ORIGINAL ARTICLE

# Cardiac Arrest during Long-Distance Running Races

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## ABSTRACT

### BACKGROUND

Approximately 2 million people participate in long-distance running races in the United States annually. Reports of race-related cardiac arrests have generated concern about the safety of this activity.

### METHODS

We assessed the incidence and outcomes of cardiac arrest associated with marathon and half-marathon races in the United States from January 1, 2000, to May 31, 2010. We determined the clinical characteristics of the arrests by interviewing survivors and the next of kin of nonsurvivors, reviewing medical records, and analyzing postmortem data.

### RESULTS

Of 10.9 million runners, 59 (mean [±SD] age, 42±13 years; 51 men) had cardiac arrest (incidence rate, 0.54 per 100,000 participants; 95% confidence interval [CI], 0.41 to 0.70). Cardiovascular disease accounted for the majority of cardiac arrests. The incidence rate was significantly higher during marathons (1.01 per 100,000; 95% CI, 0.72 to 1.38) than during half-marathons (0.27; 95% CI, 0.17 to 0.43) and among men (0.90 per 100,000; 95% CI, 0.67 to 1.18) than among women (0.16; 95% CI, 0.07 to 0.31). Male marathon runners, the highest-risk group, had an increased incidence of cardiac arrest during the latter half of the study decade (2000–2004, 0.71 per 100,000 [95% CI, 0.31 to 1.40]; 2005–2010, 2.03 per 100,000 [95% CI, 1.33 to 2.98]; P=0.01). Of the 59 cases of cardiac arrest, 42 (71%) were fatal (incidence, 0.39 per 100,000; 95% CI, 0.28 to 0.52). Among the 31 cases with complete clinical data, initiation of bystander-administered cardiopulmonary resuscitation and an underlying diagnosis other than hypertrophic cardiomyopathy were the strongest predictors of survival.

### CONCLUSIONS

Marathons and half-marathons are associated with a low overall risk of cardiac arrest and sudden death. Cardiac arrest, most commonly attributable to hypertrophic cardiomyopathy or atherosclerotic coronary disease, occurs primarily among male marathon participants; the incidence rate in this group increased during the past decade.

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Participation in long-distance running races has increased annually in the United States. In 2010, there were approximately 2 million participants in marathon and half-marathon races, as compared with fewer than 1 million participants in 2000.[1] This increase has been driven in part by heightened public awareness of the health benefits of regular physical exercise. However, the growth of long-distance running has been accompanied by studies documenting post-race cardiac dysfunction[2,3] and numerous reports of race-related cardiac arrest.[4-7] These unexpected tragedies attract considerable media attention and have led to concerns regarding the health risks of this activity.[8-11]

Sudden death in young, competitive athletes has been well characterized.[12,13] However, these data may not apply to participants in long-distance running races, who are an older population with different cardiovascular risk factors and underlying medical conditions. Prior studies have examined cases of cardiac arrest from only one or two events[14,15] or have lacked detailed clinical information.[16] The incidence, clinical profiles, and outcomes of cardiac arrests that occur during long-distance running races therefore remain uncertain.

The Race Associated Cardiac Arrest Event Registry (RACER) was designed to address these issues. The registry collected data from the most recent decade of long-distance running races to determine the incidence, clinical profile, and outcomes of cardiac arrest in these events.

## Methods

### Study Design

We studied cases of cardiac arrest that occurred during the running or at the finish-line recovery area within 1 hour after the completion of a marathon (26.2 mi) or half-marathon (13.1 mi) that took place in the United States. A database of cardiac arrests occurring during the period January 1, 2000, through May 31, 2010, was compiled prospectively. All cases were verified retrospectively at the conclusion of the study period. Detailed analyses were conducted for the subset of cases with comprehensive clinical information.

The Partners Human Research Committee approved all aspects of the study before initiation. The details of how informed consent was obtained are outlined below.

### Data Collection

#### *Race-Participation Data*

Running USA, a nonprofit running trade organization, provided participation statistics for each year of the study period. This group uses a comprehensive, computerized cataloguing system to compile accurate statistics for participation rates in marathon and half-marathon races in the United States. These data, including registered-participant numbers categorized by sex and race distance, are publicly available online and were confirmed by direct contact with the publishing organization.

#### *Cases of Cardiac Arrest*

Cases of cardiac arrest were defined by an unconscious state and an absence of spontaneous respirations and pulse, as documented by a medical professional. Nonsurvivors of cardiac arrest were defined as persons who were not successfully resuscitated in the field or who died before hospital discharge. Survivors of cardiac arrest were defined as persons who were successfully resuscitated and subsequently discharged from the hospital.

The cases of cardiac arrest and basic event information (age, sex, location of arrest, publicly released cause of arrest, and outcome) were identified and cross-referenced by means of a targeted multistep algorithm through two independent public search engines (LexisNexis and Google). First, specific keywords and phrases, including "marathon death," "marathon fatality," "sudden cardiac death, marathon," and "cardiac arrest, marathon," were entered into each search engine. Second, a list of all long-distance races in the United States was compiled from relevant websites (e.g., coolrunning.com, runnersworld.com, and marathonguide.com). We then performed additional, targeted searches, using all identified race names, the years 2000 through 2010, and all previously mentioned keywords and phrases. Finally, online databases for the local newspapers for all towns and cities with an identified marathon or half-marathon were searched in a similar fashion. Cases of cardiac arrest were retained for final analysis if they were independently identified in three separate data sources or confirmed with official race medical staff.

Letters describing the study were mailed to the survivors of cardiac arrest and to the next of kin of nonsurvivors. These mailings included formal consent forms and opt-out forms. If no response was obtained after 4 weeks, follow-up letters were

sent, along with copies of the consent forms and opt-out forms. A publicly available e-mail address was used for a third attempt at contact if no response was obtained after two mailings. Case identification and enrollment are summarized in Figure 1 in the Supplementary Appendix, available with the full text of this article at NEJM.org.

The consenting survivors and next of kin of nonsurvivors completed a questionnaire addressing demographic characteristics, history of running and other exercise, personal and family medical history, and information about the cardiac arrest. Permission was obtained to access pertinent medical records, including information regarding visits to primary care and specialist offices and testing that took place before the cardiac arrest, emergency-medical-service documentation of care at the time of the cardiac arrest, and hospital, autopsy, and outpatient records after the cardiac arrest.

*Causes of Cardiac Arrest and Death*

Cause of death was determined from cardiac-arrest clinical care documentation and autopsy data. Hypertrophic cardiomyopathy (left ventricular mass >500 g) and possible hypertrophic cardiomyopathy (left ventricular mass between 400 and 499 g for men and between 350 and 499 g for women) were diagnosed with the use of autopsy criteria that integrate cardiac mass with findings that supported the diagnosis, including family history of hypertrophic cardiomyopathy; characteristic features of the gross anatomical cardiac architecture, including marked asymmetry and mitral-valve elongation; markedly increased left ventricular wall thickness; and disease-specific histologic findings.[13] Arrhythmogenic right ventricular cardiomyopathy was defined by the presence of a lipomatous transformation or a fibrolipomatous transformation of the right ventricular free wall.[17] Diagnostic criteria for alternative causes of death were adopted from clinical guidelines.[18-20] For survivors, we used the diagnostic data documented after the cardiac arrest to determine the cause of the arrest.

### STATISTICAL ANALYSIS

Continuous variables are presented as means (±SD), and categorical variables as proportions. Comparisons between categorical and continuous variables were evaluated with Fisher's exact test and Student's t-test. Incidence rates for the total number of cases and the fatal cases of cardiac arrest were calculated as the simple proportion of events divided by the number of participants for stated time intervals. Ninety-five percent confidence intervals for event rates were computed with the use of a Poisson distribution. Cumulative incidence rates from the initial 5 years of the study period were compared with those from the final 5 years to assess temporal stability with the use of a conservative approach involving chi-square analysis to compare Poisson distributions of log-transformed event rates.[21,22] Univariate and multivariate logistic-regression analyses were performed to identify factors associated with the outcome of cardiac arrest. Perfect predictors of the outcome, with either survival or death perfectly stratified by the variable of interest, could not be analyzed with logistic regression, and their association with the cardiac-arrest outcome was therefore assessed with Fisher's exact test. Factors associated with the cardiac-arrest outcome at a P value of less than 0.10 were tested in the multivariate model by means of a backward stepwise approach. Analyses were performed with the use of Stata software, version 8.0 (StataCorp). A P value of less than 0.05 was considered to indicate statistical significance.

## RESULTS

### CHARACTERISTICS AND INCIDENCE OF CARDIAC ARREST

We identified 59 cardiac arrests, 40 in marathons and 19 in half-marathons, among 10.9 million registered race participants. The mean age of runners with cardiac arrest was 42±13 years, and 51 of the 59 runners (86%) were men. Data regarding the point in the race course where the cardiac arrest occurred are shown in Figure 1, and race-participation numbers, absolute numbers of cardiac arrests, and incidences of cardiac arrest as a function of sex and race distance are summarized in Table 1. The overall incidence of cardiac arrest was 1 per 184,000 participants (0.54 per 100,000; 95% confidence interval [CI], 0.41 to 0.70). The incidence was significantly higher during marathons (1.01 per 100,000; 95% CI, 0.72 to 1.38) than during half-marathons (0.27; 95% CI, 0.17 to 0.43; P<0.001) and among men (0.90 per 100,000; 95% CI, 0.67 to 1.18) than among women (0.16; 95% CI, 0.07 to 0.31; P<0.001). The overall incidence of cardiac arrest and the incidence as a func-

tion of race distance were similar during the initial 5 years of the study period and the final 5 years. In contrast, the incidence of cardiac arrest among men increased during the study period. Male marathon participants, the highest-risk group (overall incidence of cardiac arrest, 1.41 per 100,000; 95% CI, 0.98 to 1.98), had a higher incidence during the final 5 years of the study period than during the initial 5 years (2.03 per 100,000 [95% CI, 1.33 to 2.98] from 2005 through 2010 vs. 0.71 per 100,000 [95% CI, 0.31 to 1.40] from 2000 through 2004, P=0.01).

### OUTCOMES OF CARDIAC ARREST

Of the 59 runners with cardiac arrest, 42 (71%) died; the incidence of sudden death was 1.00 per 259,000 participants (0.39 per 100,000; 95% CI, 0.28 to 0.52). The mean age of the nonsurvivors was 39±9 years, and the mean age of the survivors was 49±10 years (P=0.002). The incidence of cardiac arrest resulting in death was significantly higher during marathons (0.63 per 100,000; 95% CI, 0.41 to 0.93) than during half-marathons (0.25 per 100,000; 95% CI, 0.14 to 0.39; P=0.003) and among men (0.62 per 100,000; 95% CI, 0.43 to 0.86) than among women (0.14 per 100,000; 95% CI, 0.06 to 0.29; P<0.001).

### CAUSES OF CARDIAC ARREST AND DEATH

The medical information necessary to determine the cause of cardiac arrest was available for 31 of the 59 runners with cardiac arrest. These 31 runners did not differ significantly with respect to age (mean, 39±12 years; range, 22 to 65) or sex (26 [84%] were men) from the entire group of 59 runners described above or from the 28 for whom consent or full medical records could not be obtained. Of the 31 runners for whom complete clinical data were obtained, 23 had died. Hypertrophic cardiomyopathy (in 8 of 23) and possible hypertrophic cardiomyopathy (in 7 of 23) were the most common causes of death (Fig. 2 and Table 2). Notably, 9 of the 15 nonsurvivors who had cardiac hypertrophy had an additional clinical factor or postmortem finding: obstructive coronary artery disease (in 3), myocarditis (in 2), bicuspid aortic valve or coronary anomaly (in 2), accessory atrioventricular nodal bypass tract (in 1), or hyperthermia (in 1). Causes of death in the absence of left ventricular hypertrophy included hyponatremia (in 1 person), hyperthermia (in 1), arrhythmogenic right ventricular cardiomyopathy (in 1), and no evident abnormality on autopsy or presumed primary arrhythmia (in 2). Data from the medical evaluation of survivors after cardiac arrest are shown in Table 2. Ischemic heart disease (in 5 of 8 runners) was the predominant cause of cardiac arrest among survivors. None of the runners with serious coronary atherosclerosis had angiographic evidence of acute plaque rupture or thrombus.

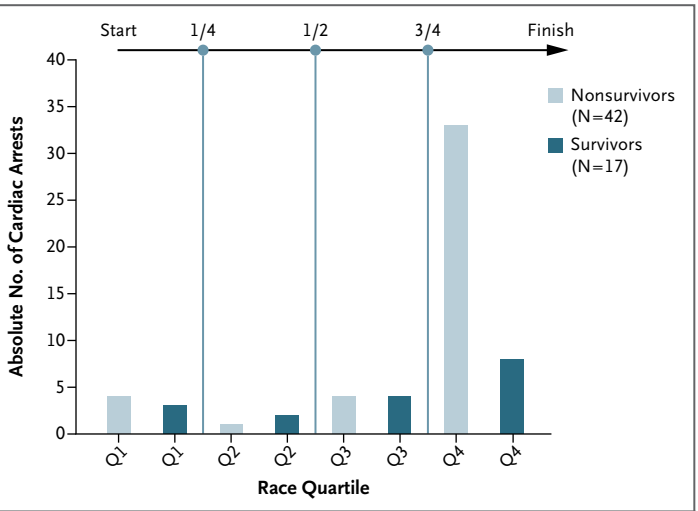


**Figure 1. Location of Cardiac Arrest According to Race Quartile.**

To account for differences in race distance between the marathon (26.2 mi) and half-marathon (13.1 mi), the point in the race course where the cardiac arrest occurred was examined as a function of the total race-distance quartile. Q1 denotes 0 to 6.5 mi (marathon) and 0 to 3.3 mi (half-marathon), Q2 6.5 to 13.1 mi (marathon) and 3.3 to 6.5 mi (half-marathon), Q3 13.1 to 20 mi (marathon) and 6.5 to 10 mi (half-marathon), and Q4 20 mi to finish (marathon) and 10 mi to finish (half-marathon).

### FACTORS ASSOCIATED WITH CARDIAC-ARREST OUTCOME

The 23 nonsurvivors and 8 survivors for whom complete clinical information was obtained are compared in Table 3. Survivors were older than nonsurvivors (53.1±6.5 vs. 33.9±9.5 years, P<0.001) and had completed more long-distance running races. Survivors were also more likely to have had a primary care physician and established atherosclerotic cardiac risk factors before the cardiac arrest. The strongest predictors of survival of cardiac arrest were initiation of bystander-administered cardiopulmonary resuscitation (CPR) (P=0.01 by Fisher's exact test) and an underlying diagnosis other than hypertrophic cardiomyopathy (P=0.01 by Fisher's exact test). In a multivariate logistic-regression model in which these two factors had

**Table 1. Participant Numbers, Absolute Number of Cardiac Arrests, and Incidence of Cardiac Arrest during Long-Distance Running Races in the United States, 2000–2010.**

| Variable | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009–2010* | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| All participants (in thousands) | | | | | | | | | | | |
| Marathon — total no. (% men) | 353 (65) | 334 (64) | 354 (64) | 365 (62) | 386 (59) | 395 (60) | 410 (60) | 412 (59) | 425 (59) | 515 (59) | 3949 (61) |
| Half-marathon — total no. (% men) | 482 (53) | 515 (52) | 550 (51) | 572 (52) | 612 (51) | 658 (47) | 724 (47) | 796 (45) | 900 (44) | 1113 (42) | 6922 (48) |
| Total — no. | 835 | 849 | 904 | 937 | 998 | 1053 | 1134 | 1208 | 1325 | 1628 | 10,871 |
| Cardiac arrests | | | | | | | | | | | |
| Marathon — total no. (no. of men) | 3 (3) | 3 (1) | 3 (1) | 3 (2) | 1 (1) | 2 (2) | 9 (9) | 5 (5) | 6 (5) | 5 (5) | 40 (34) |
| Half-marathon — total no. (no. of men) | 0 | 0 | 1 (1) | 4 (4) | 1 (1) | 0 | 1 (1) | 2 (2) | 0 | 10 (8) | 19 (17) |
| Total — no. (no. of men) | 3 (3) | 3 (1) | 4 (2) | 7 (6) | 2 (2) | 2 (2) | 10 (10) | 7 (7) | 6 (5) | 15 (13) | 59 (51) |
| | | 2000–2004 | | | 2005–2010* | | | P Value | | 2000–2010* | |
| Incidence of cardiac arrest — no./100,000 (95% CI)† | | | | | | | | | | | |
| Marathon‡ | | 0.73 (0.39–1.24) | | | 1.25 (0.83–1.82) | | | 0.11 | | 1.01 (0.72–1.38) | |
| Half-marathon‡ | | 0.22 (0.08–0.48) | | | 0.31 (0.17–0.53) | | | 0.48 | | 0.27 (0.17–0.43) | |
| Male sex§ | | 0.55 (0.30–0.93) | | | 1.17 (0.83–1.62) | | | 0.02 | | 0.90 (0.67–1.18) | |
| Female sex§ | | 0.27 (0.09–0.63) | | | 0.09 (0.02–0.27) | | | 0.15 | | 0.16 (0.07–0.31) | |
| Total | | 0.42 (0.25–0.66) | | | 0.63 (0.45–0.86) | | | 0.15 | | 0.54 (0.41–0.70) | |

* Data for 2010 include only the first 5 months (January 1 through May 31, 2010).
† Incidence rates were calculated as the simple proportion of events divided by the number of participants for stated time intervals. The 95% confidence intervals for event rates were computed with the use of a Poisson distribution. P values are for the incidence rates for 2000–2004 as compared with those for 2005–2010 and were computed with the use of a chi-square analysis of log-transformed Poisson event rates.
‡ Values represent pooled data for male and female participants.
§ Values represent pooled data for marathon and half-marathon participants.

to be excluded owing to perfect prediction, factors that were independently associated with survival of cardiac arrest were an initial cardiac rhythm of ventricular fibrillation or tachycardia (odds ratio, 0.040; 95% CI, 0.003 to 0.556) and the number of previous long-distance running races completed (odds ratio, 0.533; 95% CI, 0.291 to 0.979).

## DISCUSSION

We calculated that the incidence rates of cardiac arrest and sudden death during long-distance running races were 1 per 184,000 and 1 per 259,000 participants, respectively. We estimate that this translates into 0.2 cardiac arrests and 0.14 sudden deaths per 100,000 runner-hours at risk, using average running times of 4 and 2 hours for the marathon and half-marathon, respectively. Thus, event rates among marathon and half-marathon runners are relatively low, as compared with other athletic populations, including collegiate athletes (1 death per 43,770 participants per year),[23] triathlon participants (1 death per 52,630 participants),[24] and previously healthy middle-aged joggers (1 death per 7620 participants).[25] These data suggest that the risk associated with long-distance running events is equivalent to or lower than the risk associated with other vigorous physical activity.

This study provides several insights into race-related cardiac arrest. First, the absolute number of race-related cardiac arrests each year increased over the past decade. This is best explained by the parallel increase in participation, because overall annual incidence rates of cardiac arrest were stable. Second, men were more likely than women to have cardiac arrest and sudden death. This finding is consistent with reports on other populations and reaffirms a male predisposition to exertional cardiac arrest.[12,13,25-27] A plausible explanation for this observation is the higher prevalence of both occult hypertrophic cardiomyopathy and early-onset atherosclerosis in men.[28,29] The finding that event rates among male marathon runners increased during the study period is troubling and may indicate that long-distance racing has recently been attracting more high-risk men with occult cardiac disease who seek the health benefits of routine physical exercise. Future work is needed to further characterize this group and to determine useful prevention strategies. Third, race distance was a determinant of the incidence of cardiac arrest and death, with rates for marathons that were three to five times as high as the rates for half-marathons. A possible explanation is that longer races involve more physiological stress and thus a higher likelihood of precipitating an adverse event in a predisposed participant. Finally, cardiovascular disease accounted for the majority of cardiac arrests. Hypertrophic cardiomyopathy, the primary cause of death in young competitive athletes,[12,13] was also the leading cause of death in this population. Alternative race-related disorders, including hyponatremia[30] and hyperthermia,[31] remain important concerns but are uncommon causes of cardiac arrest and sudden death.

The overall case fatality rate was 71%. This compares favorably with previous data on out-of-hospital cardiac arrests (median case fatality rate, 92%).[32] This may be due to the fact that running

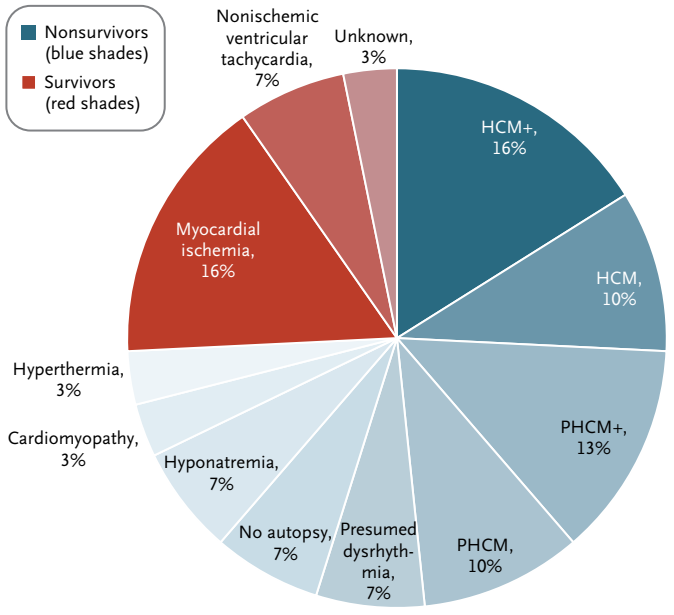


**Figure 2. Causes of Cardiac Arrest among Nonsurvivors and Survivors.**
HCM denotes hypertrophic cardiomyopathy; HCM+ denotes HCM and additional diagnoses, including coronary artery disease (in 2 persons), myocarditis (in 2), and bicuspid aortic-valve and coronary anomaly (in 1). PHCM denotes possible hypertrophic cardiomyopathy. PHCM+ denotes PHCM and additional diagnoses, including coronary artery disease (in 1 person), accessory atrioventricular nodal bypass tract (in 1), hyperthermia (in 1), and bicuspid aortic-valve and coronary anomaly (in 1). One nonsurvivor with hyponatremia was also found to have myxomatous valvular disease of the tricuspid, mitral, and aortic valves. Data include arrhythmogenic right ventricular cardiomyopathy (in 1 person). Because of rounding, percentages do not add up to 100.

**Table 2. Autopsy and Clinical Data for Nonsurvivors of Cardiac Arrest and Survivors of Cardiac Arrest.***

| Participant No. | Age | Sex | Autopsy Performed | Primary Autopsy Findings and Causes of Death | Additional Clinical and Autopsy Data |
|---|---|---|---|---|---|
| | *yr* | | | | |
| **Participants who died** | | | | | |
| 1 | 33 | Male | Yes | Hypertrophic cardiomyopathy | — |
| 2 | 35 | Male | Yes | Hypertrophic cardiomyopathy | — |
| 3 | 23 | Male | Yes | Hypertrophic cardiomyopathy | — |
| 4 | 28 | Male | Yes | Hypertrophic cardiomyopathy, myocarditis | Myocarditis with diffuse mononuclear-cell inflammation and intercellular fibrosis |
| 5 | 32 | Male | Yes | Hypertrophic cardiomyopathy, myocarditis | Myocarditis with eosinophil and granulocyte infiltration |
| 6 | 45 | Male | Yes | Hypertrophic cardiomyopathy, coronary artery disease | 75% proximal left anterior descending stenosis, 90% proximal right coronary-artery stenosis |
| 7 | 44 | Male | Yes | Hypertrophic cardiomyopathy, coronary artery disease | 85% proximal left anterior descending stenosis, 40% proximal right coronary-artery stenosis |
| 8 | 30 | Male | Yes | Hypertrophic cardiomyopathy, bicuspid aortic valve, coronary anomaly | Absent left circumflex artery |
| 9 | 26 | Male | Yes | Possible hypertrophic cardiomyopathy | — |
| 10 | 25 | Male | Yes | Possible hypertrophic cardiomyopathy | — |
| 11 | 29 | Female | Yes | Possible hypertrophic cardiomyopathy | Markedly reduced BMI of 14.9 |
| 12 | 40 | Male | Yes | Possible hypertrophic cardiomyopathy, bicuspid aortic valve, coronary anomaly | Abnormal left main and right coronary-artery origin with "slit-like" ostia |
| 13 | 23 | Male | Yes | Possible hypertrophic cardiomyopathy, accessory atrioventricular pathway | Fragmented atrioventricular node with discrete bands of conduction tissue |
| 14 | 38 | Male | Yes | Possible hypertrophic cardiomyopathy, coronary artery disease | 75% proximal left anterior descending stenosis |
| 15 | 22 | Male | Yes | Possible hypertrophic cardiomyopathy, hyperthermia | Diffuse alveolar hemorrhage, pulmonary edema, clinical documentation of hyperthermia at the time of cardiac arrest |
| 16 | 23 | Male | Yes | Hyperthermia | Diffuse alveolar hemorrhage, pulmonary edema, clinical documentation of hyperthermia at the time of cardiac arrest |
| 17 | 32 | Female | Yes | Arrhythmogenic right ventricular cardiomyopathy, coronary artery disease | Diffuse right ventricular adipose infiltration, 70% left anterior descending stenosis |
| 18 | 29 | Female | Yes | Hyponatremia | Documented altered mental status and seizures, brain-stem herniation at autopsy, myxomatous polyvalvular (mitral, tricuspid, aortic) heart disease |
| 19 | 35 | Female | Yes | Hyponatremia | Clinical documentation of profound hyponatremia during resuscitation efforts, autopsy report unavailable |
| 20 | 45 | Male | Yes | Presumed cardiac dysrhythmia | — |
| 21 | 36 | Male | Yes | Presumed cardiac dysrhythmia | — |
| 22 | 46 | Male | No | NA | — |
| 23 | 60 | Male | No | NA | — |

| | Age | Sex | Cause of Cardiac Arrest | Findings on Cardiac Catheterization | Echocardiographic Data |
|---|---|---|---|---|---|
| | *yr* | | | | |
| **Participants who survived** | | | | | |
| 1 | 48 | Female | Nonischemic ventricular tachycardia | No coronary arterial luminal narrowing, normal left ventricular function (ejection fraction, 68%) | Normal left ventricular structure and function; septal thickness, 11 mm; posterior-wall thickness, 11 mm; left ventricular end-diastolic diameter, 52 mm; left ventricular ejection fraction, 60% |
| 2 | 48 | Male | Nonischemic ventricular tachycardia | No coronary arterial luminal narrowing, normal left ventricular function (ejection fraction 62%) | Mild left ventricular dilatation†; septal thickness, 11 mm; posterior wall thickness, 11 mm; left ventricular end-diastolic diameter, 59 mm; left ventricular ejection fraction, 66% |
| 3 | 55 | Male | Myocardial ischemia | 95% mid-left anterior descending stenosis | Normal left ventricular morphology and function; septal thickness, 10 mm; posterior wall thickness, 11 mm; left ventricular end-diastolic diameter, 50 mm; left ventricular ejection fraction, 55% |
| 4 | 60 | Male | Myocardial ischemia | 95% mid-left circumflex stenosis | Mild left ventricular dilatation; septal thickness, 11 mm; posterior wall thickness, 11 mm; left ventricular end-diastolic diameter, 57 mm; left ventricular ejection fraction, 50% |
| 5 | 49 | Male | Myocardial ischemia | 95% distal right coronary-artery stenosis, 80% proximal right coronary-artery stenosis, 95% proximal left circumflex stenosis | Echocardiography not performed |
| 6 | 47 | Male | Myocardial ischemia | 85% proximal left anterior descending stenosis | Mild left ventricular concentric hypertrophy; septal thickness, 12 mm; posterior wall thickness, 10 mm; left ventricular end-diastolic diameter, 49 mm; left ventricular ejection fraction, 50% |
| 7 | 65 | Male | Myocardial ischemia | 90% mid-left anterior descending stenosis, 80% posterolateral-artery stenosis | Mild left ventricular concentric hypertrophy; septal thickness, 13 mm; posterior wall thickness, 11 mm; left ventricular end-diastolic diameter, 52 mm; left ventricular ejection fraction, 45% |
| 8 | 53 | Male | Unknown‡ | Catheterization not performed | Mild left ventricular concentric hypertrophy; septal thickness, 13 mm; posterior wall thickness, 13 mm; left ventricular end-diastolic diameter, 51 mm; left ventricular ejection fraction, 65% |

* BMI denotes body-mass index (the weight in kilograms divided by the square of the height in meters), and NA not available.
† Echocardiographic data were obtained 6 months after the cardiac arrest.
‡ The participant was found unconscious before losing pulse, underwent cardiopulmonary resuscitation, and then regained pulse before the first rhythm analysis. The electrocardiogram and blood work were unrevealing. The echocardiogram revealed no wall-motion abnormalities, and no further workup was performed.

**Table 3. Demographic Characteristics, Running History, Clinical Characteristics, Emergency Medical Treatment, and Cause of Cardiac Arrest among Nonsurvivors and Survivors.***

| Variable | Nonsurvivors (N=23) | Survivors (N=8) | P Value† | Odds Ratio (95% CI)‡ |
|---|---|---|---|---|
| Demographic characteristics | | | | |
| Male sex — no. (%) | 19 (83) | 7 (88) | 0.75 | |
| Age — yr | 33.9±9.5 | 53.1±6.5 | 0.02 | 0.78 (0.64–0.95) |
| BMI | 24.8±3.7 | 25.6±2.3 | 0.54 | |
| Running history | | | | |
| No. of years of running | 11±8 | 20±17 | 0.09 | 0.94 (0.87–1.01) |
| No. of previous long-distance running races completed§ | 1.5±1.9 | 3.5±1.5 | 0.02 | 0.57 (0.35–0.92) |
| Training regimen | | | | |
| No. of mi/wk | 41±16 | 53±10 | 0.18 | |
| Longest distance run (% of expected race distance)¶ | 86±32 | 80±18 | 0.64 | |
| Clinical characteristics — no. (%) | | | | |
| Established relationship with primary care physician | 10 (43) | 8 (100) | 0.01‖ | |
| Family history of sudden cardiac death | 1 (4) | 0 | 0.74‖ | |
| Family history of premature coronary artery disease | 4 (17) | 0 | 0.28‖ | |
| History of tobacco use | 2 (9) | 2 (25) | 0.26 | |
| Hypertension | 4 (17) | 5 (63) | 0.02 | 0.13 (0.02–0.76) |
| Hyperlipidemia | 5 (22) | 5 (63) | 0.04 | 0.17 (0.03–0.95) |
| Diabetes mellitus | 0 (0) | 0 | NA | |
| Previous positive cardiovascular review of systems** | 6 (26) | 4 (50) | 0.22 | |
| Recent viral prodrome†† | 3 (13) | 0 | 0.39‖ | |
| Emergency medical treatment | | | | |
| Bystander-administered CPR performed — no. (%) | 10 (43) | 8 (100) | 0.01‖ | |
| Time to initiation of CPR — min | 5.2±4.0 | 1.5±1.4 | 0.06 | 1.51 (0.99–2.30) |
| Time to emergency-medical-service arrival — min | 7.7±6.7 | 3.9±2.7 | 0.13 | |
| Initially documented cardiac rhythm — no. (%) | | | | |
| Ventricular fibrillation or ventricular tachycardia | 6 (26) | 7 (88) | 0.01 | 0.05 (0.01–0.50) |
| Pulseless electrical activity, asystole, or other | 17 (74) | 1 (13) | 0.01 | 19.8 (2.0–196.4) |
| Automatic external defibrillator used on scene | 8 (35) | 7 (88) | 0.03 | 0.08 (0.01–0.73) |
| Autopsy and clinical findings after cardiac arrest — no. (%) | | | | |
| Definite or probable hypertrophic cardiomyopathy | 15 (65) | 0 | 0.002‖ | |
| Ischemic heart disease | 4 (17) | 5 (63) | 0.02 | 0.13 (0.02–0.76) |

* Plus–minus values are means ±SD. Data are from the 31 cases for which complete clinical information was obtained. BMI denotes body-mass index, CPR cardiopulmonary resuscitation, and NA not applicable.
† Univariate logistic regression for predictors of nonsurvival was used to determine P values.
‡ Univariate odds ratios are provided for P values of less than 0.10.
§ The number of previous long-distance races was scored as follows: 0 (none), 1 (1 race), 2 (2 races), 3 (3 races), 4 (4 races), or 5 (≥5 races).
¶ Distance was calculated as the peak distance of the longest training run (in miles) divided by the distance of the upcoming race (marathon or half-marathon). To convert values for distance to kilometers, multiply by 1.6.
‖ P values for variables that were perfect predictors were determined with the use of Fisher's exact test.
** A positive cardiovascular review of systems was defined as chest pain, dizziness or syncope, or palpitations within 2 weeks before the race.
†† Viral prodrome symptoms were defined as generalized weakness, fatigue, or respiratory congestion within 2 weeks before the race.

races often have a high density of spectators as well as on-site medical services that facilitate timely emergency intervention. The finding that early bystander-administered CPR and use of automated defibrillators at the scene of the arrest were common for survivors of cardiac arrest underscores the notion that the race environment contributed to high resuscitation rates. There was also an association between age and cardiac-arrest outcome, with survival more common among participants who were 40 years of age or older (15 of 32, 47%) than among those younger than 40 years of age (2 of 27, 7%). This is best explained by the age-specific pattern of underlying cardiac disease. Younger persons who have cardiac arrest are more likely to have had hypertrophic cardiomyopathy, and resuscitation in cases of hypertrophic cardiomyopathy is reportedly less successful than in other conditions.[33] In contrast, older persons who have cardiac arrest are more likely to have had ischemic heart disease. In our study, runners with ischemic heart disease, most of whom were successfully resuscitated, had coronary angiographic and autopsy data suggesting a mismatch between oxygen supply and demand, not acute plaque rupture.

The absence of coronary plaque rupture in these persons was surprising, because prior data[34,35] and expert consensus documents[36] have suggested that exercise-induced acute coronary syndromes result from atherosclerotic plaque disruption and coronary thrombosis. In contrast, our findings suggest that demand ischemia (i.e., ischemia due to an imbalance between oxygen supply and demand) may be operative in exercise-related acute coronary events during long-distance running races. Although further work is warranted to clarify the mechanism (or mechanisms) that lead to cardiac arrest in runners with fixed coronary stenosis, this finding may have important clinical implications. Routine exercise testing in adults before exercise participation has not been recommended because of the low rates of exercise-related cardiac events, the high rates of false positive results in asymptomatic persons, and the concept that acute plaque rupture is the dominant cause of exercise-related cardiac events.[36] However, our observations suggest that preparticipation exercise testing, by virtue of its ability to accurately detect physiologically significant coronary-artery stenosis,[37] may be useful for identifying some persons at high risk, including middle-aged and older men with exertion-induced symptomatic or asymptomatic myocardial ischemia; this speculation requires further research for validation before it can be considered directive. The absence of plaque rupture also has important implications regarding the controversy of prophylactic aspirin use before exercise to prevent an acute event.[38,39] Our data suggest that taking aspirin before running a race may have limited efficacy, because acute coronary arterial thrombosis does not appear to be an important cause of race-related cardiac arrest.

This study has several limitations. First, our ascertainment method may have failed to detect all race-related cardiac arrests during the study period. However, the use of Internet search engines, plus direct outreach to race organizers, should have minimized this possibility. Second, we were unable to obtain complete clinical data on 45% of the nonsurvivors and on 53% of the survivors and thus cannot be certain that the detailed clinical characteristics and autopsy findings apply to all the runners who had cardiac arrest during the study period. However, age and sex were similar between those with and those without complete information, suggesting that the more comprehensively evaluated runners are representative of the entire group. Third, we examined the incidence of cardiac arrest as a function only of race distance and sex. Thus, we cannot comment on the risk or outcomes of cardiac arrest in specific populations, such as elite athletes, first-time race participants, or runners with preexisting medical conditions. Finally, some runners may have run multiple races during the decade-long study period, thereby diluting the incidence figures and leading to an underestimation of risk for an individual participant.

Findings from the RACER initiative indicate that marathons and half-marathons are associated with a low overall risk of cardiac arrest or sudden death. However, event rates have risen over the past decade among male marathon runners. Clinicians evaluating potential race participants should be aware of the risks of hypertrophic cardiomyopathy and atherosclerotic disease in this patient population.

Dr. Roberts reports holding a board membership with UCare Minnesota, receiving writing fees from *Runner's World*, and serving as an unpaid, volunteer medical director for the Medtronic Twin Cities Marathon; and Dr. Thompson, receiving consulting fees from Regeneron, Furiex Pharmaceuticals, and Lupin Pharmaceuticals, legal fees for expert testimony in cases related to cardiac arrest in exercise- and statin-related muscle injury, grant funding from GlaxoSmithKline, Genomas, Novartis, Furiex

Pharmaceuticals, B. Braun, and Aventis, lecture fees from Merck, Pfizer, AstraZeneca, Kowa, Abbott, and GlaxoSmithKline, support for the development of educational presentations from Merck, and holding stock in Zoll Medical, J.A. Wiley Publishing, General Electric, Zimmer, Medtronic, Johnson & Johnson, Sanofi-Aventis, and Abbott. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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