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Exercise and Cardiovascular Events - Placing the Risks Into Perspective: A Scientific Statement From the American heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology

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Exercise and Acute Cardiovascular Events Placing the Risks Into Perspective

A Scientific Statement From the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology

In Collaboration With the American College of Sports Medicine

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Abstract—Habitual physical activity reduces coronary heart disease events, but vigorous activity can also acutely and transiently increase the risk of sudden cardiac death and acute myocardial infarction in susceptible persons. This scientific statement discusses the potential cardiovascular complications of exercise, their pathological substrate, and their incidence and suggests strategies to reduce these complications. Exercise-associated acute cardiac events generally occur in individuals with structural cardiac disease. Hereditary or congenital cardiovascular abnormalities are predominantly responsible for cardiac events among young individuals, whereas atherosclerotic disease is primarily responsible for these events in adults. The absolute rate of exercise-related sudden cardiac death varies with the prevalence of disease in the study population. The incidence of both acute myocardial infarction and sudden death is greatest in the habitually least physically active individuals. No strategies have been adequately studied to evaluate their ability to reduce exercise-related acute cardiovascular events. Maintaining physical fitness through regular physical activity may help to reduce events because a disproportionate number of events occur in least physically active subjects performing unaccustomed physical activity. Other strategies, such as screening patients before participation in exercise, excluding high-risk patients from certain activities, promptly evaluating possible prodromal symptoms, training fitness personnel for emergencies, and encouraging patients to avoid high-risk activities, appear prudent but have not been systematically evaluated. (*Circulation*. 2007;115:2358-2368.)

Key Words: AHA Scientific Statements ■ death, sudden ■ exercise ■ myocardial infarction ■ coronary disease

Regular physical activity is widely advocated by the medical community in part because substantial epidemiological, clinical, and basic science evidence suggests that physical activity and exercise training delay the development of atherosclerosis and reduce the incidence of coronary heart disease (CHD) events.¹⁻⁴ Nevertheless, vigorous physical activity can also acutely and transiently increase the risk of

acute myocardial infarction (AMI) and sudden cardiac death (SCD) in susceptible individuals.⁵⁻⁷ This scientific statement presents the cardiovascular complications of vigorous exercise, their pathophysiological substrate, and their incidence in specific patient groups and evaluates strategies directed at reducing these complications. The goal is to provide health-care professionals with the information they need to advise

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TABLE 1. Cardiovascular Causes of Exercise-Related SCD in Young Athletes*

| | Van Camp et al ⁸ (n=100), † % | Maron et al ⁹ (n=134), % | Corrado et al ²⁵ (n=55), ‡ % |
|---|---|--|--|
| Hypertrophic cardiomyopathy | 51 | 36 | 1 |
| Probable hypertrophic cardiomyopathy | 5 | 10 | ... |
| Coronary anomalies§ | 18 | 23 | 9 |
| Valvular and subvalvular aortic stenosis | 8 | 4 | ... |
| Possible myocarditis | 7 | 3 | 5 |
| Dilated and nonspecific cardiomyopathy | 7 | 3 | 1 |
| Atherosclerotic CAD | 3 | 2 | 10 |
| Aortic dissection/rupture | 2 | 5 | 1 |
| Arrhythmogenic right ventricular cardiomyopathy | 1 | 3 | 11 |
| Myocardial scarring | ... | 3 | ... |
| Mitral valve prolapse | 1 | 2 | 6 |
| Other congenital abnormalities | ... | 1.5 | ... |
| Long-QT syndrome | ... | 0.5 | 1 |
| Wolff-Parkinson-White syndrome | 1 | ... | 1 |
| Cardiac conduction disease | ... | ... | 3 |
| Cardiac sarcoidosis | ... | 0.5 | ... |
| Coronary artery aneurysm | 1 | ... | ... |
| Normal heart at necropsy | 7 | 2 | 1 |
| Pulmonary thromboembolism | ... | ... | 1 |

*Ages ranged from 13 to 24,⁸ 12 to 40,⁹ and 12 to 35 years²⁵ for the 3 studies, respectively. Van Kamp et al⁸ and Maron et al⁹ used the same database and include many of the same athletes. All,⁸ 90%,⁹ and 89%²⁵ had symptom onset during or within 1 hour of training or competition.

†Total exceeds 100% because several athletes had multiple abnormalities.

‡Includes some athletes whose deaths were not associated with recent exertion.

§Includes aberrant artery origin and course, tunneled arteries, and other abnormalities.

patients more accurately about the benefits and risks of physical activity.

Most studies of exercise-related cardiovascular events have examined events associated with sports participation in young subjects and with vigorous exercise in adults. Vigorous exercise is usually defined as an absolute exercise work rate of at least 6 metabolic equivalents (METs), which is historically assumed to equal an oxygen uptake ($\dot{V}O_2$) of 21 mL · kg⁻¹ · min⁻¹. Six METs approximates the energy requirements of activities such as jogging. Six METs is an arbitrary threshold and does not account for the fact that the myocardial oxygen demands of any physical activity are more closely related to the $\dot{V}O_2$ requirements relative to maximal exercise capacity than to the absolute work rate per se. Consequently, exercise work rates <6 METs may still place considerable stress on the cardiovascular systems of unfit and older individuals.

Pathophysiological Basis for Exertion-Related Cardiovascular Events

Exercise-associated acute cardiac events generally occur in individuals with structural cardiac disease.

Pathological Findings in Young Individuals

Among young individuals, variously defined as <30 or <40 years of age, the most frequent pathological findings are hereditary or congenital cardiovascular abnormalities,⁸⁻¹⁰

including hypertrophic cardiomyopathy; coronary artery anomalies (eg, anomalous coronary artery origin, acute angle takeoff and ostial ridges, or intramyocardial course)^{11,12}; aortic stenosis; aortic dissection and rupture probably associated with connective tissue defects such as Marfan syndrome; mitral valve prolapse; arrhythmogenic right ventricular cardiomyopathy; and arrhythmias, including those resulting from accessory atrioventricular pathways and channelopathies such as the long-QT syndrome. Myocarditis also is associated with exercise-related deaths in young individuals. Ventricular arrhythmias are the immediate cause of death in these conditions, except for Marfan syndrome, in which aortic rupture is often the proximate cause (Table 1).

Pathological Findings in Adults

In contrast to young subjects, coronary artery disease (CAD) is the most frequent pathological finding among older individuals who die during exertion.^{13,14} Among previously asymptomatic adults, evidence of acute coronary artery plaque disruption, including plaque rupture or erosion, with acute thrombotic occlusion is common.¹⁴ The mechanism by which vigorous exercise provokes such events is not defined, but suggested triggering mechanisms^{15,16} include increased wall stress from increases in heart rate and blood pressure, exercise-induced coronary artery spasm in diseased artery segments,¹⁷ and increased flexing of atherosclerotic epicardial coronary arteries,¹⁵ leading to plaque disruption and

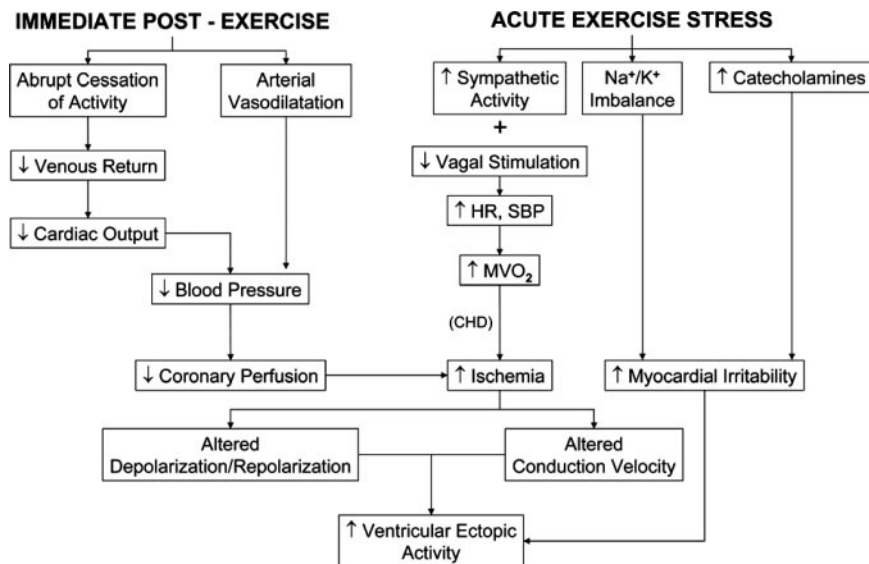


Figure 1. Physiological alterations accompanying acute exercise and recovery and their possible sequelae. HR indicates heart rate; SBP, systolic blood pressure; and MVO_2 , myocardial oxygen uptake. Reprinted from Franklin,⁷⁰ with permission.

thrombotic occlusion. Vigorous exercise also could provoke acute coronary thrombosis by deepening existing coronary fissures, augmenting catecholamine-induced platelet aggregation, or both. Spontaneous coronary plaque fissures are common and have been reported in 9% of subjects dying in motor vehicle accidents or by suicide and in 17% of people dying of noncoronary atherosclerosis.¹⁸ This observation suggests that mildly fissured coronary plaques require some exacerbating event such as vigorous physical activity to induce coronary thrombosis. An increase in thrombogenicity also could contribute to coronary thrombosis after plaque rupture or erosion. Increased platelet activation has been reported in sedentary individuals who engage in unaccustomed high-intensity exercise but not in physically conditioned individuals.^{19,20} Because circulating catecholamine levels are related more closely to the relative intensity of exercise for the individual than to the absolute exercise intensity, it is likely that platelet activation also is related to the relative intensity of the exercise session.²¹

Among individuals with symptomatic CHD, pathophysiological processes may include plaque disruption as above or ischemia-induced ventricular fibrillation from perinfarction, ischemic tissue, or scar.²² Vigorous physical exertion, which increases myocardial oxygen demand and simultaneously shortens diastole and coronary perfusion time, may induce myocardial ischemia and malignant cardiac arrhythmias. Reduced coronary perfusion can be exacerbated by a decrease in venous return secondary to abrupt cessation of activity, which possibly explains the clinical observation that collapse not infrequently occurs immediately after exercise. Ischemia can alter depolarization, repolarization, and conduction velocity and thereby trigger threatening ventricular arrhythmias (Figure 1). In addition, myocardial ischemia,²³ sodium-potassium shifts with exercise, increased catecholamine levels, and circulating free fatty acids may all increase the risks of ventricular arrhythmias.²⁴

The Importance of Age and Pathological Substrate

The present scientific statement addresses the risks of exercise in both young and adult individuals, but it is critically important to recognize that these age groups have markedly different causes of exercise-related deaths and therefore markedly different risk-to-benefit ratios for vigorous exercise. The causes of exercise-related events are not strictly separated by age, given that, for example, some young individuals with genetic defects in the low-density lipoprotein receptor may develop premature CAD, whereas some older individuals may present with structural congenital cardiac abnormalities. Nevertheless, the predominant pathological cause of exercise-related events in adults is occult CAD. Habitual vigorous physical activity appears to reduce the incidence of CHD events, and cardiac rehabilitation appears to reduce the risk of CHD death in patients with diagnosed disease, although neither conclusion has been proved by a randomized, controlled clinical trial. Thus, the benefits of physical activity in those with or at risk for CHD appear to outweigh the risks.

This situation is markedly different in young individuals with diagnosed or occult heart disease. Such subjects rarely die of CHD during exercise, and the clinical course of the responsible conditions such as hypertrophic cardiomyopathy and anomalous coronary arteries is not improved by vigorous exercise. Consequently, in populations with these diagnosed or occult cardiac diseases, the health risks of vigorous physical activity almost certainly exceed the benefits. Moderate physical activity may be justified in such patients on the basis of social and self-image considerations, as well as the benefits of physical activity in preventing obesity, obesity-related health problems, and atherosclerosis, all of which would further exacerbate the individual's cardiac risk.

Incidence of Exercise-Related Acute Cardiovascular Events

The absolute risk of an exercise-related cardiovascular event varies with the prevalence of diagnosed or occult cardiac disease

TABLE 2. Summary of Contemporary Exercise-Based Cardiac Rehabilitation Program Complication Rates

| Investigator | Year | Patient-Exercise Hours | Cardiac Arrest | MI | Fatal Events | Major Complications* |
|-------------------------------------|-----------|------------------------|----------------|------------|--------------|----------------------|
| Van Camp and Peterson ³⁵ | 1980–1984 | 2 351 916 | 1/111 996† | 1/293 990 | 1/783 972 | 1/81 101 |
| Digenio et al ³⁶ | 1982–1988 | 480 000 | 1/120 000‡ | 1/160 000 | 1/120 000 | |
| Vongvanich et al ³⁸ | 1986–1995 | 268 503 | 1/89 501§ | 1/268 503§ | 0/268 503 | 1/67 126 |
| Franklin et al ³⁷ | 1982–1998 | 292 254 | 1/146 127§ | 1/97 418§ | 0/292 254 | 1/58 451 |
| Average | | 1/116 906 | 1/219 970 | 1/752 365 | 1/81 670 | |

*MI and cardiac arrest.

†Fatal, 14%.

‡Fatal, 75%.

§Fatal, 0%.

in the study population but appears to be extremely low in ostensibly healthy subjects. Because of the rarity of exercise-related cardiovascular events, studies examining its incidence are limited by small sample sizes and large confidence intervals. In addition, small changes in the number of events can produce large changes in the calculated incidence. Given these caveats, estimates are available for various patient groups.

Young Athletes

Van Camp and colleagues⁸ estimated an absolute rate of exercise-related death among high school and college athletes of only 1 per 133 000 men and 1 per 769 000 women. These estimates include all sports-related nontraumatic deaths and are not restricted to cardiovascular events. A prospective, population-based study from Italy reported an incidence of ≈ 1 sudden death per 33 000 young athletes per year.²⁵ The rate may be higher because of the higher mean age (23 versus 16 years) of the Italian athletes, participation in sports with higher levels of exercise intensity in Italy, and the inclusion of all events, not just those directly associated with active physical exertion, in the Italian study.

Healthy Adults

Malinow and colleagues²⁶ reported only 1 acute cardiovascular event per 2 897 057 person-hours of physical activity among participants at YMCA sports centers. Vander and associates²⁷ reported only 1 nonfatal and 1 fatal event per 1 124 200 and 887 526 hours, respectively, of recreational physical activity. Gibbons and colleagues²⁸ reported only 1 nonfatal event during 187 399 hours of exercise, which corresponds to maximal risk estimates of 0.3 to 2.7 and 0.6 to 6.0 events per 10 000 person-hours for men and women, respectively. Thompson and collaborators²⁹ estimated only 1 death per 396 000 person-hours of jogging or 1 death per year for every 7620 joggers. Because half of the victims had known or readily diagnosed CHD, the estimated hourly and annual rates for previously healthy individuals were 1 death per 792 000 hours and 15 260 subjects, respectively. Siscovick and colleagues⁵ estimated a similar annual rate of exercise-related cardiac arrest among previously healthy persons of 1 per 18 000 men. Both studies have wide confidence limits because the rates were calculated with only 10 (Thompson et al²⁹) and 9 (Siscovick et al⁵) exercise-related deaths. All victims in both studies were men, and there are few estimates of event rates among women. The reasons for the rarity of exercise-related deaths among adult women are not clear but may relate to the delayed development of CHD in

women and a lower rate of participation in vigorous exercise among older women. More recently, a database consisting of >2.9 million members of a large commercial health/fitness facility chain reported 71 deaths (mean age, 52 ± 13 years; 61 men, 10 women) over a 2-year period, yielding 1 death per 82 000 members and a rate of 1 death per 2.57 million work-outs.³⁰ Nearly half of the exercise-related deaths were among members who exercised infrequently or less than once a week.

Vigorous exercise can also precipitate AMI,^{6,31,32} but even less precise estimates of the absolute incidence are available for this complication in the general population. Among 3617 men selected to participate in the Lipid Research Clinics Primary Prevention Trial because of hypercholesterolemia (plasma cholesterol ≥ 6.85 mmol/L [265 mg/dL] and low-density lipoprotein cholesterol ≥ 4.91 mmol/L [190 mg/dL]), 62 (1.7%) sustained an AMI (n=54) or SCD (n=8) definitely related to exertion during a mean follow-up of 7.4 years.³³ An additional 225 men had acute events definitely not related to exercise, but the activity of another 170 men at the onset of their event was unclear. Nevertheless, these results suggest that the annual rate of exercise-related cardiovascular events among high-risk individuals may be substantial, with 0.2% of hypercholesterolemic men having an exercise-related event annually. The risk of exercise-related AMI also may be substantial in the general population. If we use the estimated incidence of SCD among healthy subjects from Rhode Island²⁹ and the observation that exercise-related AMI is 6.75 times more frequent than SCD,³³ the annual incidence of exercise-related AMI could range from 1 AMI per 593 to 1 per 3852 apparently healthy middle-aged men.

Individuals With Diagnosed CHD

The incidence of exercise-related cardiovascular complications among persons with documented CHD has been estimated by at least 5 reports with data derived from exercise-based cardiac rehabilitation programs.^{34–38} Haskell³⁴ surveyed 30 cardiac rehabilitation programs in North America and reported 1 nonfatal and 1 fatal cardiovascular complication per 34 673 and 116 402 hours, respectively. The rate appears lower in contemporary exercise-based cardiac rehabilitation programs (Table 2) because an analysis of 4 reports estimates 1 cardiac arrest per 116 906 patient-hours, 1 myocardial infarction per 219 970 patient-hours, 1 fatality per 752 365 patient-hours, and 1 major complication per 81 670 patient-hours of participation.^{35–38} This low fatality rate applies only to medically supervised programs that are equipped to handle emer-

TABLE 3. Physical Stress as a Trigger of Acute Cardiovascular Events During Vigorous Exertion*

| Study | Effect Period | End Point | RR (95% CI) |
|---|---------------|------------------------|-----------------|
| Seattle study ⁵ (1984) | <1 h | Primary cardiac arrest | 56 (23–131)† |
| Onset study ³² (1993) | 1 h | Nonfatal MI | 5.9 (4.6–7.7) |
| TRIMM study ³¹ (1993) | 1 h | Nonfatal MI | 2.1 (1.1–3.6) |
| Hartford Hospital AMI study ⁶ (1999) | 1 h | Nonfatal MI | 10.1 (1.6–55.6) |
| SHEEP study ⁴⁰ (2000) | <15 min | Nonfatal MI | 6.1 (4.2–9.0) |
| Physician's Health Study ⁷ (2000) | 30 min | SCD | 16.9 (10.5–27) |

RR indicates relative risk and compares the risk of the cardiac event during exertion with that during sedentary activities; TRIMM, Triggers and Mechanisms of Myocardial Infarction Study; and SHEEP, Stockholm Heart Epidemiology Programme.

*Vigorous exertion is exercise intensity ≥ 6 METs (1 MET = $3.5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$).

†This RR (56) is the exertion RR for habitually sedentary men. The RR (vs no prior vigorous exercise) for the most active men (≥ 140 min/wk vigorous exertion) was 5 (95% CI, 2 to 14).

Adapted from Mittleman,⁴¹ with permission from Blackwell Publishing.

gencies because the death rate would be 6-fold higher without the successful management of cardiac arrest.^{35–38} Furthermore, patients typically are medically evaluated before participation, which could decrease event rates, as could the serial surveillance provided by rehabilitation staff. Such considerations support the use of supervised exercise-based cardiac rehabilitation programs for patients after acute cardiac events.

Does Exercise Increase the Risk of Acute Cardiovascular Events?

Compelling evidence indicates that vigorous physical activity acutely increases the risk of cardiovascular events among young individuals and adults with both occult and diagnosed heart disease.^{5,7,25,29}

Young Athletes

Corrado and colleagues²⁵ prospectively collected reports of SCDs among individuals 12 to 35 years of age over a 21-year period in the Veneto region of Italy. There were 2.3 and 0.9 SCDs per year per 100 000 athletes and nonathletes, respectively, or a 2.5-fold higher risk among the athletes.²⁵ The death rate was higher among athletes despite the fact that all Italian athletes are required by law to undergo cardiovascular screening before participation.³⁹ This report was not limited to SCD during exertion; therefore, the increased death rate among athletes cannot be attributed to exercise alone.

Healthy Adults

Studies in adults also suggest that exercise acutely increases the risk of cardiovascular events, despite a reduction in CHD with habitual physical activity. Both the Rhode Island study of exercise-related deaths²⁹ and the Seattle study of exercise-related cardiac arrests⁵ report a higher estimated hourly death rate during exertion than during more leisurely activities. In Rhode Island, the SCD rate was 7.6 times the hourly death rate during sedentary activities.²⁹ In Seattle, among previously asymptomatic individuals, the incidence of cardiac arrest during exercise was 25-fold higher than the incidence at rest or during lighter activity. The relative risk was greatest in the least compared with the most physically active men (56 and 5 times greater among the least and most active men, respectively).⁵

There is a similar pattern of increased risk with low levels of habitual activity for exercise-related AMI. Vigorous physical activity has been reported within 1 hour of AMI in 4% to 10% of AMI patients.^{6,31,32} This rate is 2.1 (Willich et al³¹) to 10.1 (Giri et al⁶) times higher than the rate during sedentary activities. As with SCD, the relative risk varies inversely with habitual physical activity and is greatest in the least physically active individuals. For patients with CHD, the relative risk of cardiac arrest during vigorous exercise is estimated as 6 to 164 times greater than expected without exertion.²²

Collectively, these data (Table 3)^{5–7,29,31,32,40,41} suggest that vigorous exertion transiently increases the risk of AMI and SCD, particularly among habitually sedentary persons with occult or known CAD performing unaccustomed, vigorous physical activity. In fact, the Onset Study estimated that the risk of AMI during or soon after vigorous exertion was 50 times higher for the least active than for the most active cohort (Figure 2).³²

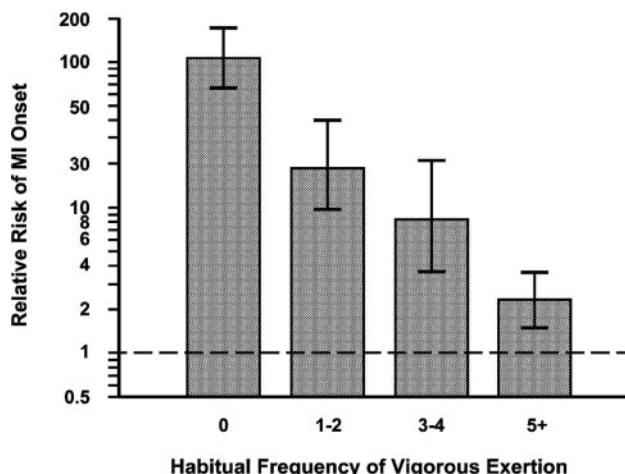


Figure 2. Relative risk of MI associated with vigorous exertion (≥ 6 METs) according to habitual frequency of vigorous exertion. The T bars indicate 95% confidence limits. The dotted line indicates risk of MI with no prior vigorous exertion. Adapted from Mittleman,⁴¹ with permission from Blackwell Publishing.

Relative Risk of Cardiovascular Events During Exercise Versus Total Risk

Vigorous exercise increases the risk of a cardiovascular event during or soon after exertion in both young subjects with inherited cardiovascular disease and adults with occult or diagnosed CHD. Nevertheless, no evidence suggests that the risks of physical activity outweigh the benefits for healthy subjects. Indeed, the converse appears to be true. In the Seattle study, the relative risk of cardiac arrest was greater during exercise than at rest for all levels of habitual physical activity, but the total incidence of cardiac arrest, both at rest and during exercise, decreased with increasing exercise levels.⁵ Specifically, the overall incidence decreased from 18 events per 1 million person-hours in the least active to only 5 in the most active subjects. The risk of an exercise-related AMI also decreases with increasing amounts of physical activity.^{6,31,32} Considerable other epidemiological evidence, albeit no random-assignment, controlled study, supports the concept that regular physical activity, including vigorous activity, reduces CHD events over time.³

In contrast to adults in whom vigorous exercise appears to reduce the overall risk of CHD, exercise in young subjects with occult cardiovascular disease may increase both exercise- and non-exercise-related sudden death. SCD during exertion in a young athlete results from the interaction between the underlying heart disease or substrate and the acute trigger of exertion plus other possible triggers associated with exercise, including emotional stress, hemodynamic changes, altered parasympathetic tone, and myocardial ischemia. Athletic training itself may increase the risk of sudden death in the young athlete with heart disease by altering the substrate. This alteration could occur by promoting disease progression or by increasing the risk of cardiac arrhythmia by structural or electrical changes. For example, in patients with hypertrophic cardiomyopathy, recurrent episodes of exercise-induced myocardial ischemia during intensive training could produce cell death and myocardial replacement fibrosis, which in turn enhance ventricular electrical instability. In patients with arrhythmogenic right ventricular cardiomyopathy, regular and intense physical activity could provoke right ventricular volume overload and cavity enlargement, which in turn may accelerate fibrofatty atrophy. In Marfan syndrome, the hemodynamic stress placed on the aorta by increased blood pressure and stroke volume during intense activity could increase the rate of aortic enlargement, thereby increasing the risk of aortic rupture. Consequently, the risk-to-benefit ratio of exercise differs between young and older subjects with occult cardiovascular disease.

The Risk of Special Situations and Activities

The rarity of exercise-related events makes the examination of special situations and activities difficult because of small sample sizes.

Morning Versus Afternoon Exercise

AMI and SCD in adults are more frequent in the early morning hours. This has prompted speculation as to whether vigorous exercise should be best restricted to afternoon hours in individuals at increased risk.

Young Athletes

In contrast to adults, sudden death and cardiac arrest among young athletes occur primarily in the afternoon and early evening and are associated with training and competition.⁹ However, sudden death among nonathlete patients with hypertrophic cardiomyopathy is more frequent in the early waking hours, much like CHD.⁴² The explanation for this observation is not clear, and the timing of cardiac events in other young subjects with inherited cardiac disease is not known.

Adults

Murray and colleagues⁴³ found 5 cardiovascular events in 168 111 patient-hours of supervised cardiac rehabilitation exercise in the morning (3.0 events per 100 000 patient-hours) and 2 events during the 84 491 patient-hours of afternoon exercise (2.4 events per 100 000 patient-hours). This difference was not significant, but conclusions are limited by the number of subjects and available events. Similarly, Franklin and collaborators³⁷ reported that time of day had little or no influence on the rate of cardiovascular complications during exercise-based cardiac rehabilitation. Given the likely benefits of exercise in reducing cardiovascular events and the low overall rate of exercise-related events, it is probably more important that individuals exercise regularly at a convenient time of day than at a specific time of day.

High-Risk Activities

Few systematic studies have identified high-risk activities, again because of the rarity of exercise-related cardiovascular events. In general, the risk of any vigorous physical activity is an interaction of the exercise per se and the individual's physical fitness because identical physical tasks evoke lower cardiac demands in physically fit subjects than in unfit persons. Snow shoveling has repeatedly been associated with increased cardiovascular events,^{44,45} probably because it can elicit higher rate-pressure products than does treadmill exercise testing,⁴⁶ because it is often performed out of necessity by unfit individuals, and because some cardiac patients develop angina at lower rate-pressure products, suggesting a coronary vasoconstrictor response, during exercise in cold temperatures.⁴⁷

Strategies to Reduce Exercise-Related Cardiovascular Events

No strategies have been adequately studied to evaluate their ability to reduce exercise-related acute cardiovascular events. Physicians should not overestimate the risks of exercise because the benefits of habitual physical activity substantially outweigh the risks. From observational studies,⁴ it appears that one of the most important defenses against exercise-related cardiovascular events in adults is to maintain physical fitness via regular physical activity because a disproportionate number of exercise events occur in the least physically active subjects performing unaccustomed vigorous physical activity.^{5,6,32} Several strategies to reduce events appear prudent although unproven. These include the following: preparticipation screening, excluding high-risk patients from some activities, reporting and evaluating prodromal symptoms, preparing fitness personnel and facilities for cardiovascular emergencies, and recommending prudent exercise programs. Each of these is discussed below.

TABLE 4. ACC/AHA, ACSM, and USPSTF Recommendations for Exercise Testing Before Exercise Training

| ACC/AHA | ACSM | USPSTF |
|---|--|---|
| Asymptomatic persons with diabetes mellitus who plan to start vigorous exercise (<i>Class IIa</i>) | Asymptomatic persons with diabetes mellitus (or other metabolic disease) who plan to start moderate (40% to 59% $\dot{V}O_2$ reserve) to vigorous ($\geq 60\%$ $\dot{V}O_2$ reserve) exercise | Recommends against routine exercise testing of low-risk adults in general and finds insufficient evidence for exercise testing before exercise training |
| Asymptomatic men >45 y of age and women >55 y of age who plan to start vigorous exercise (<i>Class IIb</i>) | Asymptomatic men >45 y of age and women >55 y of age or those who meet the threshold for >2 risk factors who plan to start vigorous exercise | |

ACC/AHA Class IIa indicates that the weight of evidence/opinion is in favor of usefulness/efficacy; Class IIb indicates that the usefulness/efficacy is less well established by evidence/opinion. Reproduced from Northcote et al,⁵⁷ with permission from the BMJ Publishing Group.

Preparticipation Screening

Young Athletes

The American Heart Association (AHA) recommends cardiovascular screening for high school and college athletes before athletic participation and at 2- to 4-year intervals.^{48,49} The examination should include a personal and family history and a physical examination focused on detecting conditions associated with exercise-related events.⁴⁸ The AHA does not recommend routine, additional noninvasive testing such as a routine ECG. The omission of routine noninvasive testing is controversial because the Study Group on Sports Cardiology of the European Society of Cardiology has recommended that routine ECGs be obtained on all athletes as part of a preparticipation evaluation.⁵⁰

The European recommendation is based largely on an observational study performed in the Veneto region of Italy.⁵¹ Italy has mandated the preparticipation screening of athletes, including an ECG, since 1982. The annual incidence of sudden death among athletes 12 to 35 years of age decreased 89% with screening, from 3.6 deaths to 0.4 deaths per 100 000 athletes. There was no change in deaths among nonathletes, which suggests that screening mediated the decrease. These results provide the best evidence to date in support of the preparticipation screening of athletes but have several limitations.⁵² The study did not directly compare the screening and nonscreening of athletes but was a population-based, observational study. Other changes in the management of the athletes could have contributed to the improvement. In addition, the study did not directly compare screening performed with and without an ECG. Finally, there could be small differences in the screened and comparison populations because the athletes were screened at the Padua Center for Sports Medicine, whereas the comparison population consisted of subjects from the larger Veneto region.

Healthy Adults

Although no data from controlled trials are available to guide the use of exercise testing in asymptomatic adults without known or suspected CAD before beginning an exercise training program, the writing groups from the American College of Cardiology (ACC)/AHA Guidelines on Exercise Testing⁵³ and the American College of Sports Medicine (ACSM)⁵⁴ have addressed this important issue by consensus. Although each group provides slightly different specific recommendations (see Table 4), the main theme of these recommendations is unified and clear: Individuals who appear to be at greater risk of having underlying CAD should be considered for exercise testing before beginning a vigorous ($\geq 60\%$ $\dot{V}O_2$ reserve)

exercise training program (where $\dot{V}O_2$ reserve = percent intensity $\times [\dot{V}O_2$ peak - $\dot{V}O_2$ rest] + $\dot{V}O_2$ rest). This is particularly evident in that both groups recommend exercise testing before exercise training for patients with diabetes mellitus. In contrast, the US Preventive Services Task Force (USPSTF) states that insufficient evidence exists to determine the benefits and harm of exercise stress testing before exercise programs.⁵⁵

A major limitation of exercise testing is that "positive" exercise test results require the presence of a flow-limiting coronary lesion, whereas most acute cardiac events in previously asymptomatic subjects are due to vulnerable plaque disruption. Consequently, an exercise stress test with or without imaging can be normal despite the presence of coronary plaque that may rupture. This requires that health professionals evaluate the entire atherosclerotic risk profile in patients when advising on the feasibility of a vigorous exercise program.

Exclusion of High-Risk Subjects

Cardiovascular screening necessitates a strategy of excluding high-risk subjects from athletic and vigorous exercise participation. Both the ACC/AHA⁵³ and the ACSM⁵⁴ recommend exercise testing before vigorous exercise training in persons with known cardiovascular disease.

Guidelines for determining eligibility for competitive athletics among children and adults have been presented in the 36th Bethesda Conference on this topic.⁵⁶ These guidelines specifically address athletic competition but can be extrapolated to recommend or restrict vigorous exercise in patients with diagnosed cardiac conditions.

Reporting and Evaluating Possible Prodromal Symptoms

Several reports suggest that many individuals with exercise-related cardiovascular events had prodromal symptoms that were ignored by the victims or their physician. Of 134 young competitive athletes with SCD, 121 of whom (90%) died during or immediately after exertion, 24 (18%) experienced probable cardiac symptoms in the 36 months preceding death.⁹ Similarly, among adults, 50% of joggers,¹³ 75% of squash players,⁵⁷ and 81% of distance runners⁵⁸ who died during exercise had probable cardiac symptoms before death (Table 5). Most reported these symptoms only to relatives, and few sought medical attention. Consequently, it is prudent for exercising adults to know the nature of prodromal cardiac symptoms and the need for prompt medical attention. In addition, physicians should carefully evaluate possible cardiac symptoms in physically active individuals. Both patients and physicians may ignore or

TABLE 5. Prodromal Symptoms Reported by 45 Subjects Within 1 Week of Their SCD

| Symptom | Reports, n |
|---|------------|
| Chest pain/angina | 15 |
| Increasing fatigue | 12 |
| Indigestion/heartburn/gastrointestinal symptoms | 10 |
| Excessive breathlessness | 6 |
| Ear or neck pain | 5 |
| Vague malaise | 5 |
| Upper respiratory tract infection | 4 |
| Dizziness/palpitations | 3 |
| Severe headache | 2 |

Adapted from Northcote et al.⁵⁷

not adequately evaluate symptoms in highly active individuals in the mistaken belief that high levels of fitness protect against, rather than only reduce, the risk of cardiac disease.

Preparing Fitness Personnel and Exercise Facilities for Cardiovascular Emergencies

The death rate from exercise-related cardiovascular events might be reduced if personnel and facilities involved with exercise activities were prepared to handle cardiac emergencies. The AHA has recommended that coaches and trainers attending high school and college athletes be trained in cardiopulmonary resuscitation.⁴⁸ The AHA and ACSM recommend that participants in fitness facilities be screened for heart disease with a specially designed questionnaire⁵⁹ and that facility staff be trained in managing cardiovascular emergencies. These organizations also have strongly encouraged fitness facilities to have automatic external defibrillators available for cardiac emergencies.⁶⁰ The AHA and the ACSM have developed a preparticipation screening questionnaire for health-fitness facilities to identify individuals at risk from exercise.⁵⁹ Nevertheless, a survey of 65 health clubs in Ohio revealed that 28% of the clubs failed to use pre-entry cardiac screenings, most had no written emergency response plans, >90% failed to conduct emergency drills, and only 3% had an automatic external defibrillator.⁶¹ Although it is unclear whether these findings are typical of clubs nationwide, the results suggest that a significant gap exists between national recommendations and practices. At minimum, it would be prudent for health-fitness facilities to perform pre-entry screenings, to have written emergency policies, to conduct regular emergency drills and cardiopulmonary resuscitation practice, to have automatic external defibrillators available for immediate use by trained personnel,⁵⁹ and to establish a “hotline” to summon emergency medical services.

Recommending Prudent Exercise Programs

Ostensibly healthy adults without known cardiac disease should be encouraged to develop gradually progressive exercise regimens. Because the least fit individuals are at greatest risk for exercise-related events, gradually progressive programs should theoretically increase fitness and reduce acute CAD events without excessive risk. Patients with known cardiac disease also should be counseled to include at least 5

minutes each of warm-up and cool-down in their exercise training sessions to reduce the likelihood of inducing cardiac ischemia with sudden, intense physical effort^{62,63} and to avoid the decrease in central blood volume that can occur with the abrupt cessation of physical activity. Patients with cardiovascular disease who are interested in participating in competitive sports should be evaluated and advised in accordance with the 36th Bethesda Conference guidelines.⁵⁶ Physically inactive individuals and patients with known cardiovascular disease should avoid strenuous, unaccustomed exercise in both excessively cold and hot environmental conditions. Vigorous exercise in the cold such as snow shoveling has repeatedly been associated with acute cardiovascular events,^{44,45,64} and hot, humid environments require an increased heart rate response to handle the increased thermal load.⁶⁵ Increased altitude reduces oxygen availability and augments the cardiorespiratory and hemodynamic responses to a given submaximal work rate, thereby increasing cardiac demands. Individuals exercising at altitudes of >1500 m should limit the intensity of their exercise until acclimatized.^{54,66}

Summary

No sufficiently powered, randomized controlled studies have evaluated the contribution of exercise training to reducing CAD events. Nevertheless, a variety of epidemiological, basic scientific, and clinical evidence suggests that habitual physical activity decreases the risk of fatal and nonfatal CAD events and that the benefits of regular physical activity outweigh its risks. Consequently, physical activity should be encouraged for most individuals in accordance with the Centers for Disease Control and Prevention/ACSM recommendations for ≥ 30 minutes of moderate-intensity physical activity such as brisk walking on most, preferably all, days of the week.^{67,68} Vigorous exercise, however, transiently increases the risk of AMI and SCD, even in exercise-conditioned individuals, and several strategies are recommended to potentially reduce this risk:

- Healthcare professionals should know the pathological conditions associated with exercise-related events so that physically active children and adults can be appropriately evaluated.
- Active individuals should know the nature of cardiac prodromal symptoms and seek prompt medical care if such symptoms develop.
- High school and college athletes should undergo preparticipation screening by qualified professionals.^{49,69}
- Athletes with known cardiac conditions should be evaluated for competition according to published guidelines.⁵⁶
- Healthcare facilities should ensure that their staffs are trained in managing cardiac emergencies, have a specified plan, and have appropriate resuscitation equipment.
- Active individuals should modify their exercise programs in response to variations in their exercise capacity, their habitual activity level, and the environment.

Although these interventions have not been rigorously evaluated and documented to reduce exercise-related cardiovascular events, they appear prudent given our present understanding of the risks and benefits of exercise.

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*Modest.

†Significant.

‡Dr Costa was affiliated with the American Heart Association at the time this statement was written.

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