

Cardiovascular risks of physical activity in apparently healthy individuals

Risk evaluation for exercise clearance and prescription

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Exercise-induced cardiovascular (CV) events, particularly sudden cardiac death (SCD), attract considerable media attention in the context of the safety of exercise for the general population. As a result, concern about the safety of exercise participation is a common topic during routine office checkups and with the prescribed recommendation of increased physical activity (PA). In reality, it is estimated that only 4% to 17% of myocardial infarctions in men are linked to physical exertion, with much lower rates observed for women.^{1,2} Of these exercise-related events, it is also true that few occur in the absence of pre-existing cardiovascular disease (CVD), for which risk factors might (or might not) have already been evident.

This article provides an executive summary of findings from a systematic review of the risks of PA in apparently healthy individuals.³ It is one in a comprehensive series of reviews examining the risks of PA in healthy individuals and patients with various chronic diseases. The evidence thus obtained provides the foundation for new tools that will simplify the tasks of exercise clearance and prescription: the revised Physical Activity Readiness Questionnaire (PAR-Q+) and the electronic Physical Activity Readiness Medical Examination (ePARmed-X+) procedure.⁴ We present background evidence and mechanistic pathways regarding the risks of exercise in apparently healthy patients. The intention of this article is to facilitate the family physician's tasks of screening patients for PA participation and providing risk-appropriate PA prescriptions.

Growing evidence indicates that a range of PA confers some benefit in a dose-response pattern, demonstrating a continuum of increasing benefit and risk reduction as one progresses from low-intensity to more vigorous PA. In healthy individuals, low-intensity exercise performed regularly (3 to 5 times per week) can elicit substantial improvements in measures of quality of life, body composition, and CVD risk factors. More vigorous PA has been associated with pronounced reductions in risk and all-cause mortality rates in individuals with various chronic diseases. Energy expenditure through vigorous PA of at least

1000 kcal per week, but optimally closer to 2000 kcal per week, has yielded the greatest risk reductions for CVD.^{5,6}

Physical activity as a trigger of CV events

Despite the evidence supporting long-standing participation in vigorous PA as a means of reducing long-term morbidity and mortality, each individual exercise session acutely increases the risk of both nonfatal CV adverse events and SCD. This is the “risk paradox” of exercise—the long-term risk reductions obtained through vigorous PA are linked to acute, transient risk elevations. Numerous reports in the medical and lay literature describe adolescents and adults dying suddenly during or immediately after PA, regardless of their long-standing participation history. Given these concerns, a clear understanding of the risks of PA and exercise testing is warranted to inform and enhance screening procedures to reduce the likelihood of adverse events without unduly restricting individuals from the benefits PA can provide.

Risks of PA and triggering CV events

To date, most analyses of PA risk are retrospective studies obtained from recreational facilities, questionnaires, registries, or large-scale sporting events. A gradient of risk with increasing exercise intensity is consistently observed, with a relative risk of a fatal CV event increasing as much as 56 times (above that expected at rest),⁷ or as little as 2.1 times.⁸ Women appear to have a considerably lower incident rate of fatal CV events related to exercise than men do, likely owing to the delay seen in coronary artery disease development and lower participation rates in vigorous PA.⁹ Several reports describe the risks of individual endurance activities, specifically marathon running. This is of particular interest given the trend of increasing participation in marathons (rising more than 12-fold since 1976) and, more important, the shift in the age of participants: the fastest growing cohort in these events is those older than 40 years of age; 40% of current runners are older than 40 years of age, compared with 23% in 1980.¹⁰ This trend is expected to continue as the population ages and the “baby boom” generation continues to engage in this form of activity. Media reports of fatal cardiac events at various marathons in Canada and the United States have heightened the concern and have led to a number of retrospective analyses of risk. Recent data indicate that the risk of a fatal CV event during marathon



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running ranges between 1 per 80 000 participants¹¹ and 1 per 200 000 participants.¹²

The CV risks of resistance training appear to be reasonably low; however, existing data are from relatively small studies and are insufficient to provide accurate estimates of risk for the general population. The use of appropriate exercise technique, including avoiding holding the breath during the contraction phase of a lift (the Valsalva maneuver), has been shown to elicit blood pressure responses similar to aerobic exercise, providing the effort is within a range of 80% to 100% of the 1-repetition maximum, suggesting that at least some of the assumed risk can be controlled.¹³

The cause of adverse CV events occurring during or following exercise in young adults and adolescents has been well documented, but the incidence of events in this cohort is poorly described. In any case, it is generally accepted that the risks are well below those seen in adult populations. Screening young individuals before participation in sport, particularly screening involving electrocardiography, remains controversial. Such screening is mandatory in Italy, and despite strong support in some countries, it has not been widely accepted in North America. The correct identification of occult disease remains a primary challenge, as most SCD cases are associated with clinically silent conditions and are rarely associated with prodromal symptoms.

The presence of exercise-induced ventricular arrhythmias during exercise testing in athletes or the sedentary population has uncertain prognostic value but likely indicates elevated risk.^{14,15} Abnormal repolarization patterns are rare in athletes 18 to 35 years of age (1% to 4%). In older individuals, increasing frequency of ectopic beats is associated with poor clinical outcomes and increased risk of atherosclerosis.¹⁶ The increased presence of electrocardiogram abnormalities in young, trained athletes is more likely secondary to increased vagal tone and training-induced morphologic changes.¹⁷ While most anomalies of this type are a reflection of nonpathologic training adaptations and do not warrant follow-up, their presence poses additional challenges in ruling out an increased risk of CV events and potential pathology including hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy. The presence of any cardiac arrhythmia or symptoms, particularly syncope, might increase risk and should be investigated aggressively.

A key observation is that the increased relative risk of CV events during exercise is considerably lower if the individual regularly participates in routine exercise, particularly when it is frequent and vigorous in nature. This has been demonstrated in men,¹⁸⁻²⁰ women,²¹ and even “weekend warriors” who only exercise 1 to 2 times per week.²²

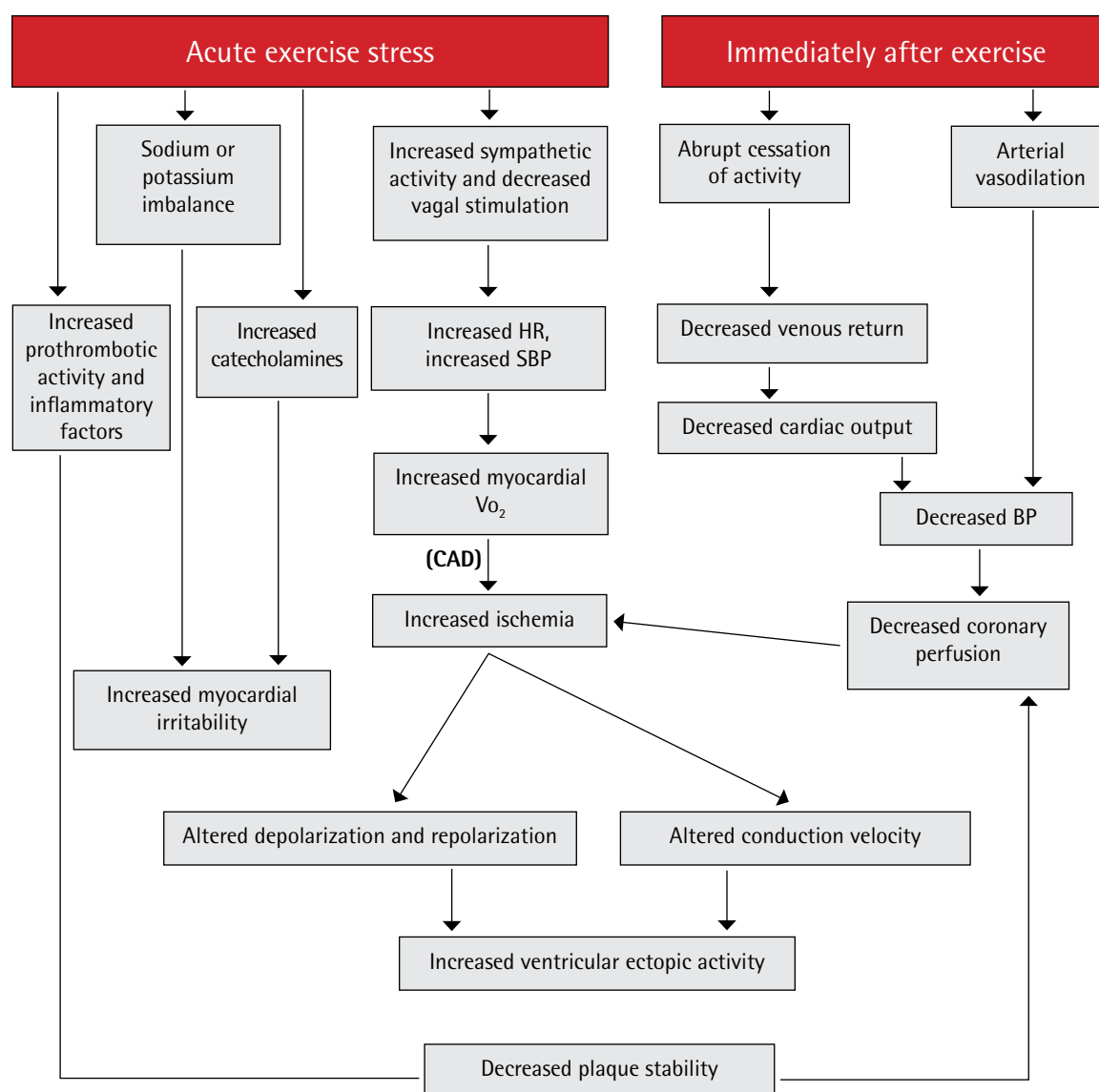
Underlying causes of adverse CV events triggered by PA

Numerous reports have described the pathophysiology contributing to exercise-induced SCD. The consensus is that by far most exercise-related SCD in those older than 30 to 35 years of age is secondary to acute complications of atherosclerosis, whereas SCD in those younger than 30 to 35 years of age is most often ascribed to disorders of myocardial structure or conduction. These include inherited genetic diseases that account for most pathologic findings in cases of SCD. Disturbances in electrical conduction might be a “concealed” cause of death in young athletes despite normal histology, because conduction systems are rarely examined thoroughly and rarely have gross abnormalities upon inspection at autopsy.

Atherosclerotic disease is associated with more than 80% of exercise-related SCD in those older than 35 years of age, and more than 95% of cases in those older than 40 years. Autopsy findings generally indicate previous or acute myocardial infarction, but evidence of coronary thrombosis is not always identified. The early identification of disease remains the limiting factor for prevention, given that in most cases of SCD no previous symptoms are reported and screening has not been performed before activity.²³ The occult nature of coronary disease remains a primary challenge of screening procedures. It is likely that SCD involves an acute and rapid progression in the disease state without warning in the moment immediately preceding death.⁹ Consequently, ascertaining the overall risk profile might help to minimize the risk of adverse events during vigorous exercise. A number of factors with suggested associations to exercise-induced CV risk during and following vigorous PA and deserving of consideration are included in **Figure 1**.²⁴ Some of these risk factors, such as poor perfusion and ischemia secondary to blood pooling after exercise, can be avoided by adoption of precautionary exercise practices. For example, blood pooling is decreased through avoidance of abrupt cessation of vigorous activity and adoption of slow walking or cycling during a “cool-down” phase (to facilitate venous return via the leg muscles) while cardiac output returns to resting levels.

Current guidelines from the American College of Sports Medicine²⁵ and the American Heart Association²⁶ call for pre-participation exercise testing in individuals considered to be at “moderate risk”²⁵; these guidelines are based largely on the knowledge of increasing CVD prevalence in the population. Specifically, exercise testing is not recommended for men and women younger than 45 and 55 years, respectively, if they do not have coronary risk factors.²⁶ However, testing should be considered for those over these age thresholds when 1 risk factor is present, and should be strongly considered when 2 or more risk factors have been identified.^{25,26} In

Figure 1. Factors contributing to exercise-induced cardiovascular risk during and following vigorous physical activity in those with occult cardiovascular disease



BP—blood pressure, CAD—coronary artery disease, HR—heart rate, SBP—systolic blood pressure, Vo_2 —oxygen consumption.
 Adapted from Franklin.²⁴

low-risk patients, a low likelihood of coronary artery disease and, in many cases, the inability of an individual to reach maximal effort during exercise testing, yields a lower sensitivity for true-positive findings. This limits the efficacy of stress testing in low-risk patients, particularly women.²⁶ Even when performed in conjunction with cardiac imaging modalities (perfusion scanning or stress echocardiography), a positive test result remains dependent on the presence of a well-established flow-mediated lesion or a spontaneous disruption in plaque that elicits ischemia⁹; as plaque fissuring and lethal

arrhythmia might not occur during stress testing, but rather during subsequent exercise, exercise testing alone might be insufficient for screening.

Conclusion

Based upon the available evidence, and a thorough review of documented incidence,³ we have arrived at a number of practical recommendations that can be useful in the primary care setting (Table 1). The risk of adverse CV responses during PA is extremely low for apparently healthy adults and adolescents and is outweighed by

Table 1. Evidence-based recommendations for risk of CV events during PA

RECOMMENDATION	LEVEL*
Exercise transiently increases the relative risk of CV events anywhere from 2- to 56-fold above what is expected at rest by chance alone	II or III
There is evidence for greater risk with PA in the following patients or circumstances: when performing increasingly vigorous intensity (≥ 6 METs); in men, especially with limited previous PA history; and in older individuals	II or III
Symptoms of dizziness or syncope, chest discomfort, and unexplained shortness of breath during or following PA are associated with nonfatal CV events or SCD and should be followed up. However, in most cases of SCD, death is the first clinical event, thus underlying pathology is not recognized. Despite the limitations of written or verbal screening alone (without ECG) for the detection of cardiac disease in apparently healthy individuals, efforts to identify those at higher risk using this approach are warranted; arguments in support of this method of screening are the low risk of adverse events in this population, the consequences of false-positive or false-negative results, and the costs of nonessential advanced screening technologies	III
Most events in individuals older than 35 to 40 y are secondary to coronary artery disease; by far most cases in those younger than 30 to 35 y are linked to undetected congenital or inherited heart conditions related to conduction or myocardial and vessel structure. In both cases, adverse events are likely triggered by various malignant substrates related to the physiologic stress of exercise in the presence of disease	III
The routine use of exercise testing in apparently healthy individuals is relatively safe and the risks of testing have been overstated by 20% to 50%, based on limited data from individuals with and without cardiac disease. The estimated risk of a fatal event during maximal exercise testing ranges from 0.3 to 0.8 per 10 000 tests (rather than 1 per 10 000 tests). Approximately 1.4 nonfatal events occur per 10 000 tests	III
The risk of an adverse CV response during PA is extremely low for apparently healthy adults and adolescents; the risk of participation is outweighed by substantial health benefits conferred by PA	II

CV—cardiovascular, ECG—electrocardiogram, METs—metabolic equivalent task unit, PA—physical activity, SCD—sudden cardiac death.

*Level I evidence includes randomized controlled trials; level II evidence includes randomized controlled trials with important limitations or observational trials with overwhelming evidence; level III evidence includes observational trials; and level IV evidence includes anecdotal evidence or expert opinion.

the considerable health benefits conferred by PA. We conclude that in the absence of overt signs and symptoms of disease (in which case, modified exercise should be prescribed), PA should be promoted.

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Competing interests

None declared

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