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Review

My patient wants to perform strenuous endurance exercise. What's the right advice?

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ABSTRACT

Prolonged strenuous endurance exercise (SEE) such as marathon running has recently been associated with potential deleterious cardiac effects, particularly increased risk of atrial fibrillation (AF). This topic is medically important due to the increasing number of participants in SEE events lasting several hours, including older people. The aim of this narrative review is to provide a summary of the evidence available on SEE and related issues such as cardiovascular mortality, AF, potential cardiac remodeling, cardiovascular events during exertion, or the need for pre-participation screening (with a special focus on beginners). This type of information can help physicians giving advice to their patients and the general public regarding safe SEE practice.

1. Introduction

The marathon running race (42.195 km) commemorates the death of Pheidippides (530–490 BC), a Greek messenger who is said to have died (perhaps of cardiac arrest (CA)) shortly after running from Marathon to Athens (~40 km) to announce that the invading Persians had been defeated. Whether this event is myth or real, prolonged strenuous endurance exercise (SEE) has recently been hypothesized to have potential deleterious cardiac effects, and a 'safety' threshold of ~1 h/day been recently postulated [1]. The "too much exercise" topic is medically important due to the increasing number of participants in SEE events lasting several hours. Thus, the aim of this narrative review is to summarize the evidence available so that physicians can adequately advise their patients and the general public regarding SEE training and participation. We searched for publications on SEE and mortality, atrial fibrillation (AF), cardiac remodeling, cardiovascular events and pre-participation screening (with no restriction on the starting date and up to April 30, 2015). The abovementioned terms were used primarily in the literature search, or combinations of 1 or more of these terms, with restrictions to English-language scientific articles (excluding congress abstracts) indexed in the Medline and Web of Science databases. We also extended the search spectrum to the "related articles", and additional studies were identified from reference lists and the authors' knowledge of in press studies. Two authors independently assessed the records obtained for each of the main topics we addressed.

1.1. SEE and mortality

Around ~1/3 of adults are essentially totally inactive [2], which remarkably increases the risk of chronic diseases and mortality [3]. Conversely, there is strong evidence that moderately-vigorous endurance ('aerobic') exercise (e.g., brisk walking, intensity ~3–6 metabolic equivalents (METs), with 1 MET equaling resting energy expenditure, 3.5 mL O_2/kg/min) is associated with longer life expectancy, especially as weekly exercise time increases to 450+ min [4].

The existence of a dose–response benefit of SEE remains more uncertain compared with less intense exercise, although no dose-related harm has been convincingly demonstrated. In a 15-year follow-up of 55,137 adult men/women, even low-volume running (<51 min/week)

Abbreviations: AF, atrial fibrillation; AHA, American Heart Association; CA, cardiac arrest; CHD, coronary heart disease; CRF, cardiorespiratory fitness; CVD, cardiovascular disease; ESC, European Society of Cardiology; HCM, hypertrophic cardiomyopathy; HR, hazard ratio; LA, left atrium; LV, left ventricle; PA, physical activity; RA, right atrium; RV, right ventricle; SCD, sudden cardiac death; SEE, strenuous endurance exercise; SMR, standard mortality ratio; OR, odds ratio; PPS, pre-participation screening.

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reduced the risk of mortality due to cardiovascular disease (CVD), and persistent running over time was more strongly associated with mortality reduction, but no dose–response benefit was found [5]. A study of 1878 joggers reported highest mortality benefits for ≤150 min/week at a slow/average speed, but mortality was lower among joggers than non-joggers irrespective of training loads [6]. A study with 416,175 adults of both genders found no additional mortality benefits for >50 min/day of SEE [7]. A 21-year follow-up showed that 538 runners of both genders aged ≥50 years and performing SEE ~ 270 min/week had 39% lower mortality than those engaging in ~70 min/week [8]. A 7.7-year longitudinal analysis of 35,402 male runners showed that, compared to <3 km/day, running >9 km/day decreased angina (−65%), nonfatal CHD (−29%), and both fatal/nonfatal CHD risk (−26%) [9]. A recent prospective cohort study with 204,542 Australian adults aged 45–75 years found that, among those who reported performing any physical activity (PA), engaging in SEE (e.g., jogging, cycling) was associated with risk reductions for all-cause mortality of 9% to 13%, even after adjusting for the total amount of PA [10]. Another recent prospective study on a large sample cohort reported that the upper threshold for all-cause mortality benefit occurred at 3 to 5 times the minimum 2008 PA Guidelines for Americans (150 min of moderate-intensity PA, e.g., walking, or 75 min of vigorous-intensity PA, e.g., brisk walking, jogging) and showed no evidence of harm at 10 times the recommended minimum [11].

Exercise-related CVD-mortality benefits are still present in extreme endurance exercisers. A recent meta-analysis estimated a 27% lower CVD standard mortality ratio (SMR) in elite athletes (n = 12,119, mostly men, including Tour de France finishers or former Olympic marathoners), compared with the general population [12]. Albeit the heterogeneity of athletes' specialties (endurance but also 'explosive'/'power' sports) is a major limitation, these findings do not support the notion that SEE above some sort of safety threshold may lead to a chronic cardiac damage that would ultimately limit the longevity benefits of exercise. A recent 50-year follow-up of Finnish athletes found higher life expectancy in endurance athletes (79.1 years; 95% CI: 76.6–80.6) than in controls (72.9 years; 95% CI: 71.8–74.3) [13]. Data from 49,219 men and 24,403 women participating in 90 km or 30 km cross-country ski races, respectively, showed a CVD-SMR of 0.43 (95% CI: 0.35–0.51), with the lowest SMRs found among older participants and those who participated in several races [14].

1.2. Long-term SEE and AF

Light-moderate exercise (e.g., walking) is associated with lower AF risk in older adults [15]. A recent meta-analysis in non-athletes (n = 96,526) found no significant association between regular exercise and higher AF risk compared with sedentary lifestyle (odds ratio (OR) = 1.08; 95% CI: 0.97–1.21) [16]. A recent pooled analysis of 4 studies (n = 112,784 participants) showed no association between increasing amount of time spent on exercise and AF (0.95; 95% CI: 0.72–1.26) [17]. In contrast, long-term practice of SEE can be associated with higher risk of AF, particularly lone AF [18–22]. Although there is no universal consensus [23,24], the association seems stronger in highly competitive athletes.

A meta-analysis including 655 athletes and 895 controls found a 5.29-fold higher risk (95% CI: 3.57–7.85) in the former [25]. A longitudinal study of 309,540 Norwegian men and women aged 40–45 years showed that men who reported SEE were more often prescribed flecainide than sedentary people (HR = 3.14; 95% CI: 2.17–4.54) [26]. In 52,755 long-distance cross-country skiers, higher competition and experience level were associated with higher risk of any arrhythmias (HR = 1.30; 95% CI: 1.04–1.62) and AF (HR = 1.20; 95% CI: 0.93–1.55) [27]. A recent meta-analysis also found a significant association between history of sports participation and AF risk (1.98; 95% CI: 1.00–3.94) [17]. Elderly men with a history of long-term SEE practice had a 6% higher AF risk (95% CI: 0.8–11.1) compared with elderly men in the general population [28]. Grabs et al. recently performed continuous ECG monitoring in 20 male runners (age 45 ± 8 years) during a marathon race [29]. Interestingly, the prevalence of arrhythmias (atrial and ventricular premature complexes) decreased during and after the run and no malignant arrhythmias were reported.

Potential factors triggering AF in previously healthy long-term exercisers include left-atrial (LA) enlargement or fibrosis, increased parasympathetic tone and inflammation [30–33]. Self-reporting of AF is a significant limitation of some studies in this field [28], since this might include not only paroxysmal (vs. stable) AF, but also palpitations and other symptoms that might be erroneously interpreted as AF by sportspeople. Other types of arrhythmias (e.g., ventricular tachycardia) which are relatively common in CVD/CHD-free people who are starting to practice exercise can also be interpreted as palpitations.

1.3. Long-term SEE-induced remodeling?

SEE sports events (marathon, half-ironman triathlon, full-ironman triathlon, alpine bicycle racing) can cause acute cardiac changes such as RA and right ventricle (RV) dilation, accompanied by decreased RV ejection fraction and elevation of biomarkers of myocardial stress/injury (troponin, B-type natriuretic peptide) [7,34,35], with an apparent dose–effect of event duration [34,35]. A recent meta-analysis found that RV function is the most impaired variable post-SEE, while left ventricle (LV) function is relatively unaffected [36]. Short-term recovery of the SEE-induced disturbances is usually complete, with no evidence of actual tissue damage [37–39]. However, LV or RV diastolic dysfunction might persist in some participants for 1 [35,40] up to ~4 weeks post-race [41]. No significant post-marathon changes in cardiac-troponin have been reported in old experienced (>60 years) runners [42]. When these do occur in older runners, post-marathon alterations follow a similar pattern compared to younger runners [43], and return to normal within 2 weeks [43]. Post-marathon occurrence [44] or persistence of cardiac alterations were found to be more frequent in less trained runners (<56 km/week) [41], although this evidence was contradicted in another study [35]. The long-term clinical consequences of repeated exposure to the abovementioned SEE-induced alterations remain to be clearly determined.

Rats exposed to long-term, daily forced (tail shock) intense treadmill-running developed arrhythmogenic areas of RA and RV fibrosis [45]. Yet these findings cannot be easily translated to humans because training intensity was beyond that sustainable by extreme endurance elite athletes, including Tour de France participants [46]. Highly endurance-trained athletes might show a significant increase in the LV mass-to-volume ratio instead of a proportional increase in both LV wall thickness and internal diameter [47], with an ~15% subset showing striking LV cavity enlargement [48], or also enlarged RA and RV [49]. A mildly dysfunctional RV might be the substrate for ventricular arrhythmias even in asymptomatic athletes [50,51], although the RV systolic function of former highly elite endurance athletes, most of whom were still active competitors (mean age 55 years), was recently reported as normal [52]. Moreover, competitive Master's level (>65 years) endurance athletes were found to have preserved, youthful levels of LV compliance and distensibility [53,54] and highly trained endurance runners (33–65 years) demonstrated greater dilating capacity of their epicardial coronary arteries compared with inactive men [55].

Solid evidence is lacking that athlete's heart remodeling leads to long-term CVD, but this possibility, especially RV enlargement, cannot be excluded in some high-level athletes and deserves further scrutiny [48]. On the other hand, unsuitable cardiac remodeling is unlikely to affect runners with a lower training/competition level. In sedentary people who trained intensively for 12 months to compete in a marathon, the LV showed concentric remodeling during the first 6–9 months, and thereafter dilated and restored the baseline mass-to-volume ratio whereas the RV responded with a balanced remodeling throughout the program [56].