

[Primary Care]

Cardiac Risks Associated With Marathon Running

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Context: A recent cluster of sudden cardiac deaths in marathon runners has attracted considerable media attention and evoked concern over the safety of long-distance running and competition. This review discusses the acute and potential long-term risks associated with marathon running and puts these into perspective with the many health benefits afforded by habitual vigorous exercise.

Evidence Acquisition: Data sources included peer-reviewed publications from 1979 to January 2010 as identified via PubMed and popular media.

Results: Marathon running is associated with a transient and low risk of sudden cardiac death. This risk appears to be even lower in women and is independent of marathon experience or the presence of previously reported symptoms. Most deaths are due to underlying coronary artery disease. The value of preparticipation screening is limited by its insensitivity and impracticality of widespread implementation. Appropriate preparation and deployment of trained medical personnel and availability of automatic external defibrillators are expected to have a major impact on survival from cardiac arrests during marathons. Cardiac biochemical and functional abnormalities are commonly observed transiently following completion of a marathon, although their clinical significance is unknown.

Conclusions: Sudden cardiac deaths associated with marathon running are exceedingly rare events. Prevention should focus on recognition and investigation of prodromal symptoms, if present, and access to rapid defibrillation and trained medical personnel. The robust association of endurance running with improved quality of life and longevity underscores the importance of putting risks into perspective with other well-established health benefits of regular vigorous exercise.

Keywords: marathon; running; sudden cardiac death; cardiac arrest; preparticipation screening; exercise

Every year, more than 150 marathons are run in the United States, and more than 800 are run worldwide. Larger marathons have tens of thousands of participants. Generally, marathon runners represent some of the healthiest members of our society; therefore, a sudden death in the midst of competition attracts a great deal of media attention. A cluster of sudden deaths—such as those that occurred in the Detroit Marathon and Half Marathon in 2009 (3 men: ages 26, 36, and 65 years)—generates public concern over the risks of vigorous exercise and competition, and it may discourage individuals from even modest physical activity. This report reviews the risks associated with vigorous exertion, with a focus on marathon running, and puts them into perspective with the many well-established health benefits that regular exercise affords. Also presented are issues related to preparticipation screening and

marathon race medical preparation, with advanced life support and access to rapid defibrillation.

INCIDENCE AND CAUSES OF EXERCISE-RELATED SUDDEN CARDIAC DEATH

Vigorous exercise is associated with a transient increase in risk of sudden cardiac death (SCD). For young athletes (12 to 35 years) participating in competitive sports, the total relative risk of SCD is approximately 2.5 times higher than in nonathletes.⁷ The increased risk in this study was not limited to the risk during exercise. However, absolute event rates are low, about 1 in 50 000 to 200 000 annually.^{23,43} SCD in athletes occurs most commonly during or shortly after intense training or competition.^{23,26} For young athletes participating in

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organized individual or team sports, the most common cause of SCD in the United States is hypertrophic cardiomyopathy (36%), followed by coronary artery anomalies (17%).^{24,26} Myocarditis, premature coronary artery disease, other inherited cardiomyopathies, and ion channelopathies make up most of the remainder. The majority of athletes who suffer SCD are men (approximately 90%), and a disproportionate number are nonwhite (ie, 64% [nonwhite] versus 51% [white] of deaths due to cardiovascular disease, $P < .001$).²⁴ Certain sports appear to pose a higher risk than others—including basketball, football, soccer, track and field, and baseball—although it is difficult to reconcile whether the higher absolute number of SCDs in these sports is a reflection of their popularity in the United States or an inherently higher risk of SCD because of the intensity required for training and competition.

The incidence of SCD in older athletes (> 35 years old) is reportedly more frequent than in the young, with an estimated annual incidence of approximately 1:11 000 to 1:80 000 in men.^{1,36,39,40} Like SCD in young athletes, the incidence is strikingly lower in women. The annual incidence of exercise-triggered SCD in the Nurses' Health Study cohort was approximately 1:185 000, with an absolute risk of 1 per 36.5 million hours of exertion.⁴⁶ In comparison, in the Physicians' Health Study¹ the relative risk during an episode of vigorous exercise was approximately 19-fold higher among men than among women. The reasons for this sex discrepancy are unknown, but they may be related to differences in prevalence or susceptibility to the pathologic substrate for SCD. The predominant pathological finding in older athletes is coronary artery disease,⁴⁴ accounting for 73% of SCDs in joggers and marathon runners.⁴⁵ This is consistent with observations that vigorous exercise can trigger acute myocardial infarction, with annual incidence rates at about 1:600 to 1:4000 of apparently healthy individuals.^{28,47} The lower incidence of SCD in women could therefore be explained by delayed onset of coronary heart disease, decreased susceptibility to exercise-provoked plaque disruption or platelet activation, or resistance to ventricular fibrillation. Lower rates of participation in vigorous sports among older women could also account in part for differences in event rates.³⁹

THE PARADOX OF EXERCISE: BALANCING THE RISKS AND BENEFITS

Ironically, although physical exertion can trigger SCD or MI, habitual exercise imparts many well-established long-term health benefits. Large prospective epidemiologic studies consistently document reduced rates of coronary heart disease and its associated risk factors with regular exercise.^{9,38} Physical inactivity universally emerges as a strong predictor of mortality, with risk being directly proportional to exercise capacity.^{5,13,21,30,37} Habitual exercise also substantially decreases the overall risk of SCD and the risk of cardiac arrest associated with vigorous exertion in both men and women.^{1,46} For example, in a case series of 133 men with primary cardiac

arrest, the relative risk of SCD during vigorous exercise versus rest was 56 for those with low levels of habitual exercise, compared with a relative risk of 5 for those at the highest level of habitual exercise.³⁶ Regular exercise also lowers the probability of an exertion-triggered myocardial infarction, with a relative risk of 1.3 versus 6.9 for men who exercised 4 or more times versus less than 4 times per week, respectively.⁴⁷ With these compelling data in mind and given the low overall incidence of exercise-induced SCD, the risk:benefit ratio is generally in favor of routine vigorous exercise, particularly in older individuals, for whom coronary heart disease is the most common cause of cardiovascular morbidity and mortality.

RISK OF SCD IN MARATHON RUNNERS

SCDs during marathons have been reported throughout the world. Several publications have catalogued these deaths in a subset of marathons over many years (Table 1).^{25,33,34,42} The overall incidence of SCD is low, ranging from 1:50 000 to 1:220 000. Cumulatively, there were 39 reported sudden deaths among more than 4 million runners, for a total incidence of 1:114 000. If nonfatal cardiac arrests are included, the incidence is higher: 1:31 000 to 1:55 000. Observations made in the same marathons (Twin Cities and Marine Corps) over time suggest that the SCD rate may be declining.³⁴ Given that the combined incidence of nonfatal arrests and SCDs has remained relatively steady over the reported years, the decrease in mortality from these events may be due to expanded access to external defibrillators, leading to improved survival in cardiac arrest victims.

Like other data on risk of SCD with vigorous exercise, the incidence of SCD in women is lower than it is in men. Only 15% of reported SCDs occurred in women across all marathon studies. However, the participation rate for women is also lower, so the absolute incidence may not be significantly different.

The major causes of nonfatal and fatal cardiac arrests are related to coronary artery disease. In the Twin Cities and Marine Corps marathons,²⁵ a 19-year-old female had a high-risk left main coronary artery anomaly. Seven of the 8 men had significant coronary atherosclerotic disease, and 1 also had marked left ventricular (LV) hypertrophy and a family history of sudden death. In the London Marathon,⁴² 11 of 14 cardiac arrests resulted from coronary artery disease; the other 3 were from unexplained LV hypertrophy or hypertrophic cardiomyopathy. Finally, of the 26 sudden deaths reported in a series of 26 US marathons, 21 were attributable to coronary artery disease. Other contributing factors included coronary artery anomalies ($n = 2$), electrolyte abnormalities ($n = 4$), and heat stroke ($n = 1$).

More than half the victims had completed at least 1 previous marathon, indicating that events occur in experienced runners. Few had reported symptoms before the race, and in at least one instance, stress testing 2 months before competition revealed negative results.³³ Cardiac arrests appear to cluster in the latter stages of the race, with the highest numbers in the final mile or at the finish line (Figure 1), a finding that

Table 1. Reported incidence of fatal and nonfatal cardiac arrests in marathons.^a

Events	Years	Cumulative Finishers, n (Female, %)	Nonfatal Cardiac Arrests, n (Female, n)	SCDs, n (Female, n)	Incidence	
					SCD	SCD + Nonfatal Arrests
Marine Corps and Twin Cities marathons ²⁵	1976-1994	221 318 (18)	1 (0)	4 (1)	1:50 000	1:44 000
Marine Corps and Twin Cities marathons ³⁴	1995-2004	220 606 (37)	3 (0)	1 (0)	1:220 000	1:55 000
London Marathon ⁴²	1981-2006	650 000 (17)	6 (0)	8 (0)	1:81 000	1:46 000
26 US marathons ³³	1975-2004	3 292 368 (—)	—	26 (5)	1:127 000	—
36-km beach cycling and half marathon (Netherlands) ⁴	2002-2006	62 862 (24)	2 (0)	0	0	1:31 000
Total	1976-2006	4 447 154	12	39 (6)	1:114 000	1:46 000

^aSCD, sudden cardiac death. Dash (—) indicates *not reported*.

has important implications for the deployment of medical personnel and external defibrillators.

RISK OF SCD DURING MARATHONS IN PERSPECTIVE

The reality is that cardiac arrests associated with marathon running are rare events. Compared with the risk of running 1 marathon, the annual risk of premature death is estimated to be 120 times higher during general living.²⁵ Running the London Marathon in 4 hours is estimated to have an equivalent risk to riding a motorcycle for 2 hours, cycling for 10 hours, or being in a car or flight for 28 hours.⁴¹ Another study calculated the relative risk reduction for motor vehicle accidents to be 35% because of road closures for the marathons,³³ which amounted to a net reduction of 1.8 crash deaths for each case of sudden death during a marathon. So, from a societal perspective, sudden deaths during marathons are less of a public health threat than that perceived by the media. This does not mitigate the tragedy of each marathon death and the need to pursue strategies to prevent future events.

IS PREMARATHON PARTICIPATION SCREENING PRACTICAL OR WORTHWHILE?

This journal recently reviewed cardiovascular screening for young individuals participating in competitive sanctioned sports.¹⁴ Because the predominant cause of death among

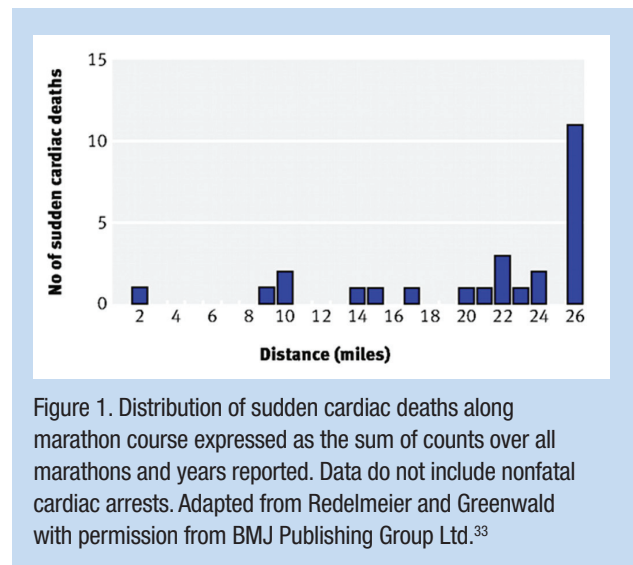


Figure 1. Distribution of sudden cardiac deaths along marathon course expressed as the sum of counts over all marathons and years reported. Data do not include nonfatal cardiac arrests. Adapted from Redelmeier and Greenwald with permission from BMJ Publishing Group Ltd.³³

marathon runners is coronary artery disease (even in younger participants), the screening tool of the highest potential utility is an exercise stress test. No randomized controlled trials have addressed the utility of exercise testing in asymptomatic individuals, even those pursuing a vigorous exercise program or competition. As such, published guidelines are based on expert consensus and thus differ among writing groups.³⁹ The American College of Cardiology and American Heart Association task force considered exercise testing a class

Ila indication (ie, weight of evidence/opinion in favor of usefulness/efficacy) for asymptomatic persons with diabetes mellitus who are planning to start vigorous exercise.¹² The group indicated that the usefulness/efficacy of exercise testing is less well established for asymptomatic men older than 45 years and women older than 55 years who are planning to initiate a vigorous exercise program (class IIB). The American College of Sports Medicine provided recommendations similar to those of the task force,¹⁹ whereas the US Preventive Services Task Force found insufficient evidence for routine stress testing before exercise training and did not endorse it.¹¹ A significant shortcoming of exercise testing is insensitivity for predicting acute coronary events, most of which result from plaque rupture of non-flow-limiting epicardial coronary lesions. There are also the more practical issues of resource utilization and cost-effectiveness of performing exercise tests on millions of marathon participants worldwide, not to mention the unnecessary secondary (and often invasive) testing that would be needed to discriminate true- from false-positive stress test results in a low-risk population. Overall, a more prudent strategy seems to be one of prevention and attention to prodromal symptoms, which both the patient and the physician tend to ignore when they occur in highly fit individuals.³⁹

PREPARATION OF MARATHON MEDICAL PERSONNEL AND AVAILABILITY OF RAPID EXTERNAL DEFIBRILLATION

Survival from cardiac arrest is highly reliant on the time interval from the onset of arrest to first defibrillation. Rapid defibrillation is easier to guarantee for sporting events held in an enclosed space but much more difficult to accomplish over a 26-mile point-to-point race course. In the Twin Cities and Marine Corps marathons, successful defibrillations were achieved within 5 minutes of collapse among 4 runners, with manually operated defibrillators and rapid response teams that included physicians, paramedics, and emergency medical technicians.³⁴ Defibrillators were located at medical aid stations at 2- to 3-mile intervals, at the finish line, and in mobile ambulances. Mobile first-response teams on bicycles and golf carts were also deployed with automatic external defibrillators. To achieve defibrillation in 1 to 2 minutes from time of arrest, one of the following is required: advanced life support personnel with automatic external defibrillators every 200 to 300 m of the course or a large number of mobile rapid-response patrols with access to the whole course.⁴¹ The logistics and expense of that strategy are great and not likely feasible. A more realistic goal of defibrillation, within 3 to 5 minutes of arrest, seems reasonable on the basis of recent studies of public access defibrillation, showing marked improvements in survival to hospital discharge with immediate bystander cardiopulmonary resuscitation accompanied by defibrillation within this time frame.^{3,15} Because cardiac arrests occur most commonly in the latter stages of the race, a reasonable approach is to increase the density of automatic

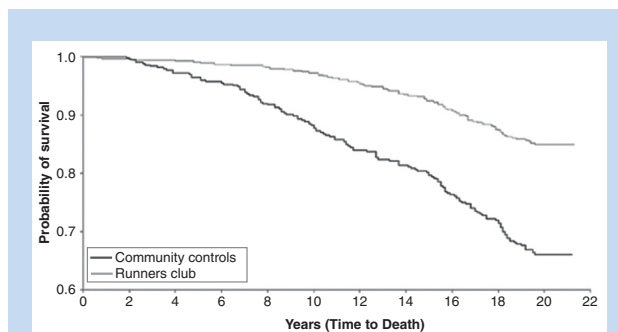


Figure 2. Kaplan-Meier unadjusted survival curves for all-cause mortality in 941 runners club members and community controls through 21 years of follow-up. There was a significant difference in survival between the groups ($P < .001$). Adapted from Chakravarty et al with permission from the American Medical Association.⁶

external defibrillators and medical response teams in the last 5 to 6 miles of the marathon and at the finish line.

ARE THERE OTHER CARDIAC HAZARDS TO MARATHON RUNNING?

In addition to the transient risk of an acute event, concerns have been raised about the potentially damaging effects of marathon running on the heart. Over the past several years, multiple studies have documented an increase in cardiac biomarkers following a marathon. By conventional assays, circulating cardiac troponin T or I is elevated beyond the assay detection limit in approximately 30% to 68% of nonelite marathon participants immediately following the race.^{10,17,18,31} This number is higher still (86% of participants) when newer-generation, more highly sensitive troponin assays are used.²⁷ A rapid decline within 24 hours,^{2,16,27} along with the absence of delayed enhancement on cardiac magnetic resonance imaging,²⁹ supports the theory that an increase in circulating troponins is due to cytosolic release (perhaps because of increased membrane permeability) as opposed to permanent myocyte damage. Some studies have shown a correlation of troponin elevation with less training mileage,³¹ less marathon experience,^{10,27} slower finishing times,¹⁸ or weight loss and increased creatinine,^{17,18} but results are not consistent. Similarly, some studies have shown correlations of troponin elevation with noninvasive measures such as pulmonary artery pressure,³¹ right ventricular (RV) systolic dysfunction,³¹ and decreased LV systolic strain,²² whereas others have not.²⁰

Many studies have documented increases in serum N-terminal pro-brain natriuretic peptide in runners immediately following a marathon or ironman triathlon.^{20,22,31} Inverse correlations have been demonstrated with training experience and LV diastolic function³¹ but not consistently,²⁰ although a baseline increase in the peptide in older runners may herald occult cardiac disease.³⁵



Clinical Recommendations

SORT: Strength of Recommendation Taxonomy

A: consistent, good-quality patient-oriented evidence

B: inconsistent or limited-quality patient-oriented evidence

C: consensus, disease-oriented evidence, usual practice, expert opinion, or case series

Clinical Recommendation	SORT Evidence Rating
Consider exercise testing for asymptomatic persons with diabetes mellitus who plan to start a vigorous exercise program. ^{11,17}	C
Exercise testing is not likely to be beneficial for asymptomatic men older than 45 years and women older than 55 years without known cardiac disease who plan to start a vigorous exercise program. ^{10,11,17}	B
Long-term health benefits of marathon running and training likely outweigh the risks. ^{5,37}	B

For more information about the SORT evidence rating system, see www.aafp.org/afpsort.xml and Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician*. 2004;69:549-557.

Acute changes in LV and RV function associated with running a marathon have been documented, albeit to varying extents. Changes in RV morphology and function are the predominant observations, with RV dilation and decreased RV systolic and diastolic function.^{20,22,29,31} LV diastolic dysfunction has been described^{8,29,31} but not universally.²⁰ In most patients, LV and RV function returned to normal within a week following the race.

Collectively, the clinical relevance of these findings is debatable, and long-term follow-up data are not available. However, it is difficult to fathom how transient biochemical and functional abnormalities so pervasive among marathon runners would be compatible with marathon running of 25 years' duration and with completion of a mean of 38 marathons.²⁰ A recent report of reduced long-term disability and marked survival advantage of older runners compared with a control group in a large study with a 21-year follow-up period⁶ (Figure 2) argued strongly that long-term benefits of vigorous exercise must far outweigh any real or theoretical risks of a vital long-distance running career.

CONCLUSIONS

As with other forms of vigorous exercise, marathon running is associated with a transient increase in, but exceedingly low risk of, SCD. Although acute coronary events are the primary cause, widespread screening of runners with cardiac stress testing is unlikely to be useful or cost-effective. Deployment of rapid medical response teams and automatic defibrillators is expected to have a significant impact on survival following cardiac arrest during a marathon. It is yet to be determined what impact, if any, increases in the number and age of marathon participants with slower average finishing times³² will have on SCD prevalence. Although more data are needed to determine the prognostic importance of acute cardiac biochemical and functional changes elicited by marathon participation, a robust association of long-distance running with improved quality of life and longevity is certainly encouraging news for the running community.

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