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Review

The Potential Cardiotoxic Effects of Exercise

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ABSTRACT

The emerging controversy related to the potential cardiotoxic effects of high doses of intense exercise need to be considered among the much stronger evidence that supports the pleomorphic benefits of exercise as a whole. However, there is fairly compelling evidence to support the association between long-term sport practice and an increased prevalence of atrial fibrillation and the fact that this relates to a chronic altered atrial substrate. This article was designed to challenge the reader with speculative science that suggests that exercise might promote permanent structural changes in the myocardium which can, in some individuals, predispose to arrhythmias. In terms of long-term health outcomes, it would seem that these small risks are outweighed by the many other benefits of exercise, including a likely decrease in atherosclerotic vascular events, although some recent results have brought into question whether the protective benefits of exercise on vascular events also extends to high-intensity exercise training. Above all else, in this article we sought to highlight current controversies to stimulate research on the many unanswered questions. In particular, there is a lack of adequately powered prospective studies from which we can measure health outcomes and their relationship to exercise-induced cardiac remodelling.

RÉSUMÉ

La nouvelle controverse relative aux possibles effets cardiotoxiques de l'exercice intensif pendant de longues périodes doit être revue à la lumière des preuves beaucoup plus probantes appuyant les nombreux bienfaits offerts par l'exercice physique en général. Il existe des preuves assez concluantes à l'effet que les sports intenses pratiqués à long terme augmentent la prévalence de la fibrillation auriculaire liée à une modification du substrat auriculaire et cet article a pour but de mettre le lecteur au défi en lui présentant l'hypothèse selon laquelle l'exercice serait susceptible d'entraîner des modifications structurelles permanentes du myocarde qui pourraient prédisposer certaines personnes à l'arythmie. Ces risques, somme toute limités, seraient toutefois amplement compensés par les bienfaits généraux de l'exercice physique, notamment la réduction des accidents vasculaires liés à l'athérosclérose, et ce, même si les résultats de certaines études récentes semblent remettre en question les bienfaits vasculaires de l'exercice intensif. Dans cet article, nous avons avant tout cherché à faire ressortir la controverse actuelle afin de stimuler l'amorce de travaux de recherche visant à fournir des réponses aux nombreuses questions qui demeurent toujours en suspens. Il y a notamment une pénurie d'études prospectives suffisamment importantes pour pouvoir mesurer les effets de l'exercice sur la santé et son association avec le remodelage cardiaque induit par l'exercice.

The science that underpins the pleomorphic benefits of exercise is concrete.[1] As has been championed by strategies such as the "Exercise is Medicine" campaign, the benefits of exercise outperform any pharmacological therapy across a broad range of biological systems and if it were a patented pill it would be promoted as a miracle.[2] Rather, this free and readily accessible therapy, which comes in a range of palatable formulations, is all too often overlooked during formulation of health plans for individuals. Against these overwhelming benefits, an article on the potential toxicities of exercise might be perceived as a barrier in the fight against sedentary behaviour and the emerging epidemic in lifestyle-associated morbidity.[3] However, this report was aimed to address an entirely different demographic, one at the other end of the spectrum from inactivity. As opposed to the unquestionable science behind the benefits of 'getting off the couch,' in this article we discuss the often questionable, incomplete, and controversial science behind the emerging concern that high levels of intense exercise might be associated with some adverse health effects. All available therapies, pharmacological or otherwise, have a dose-response relationship whereby benefits diminish at high doses and the risk of adverse events increases. An open mind would consider that this might even be possible for the very best available health therapy—exercise.

It is important to differentiate between exercise as a trigger of arrhythmias and sudden cardiac death (SCD) as opposed to exercise as a promoter of abnormalities of cardiac structure, which might itself contribute to clinical events. It has been observed that athletes might be at greater risk of

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SCD compared with nonathletes, but most if not all of this excess is due to underlying abnormalities such as familial cardiomyopthies.[4,5] Thus, the mainstream view is that adverse clinical events are explained by exercise acting as a trigger in individuals who are susceptible because of an independent underlying abnormality. In this review we address a largely separate and controversial premise, namely, that exercise might effect a change in the myocardial substrate, which might serve as a cause of arrhythmias in its own right.

Nonlinear Dose-Response Relationship With Exercise

The benefits of exercise are most clearly established for low- and moderate-intensities. As described by Blair et al.,[6] all-cause mortality decreases progressively with fitness but there appears to be an "asymptote of benefit" at an intensity that represents only approximately 50% of a well trained athlete's capacity.[7] This is reinforced by recent large studies in male and female cohorts that have reported little or no additional benefit from performing daily strenuous exercise as opposed to less frequent or less intense exercise.[8,9] Thus, there is a significant gap between the exercise intensity associated with clear health benefits and that routinely practiced by competitive athletes (Fig. 1). It is also notable that the exercise ranges associated with improved cardiovascular outcomes is less than that expected to result in significant exercise-induced cardiac remodelling ('athlete's heart'). Therefore, we should not assume that the benefit from lower intensities can be generalized to the high-level training that induces changes in cardiac morphology.

Even the Highest Trained Athletes Live Longer

There is compelling evidence that details better health outcomes and greater longevity among elite athletes compared with the general population. Landmark cohort studies from Finland reported fewer cardiovascular and cancer deaths in former elite athletes who had competed at an international level between the years 1920 and 1965 compared with referents selected from military enrollment records.[11] However, the extent to which these improved outcomes can be attributed to exercise is difficult to ascertain because there were also important differences in smoking, alcohol consumption, obesity, and socioeconomic class. What reinforces the effect of these confounders is the fact that reductions in death were greatest in obstructive airway disease, a condition that is far more likely explained by differences in cigarette exposure than exercise.[12] Similar findings were recently documented in Tour De France cyclists[13] in whom the 'healthy cohort effect' was associated with being sufficiently healthy to ride a bike at the highest level of exertion, which translated into improved short-term mortality in which the relative reduction in deaths was greatest in diseases of the digestive and respiratory systems. Thus, we might confidently conclude that the pleomorphic benefits of an athletic lifestyle results in improved health outcomes, but that the risk reduction might not be directly attributable to exercise alone.

Improved Mortality in Athletes, but What About Morbidity? Is Endurance Exercise Associated With Arrhythmias?

There is increasingly convincing evidence that long-standing endurance training might promote some cardiac

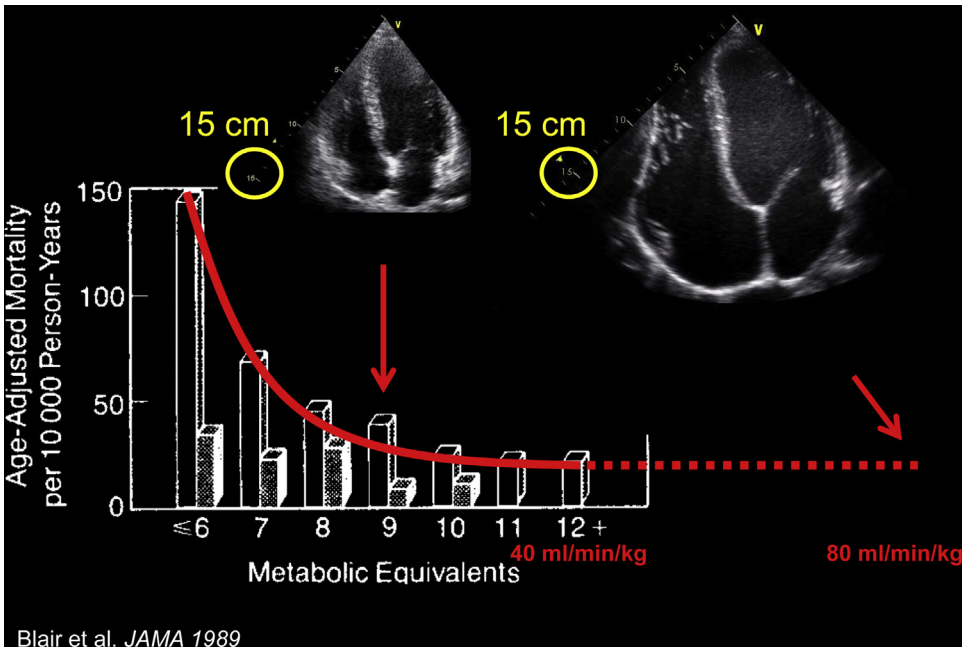

Figure 1. The benefits of moderate exercise and the issue of extrapolation. Epidemiological data, modified from Blair et al. with permission Copyright © 1989 American Medical Association. All rights reserved.,[6] shows reductions in mortality associated with increased fitness. The benefit appears to plateau at approximately 10 metabolic equivalents, which is approximately 50% of the fitness of an elite cyclist. Shown in the figure is a 23-year-old nonathlete (left) compared with a 23-year-old elite cyclist with a maximal oxygen consumption (VO_2max) of 78 mL/min/kg (approximately 22 metabolic equivalents). Note that the echocardiographic images of the heart are presented to scale (15-cm marker in **yellow circle**). Thus, the increase in cardiac size in the cyclist is considerable and the clinical consequences of such profound remodelling remain uncertain (as signified by the **dotted extrapolation of the efficacy curve**). Reproduced from La Gerche et al.[10] with permission from BMJ Publishing Group Ltd.