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Exercise Recommendations for the Athlete With Coronary Artery Disease

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Abstract

Purpose of the review We provide a framework for formulating exercise prescriptions for those with CAD in order to achieve the "optimal" dose of exercise for each individual.
Recent findings Multiple epidemiological studies demonstrate that exercise is inversely associated with atherosclerotic coronary artery disease (CAD), yet the risk of an acute coronary event is transiently elevated during vigorous exercise. In turn, CAD is the most common cause of exercise-related sudden cardiac death (SCD) in older athletes. When prescribing exercise recommendations for athletes with CAD, we should maintain equipoise between the benefits derived from sports participation and the risk of an adverse cardiac event.
Summary Athletes are not immune from atherosclerotic CAD, and we should perform risk assessments regardless of physical and athletic prowess. Cardiopulmonary exercise testing may be a useful tool to develop individualized exercise regimens for athletes with CAD.

Introduction

It is well established that exercise is important for optimal cardiovascular health and longevity [1–3]. Much like the general population, exercise should be encouraged for all patients with CAD. Unfortunately, only 20% of US adults and adolescents accumulate sufficient exercise for optimal health [4]. On the other end of the exercise spectrum, more individuals >40 years old take part in competitive endurance races than ever before [5–7]. These individuals have medical, dietary, and training backgrounds markedly different to traditional

competitive athletes. As a result, the number of older athletes with established CAD has likely increased.

Exercise has a number of athero-protective effects that prevent the progression of plaque development and rupture. At a molecular level, exercise improves endothelial function and vascular remodeling [8], reduces inflammation [9], and improves skeletal muscle fuel utilization [10]. At a system level, exercise training promotes weight loss [11], decreases blood pressure [12], and improves lipid metrics [3, 13]. Moreover, the exercise-induced effects on blood pressure [14], lipids [15], and insulin sensitivity [16] can be observed acutely after a single training session. Exercise preconditioning can also reduce cardiac insult after myocardial ischemia and ischemia reperfusion injury [17, 18]. Despite all these well-established benefits, the risk of an ischemic event or fatal arrhythmia is transiently elevated during vigorous exercise, particularly among those with underlying CAD [19–21]. In older athletes, most exercise-related sudden cardiac death (SCD) cases are due to underlying CAD [22, 23].

In this article, we discuss some deleterious effects caused by and associated with exercise and consider the optimal dose of exercise for athletes with established CAD. We provide a practical approach to assess an athlete's risk of an acute coronary event and our method for developing a safe and engaging exercise prescription. Finally we outline our approach in managing athletes in the rehabilitation phase after an acute coronary event.

The risks of exercise

The purported cardiovascular risks of exercise are categorized as either acute or chronic – the former being well established, and the latter fiercely contested.

Acute deleterious effects of exercise in patients with CAD

Although the risk of an acute coronary event in habitually active individuals is lower compared to sedentary counterparts, active individuals have a higher frequency of events during exertion than at rest [20]. Endurance exercise requires a sustained increase in cardiac output to match metabolic demand. Cardiac output may be five- to sixfold higher during periods of maximal exertion with an attendant increase in myocardial oxygen demand [24]. This, in conjunction with a shortened diastole and coronary perfusion time, may cause a demand-supply mismatch in the presence of an underlying coronary stenosis. In turn, myocardial ischemia may propagate a malignant ventricular arrhythmia and sudden cardiac arrest. When the causes of sudden cardiac arrest in long-distance races in the United States were evaluated, events in older athletes *during* these endurance events occurred due to high-grade stenosis without evidence of plaque rupture [25, 26]. Conversely, it is possible that myocardial infarction that occurs immediately *after* an endurance event is due to acute coronary thrombosis [27]. Similarly, in the general population, myocardial infarction related to physical exertion is often due to plaque rupture [28]. Although the pathophysiology behind this phenomenon is unclear, vigorous exertion and the concomitant increase in heart rate and blood pressure cause an increase in wall shear stress and flexing of atherosclerotic epicardial coronary arteries. Both may lead to rupture of an underlying vulnerable plaque. An increase in thrombotic factors, particularly in the immediate postrace period, may provoke thrombosis in a plaque ruptured during exertion. It is important to acknowledge that studies typically do not discriminate between race and postrace events, and therefore the notion that there is distinct pathophysiology

of acute coronary events during and immediately after exercise in athletes is based on limited evidence. Importantly, the data suggest that both mechanisms of myocardial infarction – fixed coronary stenoses and plaque rupture – stand to transiently increase risk of events around exercise.

Chronic deleterious effects of exercise in patients with CAD

In addition to the transient increase in the risk of an acute coronary event during, or immediately following exercise, there is also a concern that chronically high levels of exercise can have long-term deleterious effects. This debate largely centers on the association of coronary artery calcification (CAC) in those whose activity levels place them at the upper end of the exercise dose spectrum. CAC is a validated marker of atherosclerotic CAD and assists in risk stratification in the general population [29–31]. Male endurance masters athletes demonstrate a higher burden of CAC and calcified plaques compared with sedentary controls matched for age and traditional risk factors [32••, 33••, 34].

The question, therefore, is whether high volumes of endurance exercise can promote coronary calcification. This apparent paradox has been discussed by several authors [7, 35–37], who emphasize the need for cautious interpretation of the available evidence. This, they argue, is primarily for three reasons including the limitations of cross-sectional studies to establish causal relationships, the existence of a potential of unmeasured confounders, and the paucity of data regarding clinical outcomes of CAC in athletes. In an attempt to reconcile the limitations of cross-sectional data, coronary artery plaque volume was longitudinally examined before and after an extreme dose of endurance exercise in eight runners partaking in Race for America [38]. Half of the runners, all of whom had at least one preexisting CAD risk factor, had baseline luminal stenosis in the proximal or mid-left anterior descending artery. While CAD did not newly appear in any runners without baseline disease, plaque volume increased in all runners with CAD identified prior to the race. This was largely driven by an increase in non-calcified plaque. While the study supports the notion that an extreme dose of exercise may accelerate plaque volume in susceptible individuals, high cardiorespiratory fitness attenuates the risk of cardiovascular disease events in those with high CAC [39]. Moreover, the majority of masters athletes do *not* demonstrate CAC [32••], and the association of CAC and high levels of endurance exercise is not seen as frequently in female athletes [32••]. Therefore, based on the available evidence, it appears that high dose of endurance exercise is neither necessary nor sufficient to cause coronary artery disease in older individuals. Indeed, it is plausible that diligent management of atherosclerotic risk factors at a younger age would reduce the burden of CAC observed in older athletes.

Is there an optimal dose of exercise?

We have established that exercise training has a plethora of cardiovascular and non-cardiovascular benefits, yet vigorous exercise in athletes with underlying CAD may transiently increase the risk of an ischemic event. Given that exercise training is an integral part of an athlete's well-being and is a prerequisite for success in competition, we should address the concept of an "optimal dose of exercise" for athletes.

Broadly speaking, the "optimal" dose (dose encompassing intensity, duration, and frequency) will depend on what one is attempting to optimize. If optimal refers to a pure increase in longevity for athletes with underlying CAD, moderate levels of exercise should suffice. The greatest incremental reduction in risk of cardiovascular events occurs at the lowest levels of physical activity (i.e., from no exercise to low/moderate levels of exercise) [40, 41]. An increase in the volume of exercise beyond moderate levels yields progressively smaller reduction in cardiovascular events. Large epidemiological studies demonstrate that maximal benefit of physical activity is achieved by 150 to 300 minutes per week of moderate-intensity or 75 to 150 minutes per week of vigorous-intensity activity or an equivalent combination of moderate- and vigorous-intensity aerobic activity [41, 42].

Conversely, "optimal" may refer to performance, in which case the dose of exercise is the level required to achieve success in competition, regardless of the risk of an adverse cardiac event. In an observational study of >1000 patients with CAD, self-reported physical activity levels of 2–4x/week conferred the greatest survival benefit, while exercising ≥5x/week was associated with increased hazard of cardiovascular mortality [43]. However, generally the data is limited in relation to the risks of high levels of exercise in athletes with CAD due to paucity of such individuals for inclusion in epidemiologic studies.

Taken together, it is reasonable to consider the "optimal" dose to encompass a balance between maximizing longevity benefits of exercise with minimizing performance losses. Although this is a gray zone that relies much on conjecture and individualized data, we shall use this definition to frame the context of our exercise recommendations in athletes with CAD Fig. 1.

Risk assessment of athletes with CAD

Prescribing an exercise regime to athletes with CAD begins with an individualized risk assessment to ascertain the underlying burden of disease. It is also

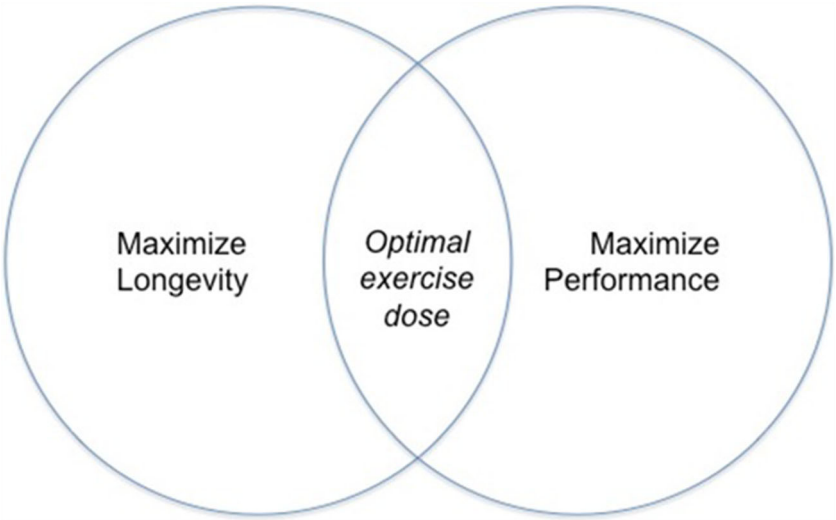

Fig. 1. Optimal dose of exercise for athletes with CAD.

important to recognize that athletes typically wish to perform at high work rates, which entails high myocardial oxygen consumption. If this myocardial oxygen demand is not met, ischemia and its attendant adverse consequences will ensue. It may be argued, therefore, that some athletes require relatively greater maximal coronary blood flow than sedentary individuals who do not regularly engage in high levels of work. The risk of an exercise-related cardiac event in an athlete may then be framed by asking the following three questions:

1) What is the degree of luminal obstruction?
2) How stable is the underlying plaque?
3) What will be the intended myocardial oxygen demand?

The European Society of Cardiology provides recommendations for participation in sports for athletes with CAD [44••]. While this serves as the most comprehensive document on the topic to date, it draws primarily upon expert opinion. In athletes with established CAD, the safety of a high exercise dose is based upon factors outlined in Table 1.

Limitations of exercise testing in athletes with CAD

The main limitation using the above features to ascertain the future risk of an exercise-related cardiac event lies largely on the reliance of functional exercise testing. Exercise testing is a useful investigation to elicit the level of luminal obstruction; however it provides little information regarding plaque stability or future risk of plaque rupture.

Another important consideration is that maximal exercise testing in athletes differs considerably from the general population. We often encounter exercise

Table 1. High- and low-risk features for an exercise-induced cardiac event (adapted from "Recommendations for participation in leisure time or competitive sports in athletes-patients with coronary artery disease: a position statement from the Sports Cardiology Section of the European Association of Preventive Cardiology") [44••]

Low probability for exercise-induced cardiac events (all features must apply)	High probability for exercise-induced cardiac events (only one criteria must be met)
Absence of critical coronary stenoses (i.e., <70%) of major coronary artery or <50% of left main stem on coronary angiography	Presence of a critical coronary stenosis in at least one major coronary artery (>70%) or left main stem (>50%) on coronary angiography
Ejection fraction ≥50% on echocardiography, CMR or angiography	Ejection fraction <50%
No motion wall abnormality	Exercise-induced ischemia
Normal age-adjusted exercise capacity	New left bundle branch block at low exercise intensity level or immediately post exercise
Absence of inducible ischemia on maximal exercise testing	Dizziness, syncope, dyspnea, or angina at low exercise intensity
Absence of major ventricular tachyarrhythmia, polymorphic, or very frequent PVCs at rest or during maximal exercise testing	Relevant ventricular tachyarrhythmia
	High degree of myocardial scarring on CMR

tests in athletes that have been terminated due to heart rate criteria as opposed to maximal exercise capacity. Athletes have a far higher exercise capacity than the general population, and calculation of maximal heart rate has a wide standard deviation [45]. As a result, termination of a maximal exercise test based on heart rate alone may be premature in an athlete. Taken together, a negative exercise test may be falsely reassuring when there is concern for an exercise-induced CAD event.

Exercise prescription for athletes with CAD

There are no carefully designed trials to adequately guide an exercise prescription for athletes with established CAD. In our experience, while an exercise ECG, exercise echocardiogram, or other imaging modalities may provide some useful information regarding the safety of exercise in patients with CAD, cardiopulmonary exercise testing (CPET) is the highest yield to determine the optimal exercise training intensity. This assessment should be performed on the subject's standard medication regimen. The CPET is able to ascertain the maximal oxygen uptake in athletes, which provides an important benchmark to objectively assess the cardiovascular response to a specific training program. The oxygen-pulse curve derived from the CPET can be used as a surrogate marker of stroke volume (assuming a normal arterial oxygen extraction). An oxygen-pulse plateau or decline toward the end of exercise may be a sign of a decrease in stroke volume due to progressive ischemia [46, 47], although this can also be a normal finding in elite endurance athletes due to rightward shift of the interventricular septum. Direct measurement of cardiac output at varying oxygen uptake levels provides a more accurate assessment of whether a central limitation to exercise is present without any assumptions made regarding peripheral oxygen extraction. These parameters, along with the exercise ECG, help identify the level of work required to induce ischemia. As such, a training regimen should focus on work rate below this level in order to minimize the risk of an ischemia-induced ventricular arrhythmia. With the increasing use of wearable heart rate monitors and cycle ergometers that provide power assessments in commercial gyms, it is feasible to reliably train at a work rate considered "safe" from the initial CPET. We encourage repeat cardiopulmonary and exercise ECG testing after the training program in order to evaluate the degree of conditioning, adaptation, and remodeling. This repeat assessment also provides crucial information regarding future safety of exercise training.

Finally, it is important to acknowledge the limitations of exercise training in athletes with CAD, particularly in relation to enhancing performance. If an athlete on optimal medical therapy places a high priority on training at a work rate at which there is evidence of ischemia in order to achieve success in competition, revascularization may be primarily considered [44••]. Despite the limited data, we can reasonably conclude that revascularization acutely improves exercise performance and invasive exercise hemodynamics [48]. Alternatively, if the athlete is content to train and compete at work rates that do not induce ischemia, medical management alone may suffice as in the general population [49]. It should be acknowledged that considering the level of sports competition in the decision to revascularize is controversial, based on low level of evidence, and is centered on a shared decision process with the athlete fully understanding the procedural and anticoagulation risks of revascularization.

High intensity interval training (HIIT) is a type of training that has become increasingly popular in the general population and has long been a form of exercise that competitive athletes have used to improve performance. Among patients with stable coronary heart disease on evidence-based therapy, HIIT performed during supervised cardiac rehabilitation achieved a greater improvement in peak exercise capacity and submaximal endurance compared to moderate-intensity continuous training [50]. However, there is a paucity of data in relation to HIIT in athletes with CAD exercising in an unsupervised setting, and we would limit its prescription to be performed under supervision. In addition, we would avoid this training modality altogether if there was evidence of inducible ischemia until further studies are performed.

Exercise recommendations post-MI or revascularization procedure

The American Heart Association/American College of Cardiology recommends prohibition of participation in competitive sports for at least 3 months after acute myocardial infarction or coronary revascularization procedure (Class IIb, LOE C) [51••]. However, competitive sports participation is not necessarily safe after this period, and some suggest a return to competitive sports only after 1 to 2 years of aggressive lipid lowering therapy in order to allow for optimal myocardial healing and atherosclerotic plaque stabilization [52]. The aforementioned risk assessment (Table 1) as well as the sporting discipline should guide the discussion regarding return to competition.

All athletes however, much like the general population, should undergo a medically supervised, exercise-based cardiac rehabilitation program after an acute coronary syndrome or revascularization procedure [53]. Specific to athletes recovering from myocardial infarction, the size of infarct, and extent of myocardial scar are important considerations to guide the timing and intensity of an exercise program. Indeed, commencing an exercise program too early in the setting of a large infarct may theoretically worsen remodeling or increase the risk of infarct extension. Other important variables to consider prior to commencing an exercise program after MI or revascularization procedure include the residual burden of CAD and ejection fraction. Cardiac rehabilitation should commence approximately 2 weeks after hospital discharge for an acute coronary event and 6 weeks after coronary artery bypass surgery with no surgical complications [53]. Animal studies suggest that exercise training early after myocardial infarction attenuates activation of the renin-angiotensin-aldosterone system and preserves cardiac function [54]. In line with these findings, a meta-analysis including 34 randomized controlled trials of >6000 patients post-MI clearly demonstrates the association of cardiac rehabilitation with reductions in mortality (odds ratio [OR] 0.64) and re-infarction (OR 0.53) [55]. It is important to note that the presence of trained medical staff to manage exercise-related cardiac events such as ventricular tachyarrhythmias likely contributes in part to the benefits observed with a cardiac rehabilitation program. As such, despite the potential and growing popularity of home-based cardiac rehabilitation and wearable heart rate monitors, we should remain cognizant of the importance of supervised programs, especially for athletes, who often grow

frustrated by the exercise limitations imposed during the acute rehabilitation phase.

Conclusion

The number of older individuals competing in endurance races has drastically increased over the past few decades. Given that their risk profiles are markedly different to traditional competitive athletes, physicians are more likely to encounter individuals with established CAD who undertake high levels of exercise. When presented with such cases, we strongly recommend an initial risk assessment in order to tailor the exercise dose. CPET is often a useful tool to help determine safe training intensities. In addition, traditional atherosclerotic risk factors should be appropriately managed in conjunction with any exercise regimen.

In light of the paucity of evidence to guide a definitive approach to prescribing exercise in athletes with CAD, a shared decision-making process becomes imperative, taking into account the individual's desire to successfully compete and the risk this may entail. We hope that as we learn more about the effects of high levels of exercise, we can take better care of our athletes and exercise enthusiasts in the coming years.

Compliance with Ethical Standards

Conflict of Interest
The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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