kg or <120% predicted [33] favor HCM.

Dilated cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy

A small proportion of endurance athletes exhibit a dilated LV dimension and a borderline low EF (at rest), which raises the suspicion of DCM. Overall, 50% of endurance athletes have been shown to have a LV end-diastolic dimension (LVEDd) > 60 mm, with 12% exhibiting an EF < 52% [34]. In such circumstances, cardiopulmonary exercise testing coupled with exercise echocardiography is valuable in making the distinction between physiological adaptation and DCM. Athletes with physiological LV enlargement and borderline low EF exhibit normal LV contraction, with an EF increase of >10% during exercise and high peak oxygen consumption in the range of 50–65 ml/min/kg (120–150% predicted). Individuals with DCM may demonstrate failure to improve LV function in response to exercise and may also exhibit a peak oxygen consumption <50 ml/min/kg (or <120% predicted). These individuals may also have myocardial fibrosis on cardiac MRI.

In athletes with a dilated right ventricle (RV outflow tract >43 mm and RV basal dimension, RVD1 > 55 mm in male athletes) and borderline reduced function at rest (RV fractional area change—RVFAC—of ≤30%), differentiation between physiological adaptation and ARVC is best facilitated by additional data from the ECG, signal-averaged ECG (SAECG), and cardiac MRI. TWIs in V1–V3 with the preceding ST segments isoelectric or depressed may be suggestive of ARVC. Again, ethnicity needs to be accounted for, as in black athletes, TWIs confined to V1–V4 with preceding convex ST segments are likely to represent normal repolarization in this group. Other ECG markers favoring ARVC include epsilon waves representing delayed repolarization, Q-waves, more than 1000 ventricular extrasystoles of RV origin, small QRS complexes in the limb lead, or late potentials on a SAECG. Echocardiographic assessment of the RV is challenging, as signs may be subtle, but a dilated RV with regional wall motion abnormalities or akinetic segments are highly specific for ARVC, as is late gadolinium enhancement on CMR.

Left ventricular non-compaction

Left ventricular non-compaction (LVNC) is a relatively new myocardial disorder characterized by increased left ventricular trabeculation and intertrabecular recesses communicating with the LV cavity. This condition manifests itself with progressive LV dilatation, impaired systolic function, thromboembolic events, and fatal arrhythmias. The diagnosis is based on imaging studies demonstrating a double-layered myocardial structure consisting of an outer (compacted) and an inner (trabeculated or non-compacted) layer, whereby the ratio of the thickness of the non-compacted to compacted layer is ≥2. Our experience of over 1000 athletes reveals that almost 20% of young athletes show increased left ventricular trabeculation and 8% fulfill diagnostic criteria for LVNC [35]. The data also suggest that ethnicity may again play a role, given that trabeculation was nearly twice more common in Afro-Caribbean athletes than in Caucasian counterparts. A subsequent study by the same group [36] went on to demonstrate that trabeculations occurred in response to increased LV loading conditions using a pregnancy model to replicate increases in cardiac preload. Hence, our group suggests that in athletes with echocardiographic criteria for LVNC, there must be concomitant markers of pathology from other investigations, such as lateral TWI on ECG, fibrosis on CMR, reduced peak oxygen consumption, or evidence of ventricular arrhythmias on Holter monitoring or exercise testing.

Sudden cardiac death in sport

On rare occasions, a young and apparently healthy athlete may die suddenly during competition or shortly afterward. Such incidents receive considerable media attention due to the well-publicized nature of sporting events and the perception that athletes are the healthiest in society. Most deaths are attributable to a plethora of structural and electrical faults that are either hereditary or congenital. It is important to note that sport is not the cause of death per se, but rather physical exertion acts as a trigger for serious ventricular arrhythmias

in the setting of an underlying heart condition. The prevalence of sudden cardiac death (SCD) among young athletes is not common, ranging from approximately 1 in 50,000 to 1 in 200,000 depending on the athletic population being studied and the methods for data collection [37,38].

In contrast, SCD in older athletes is predominantly due to atherosclerotic coronary artery disease. Many such individuals have established risk factors for CAD, suggesting that exercise may not confer the same protections from atheroma in the presence of ongoing risk factors. Most deaths in sport occur in middle-aged recreational athletes. Current strategies to prevent SCD in this cohort rely largely on bystander cardiopulmonary resuscitation (CPR) and early utilization of an automated external defibrillator (AED), which is associated with improved outcomes in 23–46% [39–41].

Cardiovascular morbidity in sport

Athletes are constantly pushing the barriers of sporting achievement, and recent decades have witnessed growing numbers of marathon runners, triathletes, and other ultra-endurance athletes both in the professional and recreational settings. Several studies have documented a rise in the concentration of biomarkers of myocyte damage after prolonged exercise. A meta-analysis of 26 studies demonstrated that half of endurance athletes have an elevated troponin response after exercise [42], and over 75% of endurance athletes have raised NT-proBNP concentrations. Such elevations in biomarkers are transient, and it is not clear whether they represent myocyte necrosis or a physiological cellular leak. It has been postulated that the former explanation may eventually lead to myocardial fibrosis that manifest as cardiac dysfunction and arrhythmias.

Atrial arrhythmias

Persuasive data from multiple case–control studies in the last 2 decades suggest that long-standing participation in high-intensity exercise may increase the prevalence of AF. A meta-analysis of 6 studies that involved 655 athletes engaging in diverse sporting disciplines reported a five-fold risk of AF [43].

Interestingly, the relationship between the intensity of exercise and the prevalence of AF exhibits a U-shaped curve, with the incidence of AF being greatest risk in those who are either sedentary or those engaging in regular vigorous activity. In a recent large study of 52,000 long-distance cross-country skiers, AF was the commonest arrhythmia (1.3%) and was related to the number of races competed and faster finishing times [44]. Some studies have assigned exercise risk thresholds for developing AF. Elosua et al. [45] studied 70 consecutive patients with lone AF and reported that a lifetime practice of sport exceeding 1500 h was associated with lone AF (odds ratio = 2.87). Similarly, a recent study of over 4000 patients diagnosed with AF reported that more than 5 h/week of exercise at the age of 30 years increased the risk of developing AF later in life (relative risk = 1.19), whereas moderate-intensity physical activities of more than 1 h/d later in life at older age decreased the risk [46].

The exact pathophysiology of developing AF in athletes is not fully understood, but shortening of the atrial refractory period due to increased vagal tone, atrial stretch, atrial inflammation, and scarring has been implicated [47]. Mont et al. [48] reported that over 50% of athletes develop AF during episodes of increased vagal tone, such as sleep, or after meals. Animal models support the theory that AF in athletes is a consequence of adverse atrial remodeling. Recently, a Canadian group demonstrated that rats exercised for 1 h/d for a total of 16 weeks, and evaluation with serial echocardiography, histopathology, and autonomic nerve testing displayed atrial dilatation and scarring and an enhanced sensitivity to AF induction [49].

Adverse cardiac remodeling and ventricular arrhythmias

There is evidence to suggest that intense exercise may promote ventricular ectopy or non-sustained ventricular tachycardia, but the clinical significance of these arrhythmias in athletes with a structurally normal heart is debatable. Baldesberger et al. [50] compared 134 former Swiss professional cyclists with aged-matched golfers and reported a much higher prevalence of ventricular tachycardias among the cyclists (15% vs 3%, $p = 0.05$). Although this observation seems somewhat alarming, the survival of all the former athletes in the study was not reduced compared with the golfers. Similarly, Biffi et al. [51] studied 355 athletes with ventricular arrhythmias ranging from frequent ventricular ectopy to non-sustained ventricular tachycardias. Over two-thirds of these athletes had structurally normal hearts, and following detraining, almost 75% of the athletes demonstrated partial or complete resolution of the arrhythmias [52]. Over an 8-year follow-up, none of the athletes with a structurally normal heart suffered any adverse cardiac events.

In context with the above, there are emerging studies that suggest that ventricular arrhythmias in a healthy athlete may have a sinister prognosis. Heidbuchel et al. [53] observed a high incidence of major arrhythmic events (39%) including sudden cardiac death (20%) among 46 young athletes who presented with frequent ventricular ectopy or non-sustained ventricular tachycardia during a 5-year follow-up period. Interestingly, 80% of the ventricular arrhythmias had a left bundle branch block appearance indicative of a right ventricular origin. Several subsequent studies from the same group suggest that chronic endurance exercise promotes right ventricle remodeling [54]. Indeed, invasive studies have revealed a high afterload on the RV, with pulmonary artery pressures reaching 80 mmHg in some athletes. La Gerche et al. studied 40 healthy athletes at baseline and after an endurance race and revealed transient right ventricular (RV) enlargement associated impaired RV function on echocardiography. Cardiac troponin and B-type natriuretic peptide levels were elevated and corresponded to duration of exercise and magnitude of reduction in right ventricular function. The researchers postulated that repeated insults of this type following prolonged and intensive endurance exercise may lead to irreversible right ventricular remodeling with a propensity to fatal arrhythmias, which has led to the concept of exercise-induced ARVC [55]. The volume of dose of exercise required for this effect is probably >20 h per week for >20

years. In a prospective study, Pellicia et al. [56] studied 114 Olympic endurance athletes who had competed in 2–5 Olympic games and did not show any new cardiac events or new diagnosis of cardiomyopathies.

Brady-arrhythmias

Sinus node dysfunction and second-degree or third-degree atrioventricular blocks have also been reported. In the study of 52,000 long-distance cross-country skiers described above, there was a 2-fold higher risk of hospitalization for brady-arrhythmias in athletes who completed five or more races compared with those only completing one race [44]. Small-scale studies of veteran endurance athletes suggest that a significant proportion require pacemaker implantation. In a 12-year follow-up study (1985–1997) of 20 Scottish veteran long-distance runners, mean age 67 years, 10% ($n = 2$) required pacemaker implantation [57].

Myocardial fibrosis

The mechanism underlying the reported arrhythmias in athletes is uncertain, but there is a suggestion that over-zealous exercise may cause fibrosis (scarring), which acts as a substrate for generating arrhythmias. Evidence from animal models tends to support some of this theory. Benito et al. [58] exercised rats on a treadmill for 16 weeks, which in human terms is equivalent to 10 years. At 16 weeks, exercised rats developed eccentric left ventricular hypertrophy, diastolic dysfunction, and diffuse fibrosis in the atria and right ventricle. More importantly, ventricular tachycardia could be induced in 42% of the exercised rats compared to only 6% in the sedentary rats. A number of rats were de-trained for 8 weeks prior to sacrifice. In these rats, the level of fibrosis was similar to that of sedentary rats, suggesting that fibrosis may be a compensatory mechanism to increased wall stress. However, this study does have important limitations. The fact that there was no dose-related fibrosis between 4, 8, and 16 weeks of exercising, rats would favor a stress response to tail shock rather than an exercise response. A stress response activates pathological signaling pathways including angiotensin II, protein kinase C, and calcineurin, which result in adverse cardiac remodeling, whereas physiological remodeling is mediated by growth factors such as IGF-1 [59]. Secondly, there was preservation of the septum and left ventricle, which is somewhat surprising given the phenomenal increase in LV filling and cardiac output during exercise.

The role of chronic endurance exercise in myocardial fibrosis has also been explored in cross-sectional studies of humans. Breuckmann et al. [60] undertook CMR imaging in 102 men aged at least 50 years who had completed at least five full-distance marathons during the past 3 years and had no history of heart disease or diabetes. Overall, 12% of the veteran marathon runners exhibited late gadolinium enhancement (LGE), an indicator of myocardial fibrosis, compared to 4% of sedentary controls ($p = 0.077$). The authors analyzed patterns of LGE and found that the majority (58%) of the runners had an atypical patchy to streaky subepicardial to midmyocardial hyperenhancement termed non-coronary artery disease (CAD) pattern compared to 42% who had patterns consistent with CAD. The study was limited by the fact that only male Caucasians were enrolled and the definition of a veteran athlete used in the study was very lenient (3 years of ultra-endurance running). A considerably smaller study from the UK evaluated 12 lifelong veteran male endurance athletes with CMR [61]. Unlike the previous study, the veteran athletes had engaged in 35–52 years of continuous training and competition. Of the 12 athletes, 50% demonstrated LGE, and this was significantly associated with the number of years spent training and number of competitive marathons completed. The small sample size of the study meant that any generalizations relating to the development of fibrosis solely due to intense exercise are difficult, and future studies using large cohorts of lifelong veteran male and female athletes are required.

Coronary artery calcification

In additional to myocardial fibrosis, Mohlenkamp et al. assessed endurance athletes for atherosclerosis by calculating calcium artery calcification scores in the same cohort of veteran runners studied by Breuckmann et al. The investigators documented that 36% of marathon runners aged > 50 years revealed coronary artery calcium scores >100 compared to 21% in controls matched for age and Framingham risk factors [62]. Shearing forces within coronary arteries during high heart rates, circulating interleukins due to inflammation, and the production of free radicals were implicated as possible factors. However, a major limiting factor of the study was that more than half of the runners in the study were previous smokers and 5% were active smokers, which could have provided an adequate explanation for the high calcium scores. A larger well-designed study that excludes confounding factors such as smoking needs to be conducted.

Conclusion

The benefits of moderate exercise are indisputable, and physical activity should be encouraged in all individuals including those with chronic cardiac disease. Indeed, there is little evidence to suggest that intense exercise in the first 3 decades of life has a detrimental effect in individuals who do not already harbor a potentially serious albeit quiescent cardiac defect. Differentiating the physiological effects of such repeated bouts of high-intensity exercise from morphologically mild phenotypes of inherited cardiac conditions requires expert interpretation of a variety of investigative tools.

Veteran athletes show a higher prevalence of AF compared with sedentary individuals of similar age. Small studies have also shown a higher prevalence of myocardial fibrosis and atherosclerosis in these individuals, yet athletes appear to live longer than sedentary individuals. Perhaps we should be prepared to accept that too much of a good thing, in the form of chronic intense exercise, may foster abnormal changes in a previously normal heart, but before we are accused of scare-mongering or generating anxiety, we believe larger studies are necessary to address the prevalence and pathophysiology of such changes, as well as their long-term outcome.

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