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Coronary Atherosclerosis in Masters Athletes: Mechanisms and Implications for Cardiovascular Disease Risk

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Abstract

Purpose of review This manuscript reviews the data on the mechanisms and significance of atherosclerotic cardiovascular disease (ASCVD) in masters athletes. It describes recent advances in understanding the biological pathway for the development and progression of ASCVD in athletes. It also reviews salient clinical trials, guidelines on managing ASCVD in masters athletes, and future research directions.

Recent findings Recent data have produced controversy as to whether high levels of physical activity and endurance training can promote ASCVD. Longstanding, vigorous endurance exercise may increase the development of calcified and non-calcified coronary plaques. There are no clinical trials to inform clinicians on how to manage masters athletes with occult ASCVD. We provide a review of the data on ASCVD in older athletes, the risks and benefits of exercise in active individuals with ASCVD, and our approach to evaluating and managing these patients.

Summary Vigorous physical exertion transiently increases the risk of acute coronary syndrome (ACS) and sudden cardiac death in patients with ASCVD. New research has demonstrated increases in both calcified and non-calcified plaque in athletes, although the dominant plaque type is usually calcific. The mechanisms mediating this possible increase in atherosclerosis in active individuals is uncertain, as is the prognostic implications of the increased atherosclerosis. The predominance of calcified plaque may indicate that coronary

plaques in athletes are less prone to rupture and to produce acute coronary events. Some guidelines offer recommendations on the management of non-athletic patients with elevated CAC but data on athletes is scarce. Until additional studies are available, we suggest that athletes with CAC values > 100 Agatston units be managed as if they have preclinical ASCVD. They should be informed of the symptoms of angina and ACS and the importance of prompt medical attention should such symptoms occur. Serum calcium and parathyroid hormones levels should be measured to exclude hyperparathyroidism. Patients should undergo symptom-limited maximal exercise stress testing and aggressive lipid treatment to achieve low-density lipoprotein cholesterol (LDL-C) values < 70 mg/dl.

Introduction

One of Paul D. White's greatest contributions to the medical community was his emphasis on regular physical activity. His walking or bicycling rather than riding in a car and climbing stairs rather than using the elevator are legendary [1]. Dr. White also reported the autopsy findings on Clarence DeMar, a 7-time winner of the Boston Marathon [2]. DeMar died at age 70 from colon cancer, but had run his last marathon only 4 years before his death. DeMar's coronary arteries were laden with atherosclerosis which extended into the media layer at a few points, with clusters of calcification. His coronary arteries were strikingly large (estimated to be two to three times the normal diameter) with only moderately narrowed lumina despite the extensive atherosclerotic plaque. Recent reports suggest that DeMar is not the only masters endurance athlete to demonstrate extensive, although asymptomatic, coronary atherosclerosis.

This review defines a masters athlete as an athlete aged ≥ 40 years. Exercise events and sport participation have increased over recent decades with a similar increase in the number of sporting participants aged ≥ 40 years [3]. This increase is likely due to older athletes seeking the health benefits of routine physical exercise. Some of these athletes have occult, subclinical, or diagnosed ASCVD. Even extreme exercise and exercise training are well tolerated by healthy individuals, but exercise can trigger acute cardiac events (ACE) including such acute myocardial infarction (AMI), arrhythmias and sudden cardiac death (SCD) in individuals with diagnosed or occult ASCVD. Therefore, clinicians must know how to advise patients with, or at risk, for ASCVD on their exercise abilities and limitations in order to reduce the acute risk of ACE during exercise training and competition. The limited available data in athletes has led the American College of Cardiology (ACC) [4••], and other professional organizations [5], to convene expert panels to devise guidelines for the management of athletes with ASCVD. We will review the most salient points of the guidelines and the available literature on this topic and will also provide our approach to the management of masters athletes with ASCVD.

Atherosclerosis development and progression in athletes

Coronary artery disease is the most common cause of SCD in athletes 35 years of age and older [6]. Vigorous physical exertion transiently increases the risk of AMI and SCD in patients with ASCVD [7, 8]. This risk increases with increasing prevalence of ASCVD [9]. However, the progression of plaques usually takes decades, and the presence of atherosclerosis does not necessarily cause clinical symptoms [10]. The arterial injury produced by ASCVD often leads to

osteogenic protein deposition and calcification of the plaques [11]. The extent of coronary artery calcification is a marker of ASCVD and is used both to assess the degree of atherosclerosis and to predict prognosis [12].

Published data over the past decade has initiated controversy as to whether high levels of physical activity and endurance training could promote or accelerate ASCVD. German researchers used CAC to examine the prevalence and prognostic significance of ASCVD in 108 healthy German male marathon runners ≥ 50 years old and who had run ≥ 5 marathons during the previous 3 years. CAC scores were higher in the marathon runners as compared with the second control group that was matched for FRS, median CAC 36 vs 12 AU, $P = 0.02$ [13]. A similar study demonstrated that American male marathoners had significantly more total coronary artery plaque volume and calcified plaque compared with a sedentary control group. The runners were older than controls ($59 \pm$ vs 55 ± 10 years, $p < 0.05$), however, which could account for some of the difference [14]. The observational nature of the above studies precludes conclusions about why highly active individuals had more CAC. Such results could indicate accelerated ASCVD due to exercise or other differences besides exercise exposure between runners and controls. For example, it is possible that the athletic individuals who were studied had relatively recently adopted an active lifestyle, which improved their risk factors and FRS, whereas their CAC scores reflected their prior exposure to higher risk factors. It is also notable that the above studies included active individuals who had significant and uncontrolled traditional ASCVD risk factors, making it more difficult to tease apart the specific impact of exercise exposure on the prevalence of CAC.

Two more recent studies have attempted to address the above issues. A Dutch group attempted to address the impact of lifelong activity levels on CAC. They divided 284 active men (55 ± 7 years) into three groups based on their levels of their self-reported exercise habits from youth onward, and found increased absolute CAC score and increased prevalence of CAC scores > 0 in individuals with the highest (> 2000 MET-min/week, $N = 75$) average exercise volume compared with individuals with the lowest (< 1000 MET-min/week, $N = 88$) exercise volume. Those individuals with > 2000 MET-min/week also demonstrated an increased frequency of calcified plaque (OR = 3.57) compared with the least active group. Though this study was useful identifying that even those individuals who had been active for their whole life still appears to have excess risk of CAC, it did not improve upon isolating the impact of exercise vs. other ASCVD risk factors as 47% of the individuals in the most active group were former or current smokers and 33% had a family history of ASCVD, compared with 44% and 33% in the least active group [15]. To address this issue, Merghani et al. studied 152 masters athletes (70% male, 54 ± 8.5 years) who were specifically selected to have low estimated ASCVD risk. They found similar percentage of athletes with normal CAC (0) compared with controls (60 vs 63%). However, among male athletes with CAC scores of > 0, more athletes had CAC scores ≥ 300 AU (11% versus 0, $P = 0.009$). Male athletes also had more stenoses ≥ 50% (7.5% vs 0, $P = 0.05$). Plaques were more

calcified in the male masters athlete cohort. The predominantly calcific plaques in the athletes suggest a potentially different pathophysiological mechanisms for plaque formation in athletic versus sedentary men [16•]. Nonetheless, some longitudinal studies have shown that increased physical activity is associated with reduced CAC scores [17, 18], but these studies were not specific to athletes so that the quantity and intensity of exercise performed was likely far less than that performed by athletes. These data in sum support a relationship between longstanding, vigorous endurance exercise and the development of calcified coronary plaques. This could indicate that exercise increases coronary atherosclerosis or that exercise facilitates calcification of existing coronary plaques, potentially rendering them more stable and less likely to rupture and cause ACE.

Mechanisms

Several mechanisms may explain the higher CAC scores reported in lifelong, older endurance athletes. Large amounts of exercise training may increase the development of coronary atherosclerosis and the increased CAC scores simply reflect this process. Atherosclerosis develops most frequently at branch points in the arterial system where laminar blood flow is disrupted creating turbulence. Such sites include the origins of the lumbar branches from the aorta and the aortic bifurcation. Such turbulence also occurs in the coronary arteries where the beat-by-beat twisting and flexing of the coronaries creates turbulence. This may explain why coronary atherosclerosis and symptomatic narrowing occurs in the coronaries before atherosclerosis occurs in straighter, less turbulent non-coronary arterial segments. The increased cardiac output and contractility during exercise could increase this coronary flexing and with other factors, such as the increase in systolic blood pressure during exercise, exacerbate the development of atherosclerotic plaques. On the other hand, this theory does not account for the resting bradycardia produced by exercise, which should decrease atherosclerotic development.

The coronary artery flexing during exercise is also a possible explanation for the increase risk of ACE during exercise. Such flexing and bending may increase the risk of atherosclerotic plaque rupture in atherosclerotic, and thereby stiffened, coronary arteries. Healing of these clinically silent ruptures could contribute to high CAC scores in athletes, since some have proposed that coronary calcification represents healed rupture plaque [19].

There are other possible explanations for how exercise might lead to CAC. Exercising acutely and transiently increases circulating inflammatory markers [20]. These repetitive inflammation episodes acutely produced by exercise could accelerate the atherosclerotic process. Exercise also increases parathyroid hormone (PTH) release, and the increase in PTH could facilitate CAC.

The best evidence that the increased CAC scores in athletes represents important atherosclerosis comes from a report on participants in the Race Across America [21]. This effort consisted of a 140-day footrace in

which participants ran 25.7 miles daily for 6 days of the week with 1 rest day. Eight runners who completed the race had computerized coronary angiography performed before and after the event. Four of the eight had atherosclerotic lesions identified, all in the left anterior descending artery, before the run. Atherosclerosis progressed in all 4 of these runners at these atherosclerotic segments and the progression was due to increased non-calcified plaque. The least progression occurred in the only runner taking a statin during the event. No runners demonstrated regression of their atherosclerosis. Importantly, none of the runners who began the race without any atherosclerosis developed new plaques during the event. This is an example of extreme exercise, but supports the possibility that large amounts of exercise accelerate the development of existing coronary atherosclerosis.

Prognosis of coronary artery calcification in masters athletes

Whether chronic, long-term exposure to high-intensity physical activity, typically of masters athletes, portends a mortality benefit has recently been debated. Studies have reported a reverse J-curve pattern associated with exercise dose and CV mortality [22]. Despite the controversy, longevity is generally observed in masters athletes. A meta-analysis of 10 cohort studies consisting of 42,807 elite athletes compared mortality in elite athletes with mortality in the general population. The study found that all-cause mortality was 33% lower in athletes compared with the general population (standard mortality ratio (SMR), 0.67; 95% CI, 0.55–0.81). ASCVD mortality and cancer mortality, the top 2 causes of death worldwide, were 27% (SMR 0.73; 95% CI, 0.65–0.82) and 40% (SMR, 0.60; 95% CI, 0.38–0.94) lower in athletes, respectively. One major limitation of this meta-analysis was significant heterogeneity among studies for all-cause mortality and cancer mortality which may have been driven by large variability among the type of sport analyzed ranging from professional baseball and American football to soccer, cycling and certain Olympic events, many of which do not involve sustained intense aerobic efforts [23].

Data from the Cooper Clinic, a preventive medicine practice initiated in 1970, evaluated the interaction between increasing CAC burden and cardiorespiratory fitness as independent predictors of ASCVD in US adults. For any baseline age and CAC level, greater fitness was associated in a continuous fashion, with lower ASCVD events. The risk of events was decreased by 14% per each additional MET of cardiorespiratory fitness [24]. However, even among fit individuals, higher CAC scores were associated with a worse prognosis. In individuals performing 15 METs, CAC scores greater than 400 AU resulted in an approximately 2-fold increase in annual total ASCVD incidence rates when compared with CAC scores of 0. In the lowest fit (5 METs) participants, the effect of CAC was even more noticeable, with close to a 5-fold increase in annual total ASCVD incidence rates in participants with CAC scores ≥ 400 compared with those with CAC score of 0. In summary, even though fitness provided protection from ASCVD events across the

spectrum of CAC scores; CAC still reclassified risk in fit individuals. The same group also assessed CAC scores, self-reported physical activity levels and clinical outcomes in 21,758 men with mean age of 51 years over a mean follow-up of 10.4 years. Consistent with prior studies, men who performed at least 3000 MET-min/week were more likely to have prevalent CAC of at least 100 AU (RR, 1.11; 95% CI, 1.03–1.20) compared with those less physically active. However, the group of men with physical activity of at least 3000 MET-min/week and a CAC score of at least 100 AU, did not have a significant increase in all-cause mortality (HR, 0.77; 95% CI, 0.52–1.15) when compared with men who reported physical activity of less than 1500 MET-min/week. In comparison, men with CAC of less than 100 AU and reported physical activity of at least 3000 MET-min/week were close to 50% less likely to die compared with men with less than 1500 MET-min/week (hazard ratio, 0.52; 95% CI, 0.29–0.91) [25••]. Findings of this study are in keeping with prior studies that high levels of physical activity are associated with prevalent CAC but this association does not seem to be linked to harm when active men with high CAC were compared with less active men with high CAC. However, active men with high CAC had about a 4-fold increased risk of mortality as active men with low CAC score (5.9 vs 1.3 IR per 1000 person years). The lack of association with increased all-cause and or ASCVD mortality despite higher prevalence of CAC is perhaps due to the presence of more benign calcified plaque and less high-risk mixed plaque. Therefore, ironically, the masters athletes seem to defy the famous saying of a sixteenth century physician philosopher Thomas Sydenham that a man is as old as his arteries, by having older arteries at a younger age and yet living longer compared with their sedentary counterparts [26].

Management

The 2015 ACC guidelines on the management of ASCVD in competitive athletes is based on consensus opinion because there are no sufficiently powered, controlled clinical trials evaluating treatment strategies in athletes. Our approach to managing masters athletes with ASCVD is based on the recommendations of this document [27].

Athletes with ASCVD can be divided into those with clinically manifest or symptomatic disease and those with clinically occult or asymptomatic disease. The former have either experienced an acute cardiac event or have symptoms or findings of inducible ischemia [27]. Patients with clinically concealed ASCVD are presently and previously asymptomatic and are diagnosed as having ASCVD by the presence of CAC or by the presence of noncalcified plaque by coronary computed tomography angiography but do not have evidence of ischemia on provocative testing.

The risk of an exertion-related ACE is greater in individuals with diagnosed ASCVD than in those with occult ASCVD. This risk increases with exertion, the extent of CAD, the degree of left ventricular dysfunction, the presence and extent of ischemia, and the presence of electrical

instability. Unstable or vulnerable atherosclerotic plaques are lipid rich so it is possible to reduce the risk of plaque instability and an ACE by aggressive lipid-lowering treatment, which reduces plaque burden [28] and can produce plaque regression.

The treatment of masters athletes with ASCVD is to reduce their risk of developing an ACE. Athletes need to know that even regular, intense endurance exercise does not offset the ASCVD risk conferred by an elevated LDL–C, and that aggressive lipid management primarily using medications is a critical part of their management. Our treatment goal is to lower the LDL-C as much as possible without producing side effects. The LDL–C reduction goal for ASCAD patients varies between guidelines. The most recent 2018 ACC/American Heart Association (AHA) cholesterol guidelines recommend a personalized approach in risk assessment, a renewed focus on LDL-C target levels, and new drug options for the highest risk patients. These guidelines recommend calculating an individual's 10-year risk of an atherosclerotic event. This calculation is less important for athletes with diagnosed ASCVD because they are all at high risk because of their symptomatic or occult disease.

The CAC score threshold to order a stress test in an asymptomatic adult has also been very controversial. The appropriateness of stress testing after CAC scanning in asymptomatic patients is directly related to the CAC score. The incidence of abnormal nuclear testing in the non-athletic population is 1.3%, 11.3%, and 35.2% for CAC scores of <100, 100 to 400, and >400, respectively [29]. The 2010 ACC/AHA guideline for the assessment of cardiovascular risk in asymptomatic adults recommends stress myocardial perfusion imaging (MPI) for advanced cardiovascular risk assessment (Class IIb) in asymptomatic adults with CAC score >400 with concomitant diabetes or with a strong family history of ASCVD. Nonetheless, the level of evidence behind the recommendation is low (level of evidence [LOE] C) [30]. The extent of CAC has been shown to be associated with prevalence of inducible ischemia by MPI in non-athletes [31]. In non-diabetic patients, the CAC score threshold at which the prevalence of ischemia increases substantially is >400 [31]. The 2016 review of evidence on the use of noninvasive testing to stratify asymptomatic patients with diabetes by the Imaging Council of the ACC recommends that a stress test with imaging be considered for asymptomatic diabetic adults over the age of 40 with CAC scores >400 [32]. Even for this population, whether coronary revascularization offers additive benefit to medical therapy when the ischemic burden exceeds any particular threshold is still unclear. There are no specific guidelines regarding the use of non-invasive testing to stratify symptomatic athletes with elevated CAC scores. This is particularly important since the mechanisms of CAC development and progression in athletes are likely different. One could suggest that athletes could be a high risk subgroup given the hemodynamic demands of training and competition on the coronary circulation. However, the association between CAC scores >400 and ischemia in this subgroup of patients is less well established. In our practice, if the CAC score is ≥ 100 or $\geq$ 75th percentile, we recommend

statin therapy. This approach is also supported by the latest ACC/AHA cholesterol guidelines. Most patients with CAC scores ≥ 100 have a 10-year risk of ASCVD ≥ 7.5%, a widely accepted threshold for initiation of statin therapy [33].

Few observational longitudinal studies have evaluated the effect of vitamin D [34] and calcium intake [35] on CAC. These studies do not support the hypothesis that high calcium and vitamin D intake increase CAC. Nonetheless, we recommend that clinicians measure serum calcium and parathyroid hormone levels to exclude hyperparathyroidism in asymptomatic athletes presenting with elevated CAC scores. Patients should undergo symptom-limited maximal exercise stress testing and aggressive lipid treatment to achieve low-density lipoprotein cholesterol (LDL-C) values < 70 mg/dl.

Diet

Few patients can achieve target goal LDL-C values by dietary therapy alone. Strict vegans and vegetarians can achieve low LDL-C levels, but most patients require pharmacological therapy. Both the 2013 ACC/AHA guidelines on lifestyle management and the 2018 ACC/AHA guidelines on blood cholesterol management encourage a dietary pattern that emphasizes intake of vegetables, fruits, whole grains, legumes, healthy protein sources (low-fat dairy products, low-fat poultry (without the skin), fish/seafood and nuts), and non-tropical vegetable oils. Both also limit the intake of sweets, sugar-sweetened beverages, and red meats [33]. We encourage athletes to follow low saturated fat diets and to practice calorie control if needed, but do not depend on these interventions to achieve target LDL-C levels.

Physical activity recommendations and cardiac rehabilitation

Masters athletes with a history of a recent ACE, stable angina or coronary artery bypass graft (CABG) surgery should undergo a medically supervised, exercise-based cardiac rehabilitation (CR) program as soon as possible after the event. This helps the athlete start back into a training program, but the athlete needs to be informed that the initial phases of cardiac rehabilitation will seem far too easy. Similarly, the rehabilitation staff needs to know that they should work with the athlete to achieve a level of physical activity that keeps the athlete interested in the program. Many athletes abandon rehabilitation because the staff is too restrictive and the athlete wants to do too much too soon. It is important to stress with the athlete that the rehabilitation program is not only for physical activity but also for learning the techniques required for risk factor modification. Patients recovering from PCI or CABG should refrain from competition and strenuous training to allow myocardial healing and atherosclerotic lesion regression. The length of this delay is not defined but we suggest aggressive lipid reduction for at least 2 years before considering return to competition because of reports reporting that regression is visible after approximately 2 years of aggressive lipid

reduction [36] and evidence that the rate of regression decreases after 2 years of treatment [36, 37].

Pharmacologic lipid lowering therapy

Perhaps the most important aspect of managing masters athletes with ASCVD is aggressive lipid lowering because such treatment can reduce plaque lipid content, thereby reducing local inflammation and the chance of plaque disruption.

3-Hydroxy-3-methylglutaryl-coenzyme-A reductase inhibitor (statin) therapy

Statin therapy is the mainstay of any lipid lowering strategy in both athletes and non-athletes. The intensity of statin therapy is divided into high, moderate, and low intensities. High-intensity therapy lowers LDL-C levels by approximately 50%, moderate by 30–49%, and low by < 30%. The 2018 ACC/AHA cholesterol management guidelines recommend high intensity statin treatment for all patients with ASCVD and moderate intensity statin treatment for those not suitable for high-intensity treatment [33]. If the athlete is > 50 years of age, has an estimated 10-year ASCVD risk > 20%, and has multiple risk factors, high-intensity statin therapy is reasonable with the goal to reduce LDL-C > 50% [33].

The American Association of Clinical Endocrinologists (ACCE) 2017 guidelines recommend an LDL < 70 for very high risk patients and < 55 mg/dl for those considered at extreme risk [38]. All patients with ASCVD, including athletes, should undergo aggressive risk factor reduction with high-intensity statin therapy to reduce the chance of plaque disruption (class I; level of evidence A).

High-intensity statin treatment limits the medication choices to rosuvastatin ≥ 20 mg or atorvastatin ≥ 40 mg daily, but approximately 10% of patients treated with a high-dose statin develop statin-associated muscle symptoms (SAMS), and this is said to occur more frequently in athletes [36], although this claim has been difficult to document [36]. Many athletes are also resistant to the concept of high-dose statin therapy. Consequently, we often use low-dose statin therapy, such as atorvastatin or rosuvastatin, every other day [39] or even twice weekly [40] with or without ezetimibe because the greatest reduction in LDL-C per mg of drug occurs with low dose statin therapy. The dose can then be increased or maintained at a low level depending on the response to therapy.

Statins increase average creatine kinase levels (CK) and increases in CK are augmented by exercise [41], and these increases can be quite high. Consequently, any increases in CK in athletes must be evaluated for their relationship to recent exercise. This increase in CK also prompts us to recommend discontinuing statins around 5 days prior to prolonged endurance events to avoid the combination of exercise-induced and statin-induced muscle injury with the theoretical possibility

that such combined injury could prompt frank rhabdomyolysis. This concern applies primarily to prolonged running events since eccentric exercise, in which the muscle both stretches and contracts, such as downhill running, is more likely to produce muscle injury.

Ezetimibe

Ezetimibe can provide an additional 20% LDL-C reduction [42] and reduces ACS when added to a statin [43]. Ezetimibe reduces intestinal cholesterol absorption by binding to the Nieman-Pick C1 Like 1 (NPC1L1) receptor, and is especially useful in athletes because it has little, if any, effect on skeletal muscle. Ezetimibe is usually administered as 10 mg daily, but can be administered intermittently such as thrice or twice weekly because it has a 22-h half-life. Intermittent dosing is worth considering in athletes because the main side effect of ezetimibe is increased bowel motility and bowel motility can be increased by exercise, especially running.

Proprotein convertase subtilisin/kexin type 9 inhibitors

PCSK9Is are indicated for patients with ASCVD whose LDL-C remains too high in the clinician's assessment despite maximally tolerated by other lipid-lowering therapy. The two available agents, alirocumab and evolucomab, reduce LDL-C by an additional approximately 50% when added to statins and have been documented to reduce ASCVD events in the two available clinical trials [44, 45]. They are well tolerated in athletes because they do not appear to increase CK levels or produce muscle pain.

Blood pressure control in the masters athletes

Arterial hypertension is another important risk factor for the development and progression of ASCVD. The ACC/AHA and the European Society of Cardiology (ESC) guidelines advocate regular physical activity as a class IA recommendation for the prevention and treatment of ASCVD. In athletes with a history of subclinical or clinical ASCVD, strict blood pressure is paramount. The goal is to reduce blood pressure to < 130/80 (class I, LOE B). Athletes who compete at a national and/or international level have to review the current list of prohibited substances and methods of the World Anti-Doping Association before starting therapy. A therapeutic exemption may be obtained in order to receive the authorization to take the needed medication.

Beta-adrenergic blocking agents may be poorly tolerated by athletes because of their negative chronotropic effect added to the baseline bradycardia in most endurance-trained athletes. Beta blockers may also negatively affect aerobic exercise performance, which may interfere with

compliance. Also, beta blockers are prohibited in some sports such as archery and shooting because the increase in diastole improves shooting accuracy by spacing the unavoidable peripheral movement produced by cardiac contraction. We prefer to use angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers in athletes because they do not affect exercise capacity, are not on the doping list, and confer a theoretical advantage by reducing peripheral resistance. These drugs can worsen renal function with volume depletion. Dihydropiridine calcium channel blockers are also a preferred choice in athletes because of their predominantly smooth muscle vasodilatory and minimal chronotropic effects. If more than one drug is required, combination drugs could be considered to maximize adherence. Diuretics are banned in many sports because they can mask performance-enhancing drugs, but are often required for pressure control. These drugs can be used in athletes who will not be subjected to doping control, but should be discontinued for a day or two before endurance events especially if those events are performed in hot, humid conditions.

Conclusion

Moderate physical activity is beneficial for heart health. Vigorous physical exertion transiently increases the risk of AMI and SCD in patients with ASCVD. New research has demonstrated an association between vigorous exercise and CAC. This could represent accelerated atherosclerosis as a result of lifelong exercise training, but it could also mean that athletes have more calcified and stable plaques that are less prone to rupture and cause acute cardiac events. The mechanism increasing CAC in masters athletes is still unclear. Additional research is needed to determine the pathophysiological pathway, clinical significance, and ultimate outcomes of asymptomatic ASCVD as measured by CAC in masters athletes.

Compliance with Ethical Standards

Conflict of Interest

Antonio B. Fernandez declares that he has no conflicts of interest. Waseem Chaudhry declares that he has no conflicts of interest.

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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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