

Trends in Sudden Cardiovascular Death in Young Competitive Athletes After Implementation of a Preparticipation Screening Program

Domenico Corrado, MD, PhD

Cristina Basso, MD, PhD

Andrea Pavei, MD

Pierantonio Michieli, MD, PhD

Maurizio Schiavon, MD

Gaetano Thiene, MD

THE MAJORITY OF YOUNG ATHLETES who die suddenly have previously unsuspected structural heart disease.¹⁻⁸ Cardiomyopathies have been consistently implicated as the leading cause of cardiac arrest in young competitive athletes, with hypertrophic cardiomyopathy accounting for more than one third of fatal cases in the United States^{1,4-6} and arrhythmogenic right ventricular cardiomyopathy for approximately one fourth of fatal cases in Italy.^{2,3,7,8}

Medical evaluation of athletic populations before competition offers the potential to identify asymptomatic athletes with potentially lethal cardiovascular abnormalities and to prevent sudden death through disqualification from competitive sports.⁹⁻¹³ Italian law mandates that every participant engaged in competitive sports activity must undergo a clinical evaluation and obtain eligibility.¹⁴ Accordingly, a nationwide systematic screening program was launched in Italy in 1982.^{15,16} This preparticipation screening essentially based on 12-lead electrocardiogram (ECG) has been shown to be effective in identifying athletes with hypertrophic cardiomyopathy and in

Context A nationwide systematic preparticipation athletic screening was introduced in Italy in 1982. The impact of such a program on prevention of sudden cardiovascular death in the athlete remains to be determined.

Objective To analyze trends in incidence rates and cardiovascular causes of sudden death in young competitive athletes in relation to preparticipation screening.

Design, Setting, and Participants A population-based study of trends in sudden cardiovascular death in athletic and nonathletic populations aged 12 to 35 years in the Veneto region of Italy between 1979 and 2004. A parallel study examined trends in cardiovascular causes of disqualification from competitive sports in 42 386 athletes undergoing preparticipation screening at the Center for Sports Medicine in Padua (22 312 in the early screening period [1982-1992] and 20 074 in the late screening period [1993-2004]).

Main Outcome Measures Incidence trends of total cardiovascular and cause-specific sudden death in screened athletes and unscreened nonathletes of the same age range over a 26-year period.

Results During the study period, 55 sudden cardiovascular deaths occurred in screened athletes (1.9 deaths/100 000 person-years) and 265 sudden deaths in unscreened nonathletes (0.79 deaths/100 000 person-years). The annual incidence of sudden cardiovascular death in athletes decreased by 89% (from 3.6/100 000 person-years in 1979-1980 to 0.4/100 000 person-years in 2003-2004; P for trend $< .001$), whereas the incidence of sudden death among the unscreened nonathletic population did not change significantly. The mortality decline started after mandatory screening was implemented and persisted to the late screening period. Compared with the prescreening period (1979-1981), the relative risk of sudden cardiovascular death in athletes was 0.56 in the early screening period (95% CI, 0.29-1.15; $P = .04$) and 0.21 in the late screening period (95% CI, 0.09-0.48; $P = .001$). Most of the reduced mortality was due to fewer cases of sudden death from cardiomyopathies (from 1.50/100 000 person-years in the prescreening period to 0.15/100 000 person-years in the late screening period; P for trend = .002). During the study period, 879 athletes (2.0%) were disqualified from competition due to cardiovascular causes at the Center for Sports Medicine: 455 (2.0%) in the early screening period and 424 (2.1%) in the late screening period. The proportion of athletes who were disqualified for cardiomyopathies increased from 20 (4.4%) of 455 in the early screening period to 40 (9.4%) of 424 in the late screening period ($P = .005$).

Conclusions The incidence of sudden cardiovascular death in young competitive athletes has substantially declined in the Veneto region of Italy since the introduction of a nationwide systematic screening. Mortality reduction was predominantly due to a lower incidence of sudden death from cardiomyopathies that paralleled the increasing identification of athletes with cardiomyopathies at preparticipation screening.

JAMA. 2006;296:1593-1601

www.jama.com

Author Affiliations: Department of Cardiac, Thoracic, and Vascular Sciences (Drs Corrado and Pavei) and Institute of Pathological Anatomy (Drs Basso and Thiene), University of Padua Medical School; and Center for Sports Medicine and

Physical Activity (Drs Michieli and Schiavon), Padua, Italy.

Corresponding Author: Gaetano Thiene, MD, Istituto di Anatomia Patologica, Via A. Gabelli, 61-35121 Padova, Italy (gaetano.thiene@unipd.it).

For editorial comment see p 1648.

providing some protection against the risk of sudden death.¹¹ However, the long-term impact of such population-based programs on mortality from sudden cardiovascular death remains to be evaluated.

Our goals were to analyze the changes in incidence rates and causes of sudden cardiovascular death in the young athletic population in the Veneto region of Italy, after introduction of systematic preparticipation screening in Italy, and to compare mortality trends between screened athletes and their unscreened nonathletic counterparts. Moreover, a parallel investigation examined the changing prevalence of cardiovascular diseases causing disqualification from competitive sports in a large series of young athletes undergoing preparticipation screening at the Center for Sports Medicine in Padua, Italy, during the same period.

METHODS

We performed a trend analysis of the annual incidence rates and causes of sudden cardiovascular death in competitive athletes aged 12 to 35 years in the Veneto region of Italy between 1979 and 2004, and examined the temporal association between mortality and systematic preparticipation screening that was introduced in Italy in 1982. The incidence rates of sudden cardiovascular death in the unscreened nonathletic population of the same age range were the control variable.

Incidence of Sudden Cardiovascular Death in Athletes

Data on sudden cardiovascular death rates between 1979 and 2004 were obtained from the Registry on Juvenile Sudden Death of the Veneto region of Italy.^{2,7,11} Sudden death was defined as unexpected death as a result of natural causes in which a loss of all functions occurred instantaneously or within 1 hour of the onset of collapse symptoms. Sudden death was considered to be cardiovascular in origin when at postmortem the primary cause leading to cardiac arrest was found in the

heart or great vessels and other non-cardiac causes were excluded.

The Veneto region of northeast Italy covers an area of 18 368 km². The vast majority of residents are white, comprising an ethnically homogeneous population. During the study period, the population was stable and averaged 4 379 900, according to the Italian Census Bureau.^{7,11}

Since 1979, all fatalities occurring in young people aged 35 years or younger in the Veneto region have been collected and investigated in the setting of a prospective clinicopathological study.¹¹ The medical centers participating in this research project constituted an active network that served 94.4% of the population and permitted an accurate monitoring of fatal events occurring in this well-defined geographic area. (Participating centers are listed at the end of this article.) Regional newspapers were also systematically used at the coordinating center (The Institute of Pathological Anatomy, University of Padua, Padua, Italy) for daily monitoring of articles on sudden death in young people that occurred in the Veneto region, either sports-related or sports-unrelated.

Athletes and nonathletes who died a sudden death were examined postmortem by the local pathologist or medical examiner at each collaborative medical center to rule out extracardiac causes of death by routine autopsy. The entire heart was subsequently forwarded to the Institute of Pathological Anatomy for detailed morphological assessment, including macroscopic examination and histopathologic study of coronary arteries, ventricular myocardium, and the specialized conduction system as reported in detail elsewhere.^{2,3,11,17} Clinical history, athletic activity, and the circumstances surrounding the cardiac arrest were investigated in each athlete who had a sudden death. According to the 1995 World Health Organization classification,¹⁸ cardiomyopathies included dilated, hypertrophic, restrictive, and arrhythmogenic right ventricular cardiomyopathy.

The study was approved by the institutional review board of the University of Padua Medical School. Italian law

does not require consent of relatives for postmortem cases.

Preparticipation Screening

As required by Italian law, since 1982 all competitive athletes from the Veneto region have undergone preparticipation screening for cardiovascular diseases at risk of sudden death during sports.¹⁵ According to the Italian guidelines for sports medicine, young competitive athletes were defined as adolescents and young adults aged 12 to 35 years who participated in an organized sports program that required regular training and competition.⁷ To examine the effects of the screening program on mortality, we considered 3 periods: prescreening (1979-1981), early screening (1982-1992), and late screening (1993-2004).

First-line screening examination included family and personal history, physical examination, and 12-lead ECG; additional tests were requested only for those athletes who had positive findings at the initial evaluation.^{7,11,13} Criteria for positive history, physical examination, and ECG are listed in the BOX. Athletes diagnosed with cardiovascular abnormalities were treated according to available guidelines. The Italian recommendations for sports eligibility are similar to those of the Bethesda Conferences, although the Italian criteria are more restrictive.¹⁹⁻²¹

To assess whether the changing pattern of cardiovascular causes of sudden death in athletes was consistent with that of cardiovascular diseases identified at preparticipation screening, we performed an analysis of causes of disqualification in a large series of young competitive athletes undergoing cardiovascular evaluation during 2 consecutive screening periods (1982-1992 and 1993-2004) at the Center for Sports Medicine. This is a leading center for sports medicine in the Veneto region and is a representative regional observatory for monitoring the outcome of the Italian preparticipation screening program.¹¹

Statistical Analysis

Annual sudden death rates were reported as the number of deaths per

Box. Criteria for a Positive History, Physical Examination, and 12-Lead Electrocardiogram at Preparticipation Screening

Family History

Close relative(s) with premature myocardial infarction or sudden death at <50 years

Family history of cardiomyopathy, coronary artery disease, Marfan syndrome, long QT syndrome, severe arrhythmias, or other disabling cardiovascular diseases

Personal History

Syncope or near-syncope

Exertional chest pain or discomfort

Shortness of breath or fatigue out of proportion to the degree of physical effort

Palpitations or irregular heartbeat

Physical Examination

Musculoskeletal and ocular features suggestive of Marfan syndrome

Diminished and delayed femoral artery pulses

Mid- or end-systolic clicks

Abnormal second heart sound (single or widely split and fixed with respiration)

Heart murmurs (systolic grade $\geq 2/6$ and any diastolic)

Irregular heart rhythm

Brachial blood pressure $\geq 140/90$ mm Hg on more than 1 reading

Electrocardiogram

Left atrial enlargement: negative portion of the P wave in lead V1 ≥ 0.1 mV in depth and ≥ 0.04 s in duration

Right atrial enlargement: peaked P wave in leads II and III or V1 ≥ 0.25 mV in amplitude

Frontal-plane QRS axis deviation: right $\geq +120^\circ$ or left -30° to -90°

Increased voltage: amplitude of R or S wave in a standard lead ≥ 2 mV, S wave in lead V1 or V2 ≥ 3 mV, or R wave in lead V5 or V6 ≥ 3 mV

Abnormal Q waves ≥ 0.04 s in duration or $\geq 25\%$ of the height of the ensuing R wave, or QS pattern in ≥ 2 leads

Right or left bundle-branch block with QRS duration ≥ 0.12 s

R or R' wave in lead V1 ≥ 0.5 mV in amplitude and R:S ratio ≥ 1

ST-segment depression or T-wave flattening or inversion in ≥ 2 leads

Prolongation of heart rate corrected QT interval >0.44 s in men and >0.46 in women

Premature ventricular beats or more severe ventricular arrhythmia

Supraventricular tachycardia, atrial flutter, or atrial fibrillation

Ventricular preexcitation: short PR interval (<0.12 s) with or without delta wave

First-degree (PR ≥ 0.21 s, not shortening with hyperventilation), second-degree, or third-degree atrioventricular block

100 000 population. In calculating annual incidence rates, we counted the events during periods of 2 years and halved the resultant (2-year) rates. Numerators used to calculate annual incidence rate consisted of the number of sudden cardiovascular deaths in young people aged 12 to 35 years. The denominator consisted of person-years, namely the average size of the young population (either athletes or nonathletes) in the Veneto region at risk \times duration of the observation period. The estimates of numbers of person-years at risk were calculated based on the Veneto region census data for the years 1981, 1991, and 2001. Population data for intercensal years were estimated by linear interpolation from decennial census data. Estimates of person-years at risk were based on the Sports Medicine Data Base of the

Veneto region, which records athletes actively participating in regional official sports competition annually.^{7,11}

Continuous variables are expressed as mean (SD). The χ^2 or Fisher exact test was used to assess the significance of differences between subgroups. We evaluated trends using Poisson regression of the count of sudden deaths in each year against calendar year, including the log of the amount of person-time at risk in each year as an offset term.²² Test for trends and 95% confidence intervals (CIs) for sudden cardiac death mortality rates were calculated by using Stata version 7.0 (StataCorp LP, College Station, Tex). Relative risks (RRs) and corresponding 95% CIs were reported for the rates of sudden cardiovascular deaths during the late screening period (1993-2004) by using prescreening (1979-

1981) rates as the baseline. All tests of significance were 2-sided, and $P < .05$ was considered statistically significant.

RESULTS

Trends in Sudden Cardiovascular Death in Athletes

During the 1979-2004 period, 55 cases of sudden cardiovascular death occurred in the screened athletic population aged 12 to 35 years in the Veneto region during an estimated 2 938 730 person-years of observation, producing an overall cohort incidence rate of 1.9 deaths per 100 000 person-years. There were no significant changes in the age and sex composition of the athlete population over the study period. The 55 cases of sudden death included 50 males and 5 females (age range, 12-35 years; mean [SD] age, 23.3 [2] years; median, 23

years). In 50 cases (91%), sudden death occurred during sports activity (44 cases) or immediately afterward (6 cases).

Number and rates of sudden cardiovascular death in young competitive athletes decreased during the 26-year period (FIGURE). The annual rate of death was 3.6 per 100 000 person-

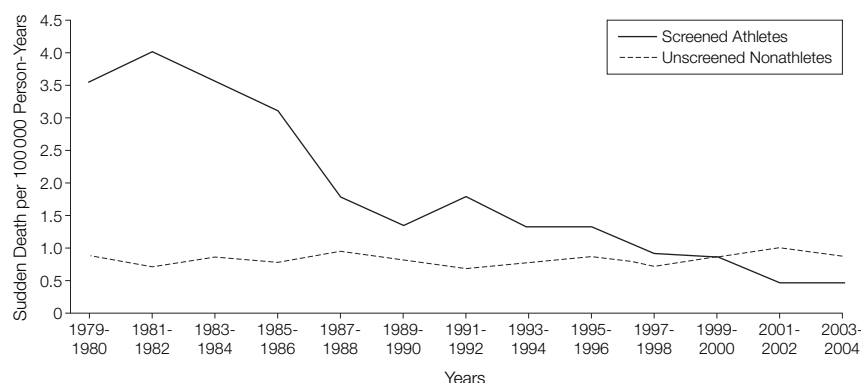
years in 1979-1980 (8 sudden deaths) and 4.0 per 100 000 person-years in 1981-1982 (9 sudden deaths). Subsequently, the annual rate of death steadily decreased over time and in the 2001-2004 period, it was 0.43 per 100 000 person-years (1 sudden death each period), which is approximately

a tenth of that recorded 2 decades before (P for trend $< .001$).

The overall changes in total incidence rates of sudden cardiovascular death in athletes in relation to the 3 screening periods are shown in TABLE 1. The decrease of sudden cardiovascular deaths in the athletic population started after the introduction of preparticipation screening and persisted to the late screening period. During the prescreening period, there were 14 deaths (13 males and 1 female; mean [SD] age, 22.9 [6] years), 12 of which were sports-related; during the early screening period, there were 29 deaths (26 males and 3 females; mean [SD] age, 23.7 [5] years), 27 of which were sports-related; and during the late screening period, 12 deaths (11 males and 1 female; mean [SD] age, 23.5 [6] years), 11 of which were sports-related.

The average incidence of sudden cardiovascular death in young competitive athletes in the prescreening period was 4.19 (95% CI, 1.78-7.59) per 100 000 person-years. The average incidence decreased to 2.35 (95% CI, 1.94-2.75) per

Figure. Annual Incidence Rates of Sudden Cardiovascular Death in Screened Competitive Athletes and Unscreened Nonathletes Aged 12 to 35 Years in the Veneto Region of Italy (1979-2004)



During the study period, the annual incidence of sudden cardiovascular death decreased by 89% in screened athletes (P for trend $< .001$). In contrast, the incidence rate of sudden cardiovascular death did not demonstrate consistent changes over time in unscreened nonathletes.

Table 1. Number and Annual Incidence Rates of Total and Cause-Specific Sudden Cardiovascular Death in Screened Athletes and Unscreened Nonathletes in Relation to 3 Screening Periods*

| | Periods | | | | | | <i>P</i> for Trend | RR (95% CI)† |
|-----------------------------------|--------------------------|-------------------------|-----------------------------|-------------------------|----------------------------|-------------------------|--------------------|-------------------|
| | Prescreening (1979-1981) | | Early Screening (1982-1992) | | Late Screening (1993-2004) | | | |
| | No. of Events | Incidence Rate (95% CI) | No. of Events | Incidence Rate (95% CI) | No. of Events | Incidence Rate (95% CI) | | |
| Total sudden deaths in athletes | 14 | 4.19 (1.78-7.59) | 29 | 2.35 (1.94-2.75) | 12 | 0.87 (0.46-1.28) | .001 | 0.21 (0.09-0.48) |
| Cardiomyopathies | 5 | 1.50 (0.21-2.78) | 7 | 0.57 (0.26-0.87) | 2 | 0.15 (0-0.36) | .002 | 0.10 (0.01-0.59) |
| Coronary artery disease | 3 | 0.90 (0-3.12) | 5 | 0.41 (0.09-0.72) | 3 | 0.22 (0-0.47) | .08 | 0.24 (0.03-1.81) |
| Cardiac conduction disease | 1 | 0.30 (0-1.56) | 2 | 0.16 (0-0.40) | 1 | 0.07 (0-0.23) | .29 | 0.24 (0.01-19.02) |
| Myocarditis | 1 | 0.30 (0-1.56) | 4 | 0.32 (0.02-0.63) | 2 | 0.15 (0-0.36) | .40 | 0.48 (0.02-28.61) |
| Congenital coronary anomalies | 1 | 0.30 (0-1.56) | 4 | 0.32 (0.02-0.63) | 2 | 0.15 (0-0.36) | .40 | 0.48 (0.02-28.61) |
| Mitral valve prolapse | 1 | 0.30 (0-1.56) | 4 | 0.32 (0.02-0.63) | 1 | 0.07 (0-0.23) | .19 | 0.24 (0.01-19.02) |
| Other‡ | 2 | 0.60 (0-1.87) | 3 | 0.24 (0-0.52) | 1 | 0.07 (0-0.23) | .06 | 0.12 (0.01-2.33) |
| Total sudden death in nonathletes | 29 | 0.77 (0.26-1.26) | 110 | 0.79 (0.69-0.88) | 126 | 0.81 (0.68-0.94) | .80 | 1.05 (0.69-1.64) |
| Cardiomyopathies | 8 | 0.21 (0.10-0.33) | 35 | 0.25 (0.17-0.33) | 40 | 0.26 (0.19-0.33) | .76 | 1.21 (0.56-2.99) |
| Coronary artery disease | 7 | 0.19 (0.07-0.30) | 23 | 0.17 (0.12-0.22) | 25 | 0.16 (0.12-0.21) | .81 | 0.87 (0.36-2.37) |
| Cardiac conduction disease | 3 | 0.08 (0-0.28) | 8 | 0.06 (0.02-0.10) | 12 | 0.08 (0.03-0.13) | .66 | 0.97 (0.26-5.36) |
| Myocarditis | 4 | 0.10 (0-0.34) | 15 | 0.11 (0.06-0.16) | 20 | 0.13 (0.08-0.18) | .58 | 1.21 (0.41-4.88) |
| Congenital coronary anomalies | 2 | 0.05 (0-0.17) | 5 | 0.04 (0.01-0.06) | 7 | 0.05 (0.01-0.08) | .87 | 0.85 (0.16-8.37) |
| Mitral valve prolapse | 2 | 0.05 (0-0.17) | 9 | 0.06 (0.03-0.11) | 8 | 0.05 (0.02-0.09) | .72 | 0.97 (0.19-9.38) |
| Other‡ | 3 | 0.08 (0-0.28) | 15 | 0.11 (0.07-0.15) | 14 | 0.09 (0.05-0.13) | .79 | 1.13 (0.32-6.15) |

Abbreviations: CI, confidence interval; RR, relative risk.

*Incidence rates are shown as events per year per 100 000 athletes aged 12 to 35 years. Number of events represent the actual number of events.

†Reported for the rates of sudden cardiovascular deaths during the late screening period (1993-2004) using prescreening (1979-1981) rates as the baseline.

‡Includes myocardial bridge, aortic stenosis, aortic rupture, and pulmonary thromboembolism.

100 000 person-years in the early screening period and to 0.87 (95% CI, 0.46-1.28) per 100 000 person-years in the late screening period, with the lowest observed rate of 0.43 per 100 000 person-years occurring between 2001 and 2004. The average rate of sudden cardiovascular death decreased by 44% from the prescreening to the early screening period and by 63% from the early to the late screening period. Compared with the prescreening period, the RR of sudden cardiovascular death was 0.56 (95% CI, 0.29-1.15; $P=.04$) in the early screening period and 0.21 (95% CI, 0.09-0.48; $P=.001$) in the late screening period.

Trends in Sudden Cardiovascular Death in Nonathletes

During the 1979-2004 period, among the unscreened nonathletic population aged 12 to 35 years in the Veneto region, 265 sudden cardiovascular deaths occurred during an estimated 33 205 370 person-years of observation, equivalent to a mortality rate of 0.79 per 100 000 person-years.

The 265 cases of sudden cardiovascular death included 198 males and 67 females (age range, 12-35 years; mean [SD] age, 23.5 [8] years; median, 23 years). At the time of death, 37 individuals (14%) were performing mild to moderate physical exercise, while 228 (86%) were engaged in sedentary activity. During the prescreening period, there were 29 deaths (21 males and 8 females; mean [SD] age, 23.7 [10] years), 3 of which were exercise-related; during the early screening period, there were 110 deaths (79 males and 31 females; mean [SD] age, 23.4 [9] years), 19 of which were exercise-related; and during the late screening period, there were 126 deaths (98 males and 28 females; mean [SD] age, 23.6 [8] years), 15 of which were exercise-related.

Systematic investigation of clinical history and prior athletic activity demonstrated that none of the cases of sudden death were former athletes who had been previously screened and disqualified from competition during the observation period.

As shown in the Figure, the trend for sudden cardiovascular death in the unscreened nonathletic young population was relatively unchanged throughout the period of observation. The average incidence of sudden cardiovascular death in unscreened nonathletes did not demonstrate significant changes over the study periods (0.77 per 100 000 person-years in the prescreening period; 0.79 per 100 000 person-years in the early screening period; and 0.81 per 100 000 person-years in the late screening period; P for trend=.80) (Table 1).

During the late screening period, the annual incidence of sudden cardiovascular death in screened athletes became equal (0.80 per 100 000 person-years in the 1999-2000 period) and less than that observed in unscreened nonathletes (0.43 per 100 000 person-years for screened athletes vs 0.90 per 100 000 person-years for unscreened nonathletes in the 2001-2002 period; and 0.43 vs 0.87 per 100 000 person-years, respectively, in the 2003-2004 period) (Figure).

Trends in Sudden Death by Specific Cardiovascular Causes

The analysis of mortality by specific cardiovascular causes among the athletic population showed that cardiomyopathies were the most common cause of sudden death (0.48 per 100 000 person-years), followed by coronary artery disease (0.37 per 100 000 person-years); congenital coronary anomalies (0.24 per 100 000 person-years); myocarditis (0.24 per 100 000 person-years); mitral valve prolapse (0.20 per 100 000 person-years); diseases of the conduction system (0.14 per 100 000 person-years); and other, such as myocardial bridge, aortic stenosis, aortic rupture, and pulmonary thromboembolism (0.20 per 100 000 person-years).

The overall changes in cause-specific incidence rates of sudden cardiovascular death in athletes in relation to the 3 screening periods are shown in Table 1. Most of the reduced incidence was due to fewer cases of death from cardiomyopathies over the 26-year period. The proportion of cases of sudden death from car-

diomyopathies decreased from 36% in the prescreening period to 17% in the late screening period, and the incidence of sudden death due to cardiomyopathies decreased by 90% (from 1.50 to 0.15 per 100 000 person-years; P for trend=.002). The greatest decline (by 84%) occurred in death rates from arrhythmogenic right ventricular cardiomyopathy (from 0.90 per 100 000 person-years in the prescreening period to 0.15 per 100 000 person-years in the late screening period; RR, 0.16; 95% CI, 0.03-1.41; P for trend=.02). There was a downward but not significant trend for sudden death from coronary artery disease and cardiac conduction disturbances.

All of the 55 athletes who died suddenly obtained eligibility for competitive sports, although 24 (44%) had at the preparticipation evaluation 1 or more positive findings, such as familial history for cardiomyopathy, sudden death, or both in 6 athletes, palpitation on exertion in 10 athletes, syncope in 7 athletes, chest pain in 2 athletes, cardiac murmur in 4 athletes, ECG changes in 14 athletes, and premature ventricular beats in 11 athletes, that were considered to be of little or no clinical relevance. The cause of sudden death in these 24 athletes included cardiomyopathy in 12, coronary artery disease in 3, mitral valve prolapse in 3, congenital coronary anomalies in 2, conduction disease in 2, and other cause in 2.

Positive history and ECG findings were found on preparticipation examination significantly more often in athletes who died of cardiomyopathy (12/14 [86%]) than in those who died of coronary artery disease (3/11 [27%]) ($P=.01$), congenital coronary anomalies (2/7 [29%]) ($P=.03$), and other causes (7/23 [30%]) ($P=.003$). Additional tests were required in 10 athletes (echocardiogram in 9 athletes, exercise testing in 3 athletes, and 24-hour Holter monitoring in 2 athletes), but failed to identify the underlying disease.

Incidence rates of cause-specific sudden cardiovascular death among nonathletes did not show significant trend changes over the study period (Table 1).

Cardiovascular Causes of Disqualification at Screening

The estimated number of competitive athletes aged 12 to 35 years in the Veneto region from 1982 to 2004 was 385 600 (186 700 during 1982-1992 and 198 900 during 1993-2004). Of these, 42 386 young athletes (11%) were screened at the Center for Sports Medicine in Padua between 1982 and 2004 (22 312 in 1982-1992 and 20 074 in 1993-2004). Among the 42 386 athletes, 3914 (9%) were referred for further examination because of positive findings and 879 (2%) were ultimately disqualified from participation in competitive sports because of the following types of cardiovascular conditions: (1) rhythm and conduction abnormalities, which worsened during physical exercise to the extent that they produced symptoms, such as impaired consciousness, significant fatigue, or dyspnea, regardless of pres-

ence of an underlying heart disease, and were inadequately treated with antiarrhythmic drugs or catheter ablation (39.0%); (2) systemic hypertension (>160/100 mm Hg at rest) unsatisfactorily controlled with drug therapy or associated with target organ damage (23.0%); (3) valvular diseases, including mitral valve prolapse complicated by ventricular arrhythmias, mitral valve regurgitation, or both (21.0%); (4) cardiomyopathies (6.8%); (5) atherosclerotic coronary artery disease (1.3%); and (6) other, such as congenital heart diseases, vascular diseases, rheumatic disease, and pericarditis (8.4%) (TABLE 2).

These conditions causing disqualification in the 879 athletes were suspected at baseline screening on the basis of positive history, physical and ECG findings, and confirmed by further examination, including echocardiography and exercise testing in 387 ath-

letes (44%); echocardiography, exercise testing, and 24-hour Holter monitoring in 335 athletes (38%); echocardiography in 128 athletes (14%); and echocardiography and 24-hour Holter monitoring in 29 athletes (3%). Cardiac magnetic resonance imaging, electrophysiologic study, or contrast angiography were required in 47 athletes (5%).

Despite positive findings at first-line screening evaluation, 3035 athletes obtained eligibility for competition after cardiovascular disease was ruled out by additional test results (false-positive results), such as echocardiography in 2458 athletes (81%); echocardiography and exercise testing in 424 athletes (14%); and echocardiography, exercise testing, and 24-hour Holter monitoring in 153 athletes (5%). Twenty-nine athletes (0.9%) underwent cardiac magnetic resonance imaging, invasive tests (such as electrophysiologic study and contrast angiography), or both.

The analysis of cardiovascular conditions causing disqualification from competitive sports in the 879 athletes during the early and late screening periods indicated an increasing efficacy of preparticipation evaluation in identifying athletes who had cardiomyopathies over time. The proportion of athletes who were disqualified from competition due to cardiomyopathies increased from 20 (4.4%) of 455 in the early screening period to 40 (9.4%) of 424 during the late screening period ($P=.005$) (Table 2). This was predominantly a consequence of the significantly higher number of athletes who did not obtain sports eligibility because of a diagnosis of arrhythmogenic right ventricular cardiomyopathy during the late screening period compared with the early screening period (14/424 [3.3%] and 2/455 [0.4%], respectively; $P=.004$).

An increase (with a nonstatistically significant trend) of the number of athletes who were disqualified because of coronary artery disease was observed in the late screening period (2.1% vs 0.4%; $P=.05$).

Table 2. Cardiovascular Conditions Causing Disqualification From Competitive Sports in 879 Athletes Over 2 Consecutive Screening Periods (1982-1992 and 1993-2004) at the Center for Sports Medicine in Padua, Italy

| Cardiovascular Causes of Disqualification | No. (%) of Disqualified Athletes | | | P Value |
|---|----------------------------------|------------------------------------|-----------------------------------|---------|
| | Total Study Period (1982-2004) | Early Screening Period (1982-1992) | Late screening Period (1993-2004) | |
| Total No. screened* | 42 386 | 22 312 | 20 074 | |
| Total No. disqualified† | 879 (2.0) | 455 (2.0) | 424 (2.1) | |
| Rhythm and conduction abnormalities | 345 (39.0) | 166 (36.0) | 179 (42.2) | .13 |
| Ventricular arrhythmias | 173 (19.6) | 81 (18.0) | 92 (21.6) | .20 |
| Supraventricular arrhythmias | 73 (8.3) | 39 (8.6) | 34 (8.0) | .56 |
| Wolff-Parkinson-White syndrome | 55 (6.3) | 29 (6.3) | 26 (6.1) | .88 |
| LBBB or RBBB and LAD | 26 (3.0) | 8 (1.7) | 18 (4.2) | .10 |
| 2nd-degree atrioventricular block | 13 (1.5) | 7 (1.5) | 6 (1.4) | .89 |
| Long QT syndrome | 5 (0.6) | 2 (0.4) | 3 (0.7) | .93 |
| Systemic hypertension | 205 (23.0) | 118 (25.9) | 87 (20.5) | .96 |
| Valvular disease, including MVP | 184 (21.0) | 106 (23.3) | 78 (18.4) | .09 |
| Cardiomyopathies | 60 (6.8) | 20 (4.4) | 40 (9.4) | .005 |
| Hypertrophic | 30 (3.4) | 14 (3.0) | 16 (3.8) | .50 |
| Arrhythmogenic right ventricular | 16 (1.8) | 2 (0.4) | 14 (3.3) | .004 |
| Dilated | 14 (1.6) | 4 (0.9) | 10 (2.4) | .21 |
| Coronary artery disease | 11 (1.3) | 2 (0.4) | 9 (2.1) | .05 |
| Other‡ | 74 (8.4) | 43 (9.5) | 31 (7.3) | .42 |

Abbreviations: LAD, left axis deviation; LBBB, left bundle-branch block; MVP, mitral valve prolapse; RBBB, right bundle-branch block.

*All athletes were screened at the Center for Sports Medicine in Padua, Italy, between 1982 and 2004.

†A total of 721 males and 158 females (age range, 12-35 years; mean [SD] age, 18.9 [6] years; median, 17 years) comprised the disqualified athletes for the total study period; 382 males and 73 females (age range, 12-35 years; mean [SD] age, 19.1 [4] years; median, 17 years) comprised the disqualified athletes for the early screening period; and 335 males and 89 females (age range, 12-35 years; mean [SD] age, 18.6 [5] years; median, 17 years) comprised the disqualified athletes for the late screening period.

‡Includes congenital heart diseases, vascular diseases, rheumatic disease, and pericarditis.

COMMENT

The major finding of our study was the 89% decrease in the incidence rate of sudden cardiovascular death among young competitive athletes aged 12 to 35 years in the Veneto region of Italy over the 26-year period. Three lines of evidence support the conclusion that the reduction in the incidence of sudden cardiovascular death is the result of the introduction in 1982 of a nationwide preparticipation screening program. (1) There was coincident timing between decline of sudden cardiovascular death in young competitive athletes and implementation of preparticipation cardiovascular screening in Italy; (2) most of the reduced incidence of sudden cardiovascular death over the 26-year period was due to fewer cases of athletes who died from cardiomyopathies and was accompanied by the concomitant increase of the proportion of young competitive athletes who were identified and hence disqualified from competition because of cardiomyopathies during the same interval; and (3) during the study period, the incidence of sudden cardiovascular death did not change among the unscreened nonathletic population in the Veneto region of the same age range.

A large proportion of cardiovascular diseases underlying sudden death in young competitive athletes are detectable by ECG.¹³ Silent but potentially lethal conditions, distinctively manifesting with ECG abnormalities, include cardiomyopathies, such as hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, and dilated cardiomyopathy; conduction system diseases, such as Lenègre disease and Wolff-Parkinson-White syndrome; and cardiac ion channel diseases, such as long and short QT syndromes and Brugada syndrome.

The Italian screening, essentially based on 12-lead ECG (in addition to history and physical examination) has been previously shown to be effective in detecting athletes with hypertrophic cardiomyopathy.^{11,23,24} Moreover, no deaths occurred during long-

term follow-up among athletes with hypertrophic cardiomyopathy who were disqualified from competitive sports, suggesting that screening may prevent sudden death.¹¹

Our trend analysis confirms and extends these previous observations by demonstrating that sudden death from any cardiovascular cause sharply decreased in athletes after the introduction of a nationwide screening program and continued until the late screening period. This trend reflected the continuous improvement in understanding cardiovascular causes and mechanisms of sudden death during sports, which in turn led to a progressively increased awareness of cardiologists and sports physicians about clinical and ECG features of diseases at risk.^{2,3,7,11,25-35} These results were predominantly obtained from the feedback derived from the systematic monitoring and clinicopathological investigation of fatal events occurring in the Veneto region.

Most of the reduced incidence of sudden cardiovascular death in athletes was due to fewer cases of fatal cardiomyopathies over the 26-year period. The proportion of athletes who died suddenly from cardiomyopathy decreased from 36% in the prescreening period to 17% in the late screening period. Data from the Center for Sports Medicine indicate that this reduction of mortality from cardiomyopathies may be related to the concomitant, progressive increase of the proportion of athletes who were disqualified from competition because of cardiomyopathies over the study period (from 4.4% in the early to 9.4% in the late screening period). These results are expected because cardiomyopathies play a leading role in causing sudden death in athletes and distinctively present clinically with ECG abnormalities, which permit their detection at preparticipation cardiovascular evaluation, even in otherwise asymptomatic participants.

Hypertrophic cardiomyopathy has been the subject of intense investigation since its original description 40 years ago³⁶⁻³⁸ and has been recognized

as the leading cause of sudden death in athletes since 1980.¹ The Italian preparticipation screening program since its first steps has mainly focused on such well-known lethal cardiomyopathy,^{11,13,16} leading to identification and disqualification of athletes with cardiomyopathies and protecting them from the risk of sudden death during sports since the early screening period.

Accordingly, the proportion of athletes who did not obtain eligibility for competition because of a diagnosis of hypertrophic cardiomyopathy remained stable over the screening periods. Other cardiovascular conditions, such as arrhythmogenic right ventricular cardiomyopathy and coronary artery disease, have thereby come to account for a greater proportion of all sudden deaths in Italian athletes. Arrhythmogenic right ventricular cardiomyopathy was discovered approximately 2 decades later³⁹ than hypertrophic cardiomyopathy and was subsequently associated with a high risk of sudden death during sports.^{2,3} However, this condition for years was underdiagnosed by cardiologists and sports physicians, thus explaining why it was previously reported to be the leading cause of sudden death in Italian young competitive athletes, despite the high prevalence of alarming symptoms and ECG abnormalities, such as T-wave inversion and QRS prolongation in right precordial leads and ventricular arrhythmias with a left bundle-branch block morphology at preparticipation evaluation.^{2,3,7,11}

Our trend analysis showed that the incidence of sudden death from arrhythmogenic right ventricular cardiomyopathy decreased dramatically over the 26-year period and accounted for much of the change in mortality from cardiomyopathy. The downward trend of fatal events from this cardiomyopathy paralleled the concomitant increase in the number of athletes with cardiomyopathies successfully identified and hence disqualified from competition over the screening periods. All these findings suggest that screening athletes for cardiomyopathies is a life-

saving strategy and that 12-lead ECG is a sensitive and powerful tool for identification and risk stratification of athletes with cardiomyopathies.

Although the incidence of sudden cardiovascular death among the screened athletic population in the Veneto region decreased, there were no significant trend changes over the study period in total and cause-specific cardiovascular mortality among the nonathletic population of the same age range who did not undergo screening. This indicates that the reduction of sudden death selectively involved young individuals engaged in competitive sports activity, because those affected by cardiovascular diseases were successfully identified and disqualified as a result of the preparticipation mass-screening program.

Our investigation is not a controlled trial designed to compare screening and nonscreening strategies, and other environmental, socioeconomic, or medical/surgical factors may have contributed to the study results. For instance, mortality reduction could reflect more prompt cardiopulmonary resuscitation and early defibrillation interventions in later years. However, such factors are expected to affect mortality similarly in screened athletes and unscreened nonathletes, and therefore are unlikely to explain the declining trend in sudden cardiovascular death selectively recorded in the screened athletic population. Specific programs for medical surveillance and access to automated external defibrillator during athletic events were not implemented in the Veneto region of Italy over the study period.

Unlike the majority of nonathletes who died, 91% of sudden deaths in athletes were sports-related deaths, suggesting that participation in competitive sports increases the likelihood of cardiac arrest. This is in keeping with our previous observation that sports activity in adolescent and young adults is associated with an approximately 3 times greater risk of sudden cardiovascular death.⁷ This figure was calculated on the basis of the average incidence rates of sudden death among athletes and nonathletes of the same age

range over a 17-year period of observation. Our trend analysis, performed in the same young population in the Veneto region, showed that in the pre-screening period the RR of sudden cardiovascular death in the athletic population was approximately 5 times higher than that of nonathletes. However, exposure of the athletic population to preparticipation screening for a 23-year period led to the reversal of the RR of sudden death, which became twice as great among nonathletes at the end of the late screening period. This finding implies that screening the nonathletic population for cardiovascular disease at risk of sudden death may further reduce mortality in the young.

In our study, systematic investigation of clinical history and prior athletic activity demonstrated that none of the cases of sudden cardiovascular death were former athletes who had been previously screened and disqualified from competition. This is in agreement with our previous data that showed the favorable long-term outcome of athletes who were disqualified for cardiovascular causes and the subsequent close follow-up and clinical treatment aimed to prevent sudden death.¹¹ These findings indicate that screening did not merely change the mode of death from exercise-related to exercise-unrelated, but actually reduced mortality during a long-term follow-up by identifying and disqualifying individuals who were at risk of cardiac arrest during sports.

The analysis of cost of screening goes beyond the scope of our study. We previously reported that the Italian screening program was made feasible because of the limited cost of first-line cardiovascular evaluation in the setting of a mass screening.⁷ The cost of performing a preparticipation cardiac history, physical examination, and 12-lead ECG by qualified physicians at an Italian sports medical center was estimated to be approximately 30 euros per athlete (approximately US \$40). The screening cost was self-covered by the athlete or his/her athletic team, except for athletes younger than 18 years, for whom the ex-

pense was entirely supported by the National Health System.⁷ In our study of 42 386 initially screened athletes, 3914 (9%) were referred for further examination and 879 (2%) were ultimately disqualified for cardiovascular reasons. Therefore, the percentage of false-positive results (ie, athletes with a normal heart but positive screening findings) requiring additional testing, mainly an echocardiogram, was 7% with modest proportional cost impact.

Athlete disqualification could be associated with an additional cost in terms of health, insurance coverage, contentment, and even future opportunities, including professional activity. However, the increased risk of sudden death, disease worsening, or both associated with athletic training and competition in the setting of known cardiovascular disorders is a controllable factor, and the devastating impact of even infrequent fatal events in the young athletic population justifies appropriate restriction from competition.⁴⁰

CONCLUSIONS

In conclusion, the incidence of sudden cardiovascular death in young competitive athletes has substantially declined in the Veneto region of Italy since the introduction of a nationwide systematic screening. Mortality reduction was predominantly due to a lower incidence of sudden death from cardiomyopathies that paralleled the increasing identification of athletes with cardiomyopathies at preparticipation screening. These data demonstrate the benefit of the current Italian screening program and have important implications for implementing screening strategies for prevention of sudden death in athletes in other countries.

Author Contributions: Dr Corrado had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Corrado, Basso, Thiene.
Acquisition of data: Corrado, Basso, Michieli, Schiavon, Thiene.

Analysis and interpretation of data: Corrado, Basso, Pavei, Michieli, Schiavon, Thiene.

Drafting of the manuscript: Corrado, Basso, Pavei, Michieli, Thiene.

Critical revision of the manuscript for important intellectual content: Corrado, Basso, Pavei, Schiavon, Thiene.

Statistical analysis: Corrado, Pavei, Michieli.

Obtained funding: Corrado, Basso, Thiene.

Study supervision: Schiavon, Thiene.

Financial Disclosures: None reported.

The Research Project "Sudden Death in the Young," Veneto Region of Northeastern Italy, 1979-2004 Medical Center Participants: Center for Sports Medicine and Physical Activity, Padua; Institutes of Pathological Anatomy and Forensic Medicine, University of Padua; Institutes of Pathological Anatomy and Forensic Medicine, University of Verona; Service of Pathological Anatomy Civil Hospital of Adria; Service of Pathological Anatomy, Civil Hospital of Arzignano; Service of Pathological Anatomy Civil Hospital of Asolo; Service of Pathological Anatomy Civil Hospital of Bassano; Service of Pathological Anatomy, Civil Hospital of Belluno; Service of Pathological Anatomy, Civil Hospital of Camposampiero; Service of Pathological Anatomy, Civil Hospital of Castelfranco Veneto; Service of

Pathological Anatomy, Civil Hospital of Chioggia; Service of Pathological Anatomy, Civil Hospital of Cittadella; Service of Pathological Anatomy, Civil Hospital of Dolo; Service of Pathological Anatomy, Civil Hospital of Este; Service of Pathological Anatomy, Civil Hospital of Feltre; Service of Pathological Anatomy, Civil Hospital of Mestre; Service of Pathological Anatomy, Civil Hospital of Montebelluna; Service of Pathological Anatomy, Civil Hospital of Pieve di Soligo; Service of Pathological Anatomy, Civil Hospital of Piove di Sacco; Service of Pathological Anatomy, Civil Hospital of Rovigo; Service of Pathological Anatomy, Civil Hospital of San Donà di Piave; Service of Pathological Anatomy, Civil Hospital of Thiene; Service of Pathological Anatomy, Civil Hospital of Treviso; Service of Pathological Anatomy, Civil Hospital of Venezia; Service of Pathological Anatomy, Civil Hospital of Vicenza.

Funding/Support: This study was funded by the

Veneto Region, Cardiocerebrovascular Pathology Registry, Venice, Italy; the European Commission research contract QLGI CT-2000 01091; the Ministry of Health, Rome, Italy; and Fondazione Cassa di Risparmio di Padova e Rovigo, Padova, Italy.

Role of the Sponsors: The sponsors did not participate in the design and conduct of the study, in the collection, analysis, or interpretation of the data, or in the preparation, review, or approval of the manuscript.

Previous Presentations: Presented in part at the Scientific Sessions of the American Heart Association, Dallas, Tex, November 13-16, 2005.

Acknowledgment: We thank Francesco Maddalena, MD, Department of Cardiac, Thoracic, and Vascular Sciences, University of Padua Medical School, for his advice on statistical and epidemiological analyses. Dr Maddalena was not compensated for his contribution.

REFERENCES

1. Maron BJ, Roberts WC, McAllister MA, et al. Sudden death in young athletes. *Circulation*. 1980;62:218-229.
2. Thiene G, Nava A, Corrado D, Rossi L, Pennelli N. Right ventricular cardiomyopathy and sudden death in young people. *N Engl J Med*. 1988;318:129-133.
3. Corrado D, Thiene G, Nava A, Pennelli N, Rossi L. Sudden death in young competitive athletes: clinicopathologic correlations in 22 cases. *Am J Med*. 1990;89:588-596.
4. Burke AP, Farb A, Virmani R, et al. Sports-related and non-sports-related sudden cardiac death in young adults. *Am Heart J*. 1991;121:568-575.
5. van Camp SP, Bloor CM, Mueller FO, et al. Non-traumatic sports death in high school and college athletes. *Med Sci Sports Exerc*. 1995;27:641-647.
6. Maron BJ. Sudden death in young athletes. *N Engl J Med*. 2003;349:1064-1075.
7. Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol*. 2003;42:1959-1963.
8. Corrado D, Basso C, Thiene G. Sudden death in young athletes. *Lancet*. 2005;366(suppl 1):S47-S48.
9. Glover DW, Maron BJ. Profile of preparticipation cardiovascular screening for high school athletes. *JAMA*. 1998;279:1817-1819.
10. Pfister GC, Puffer JC, Maron BJ. Preparticipation cardiovascular screening for US collegiate student-athletes. *JAMA*. 2000;283:1597-1599.
11. Corrado D, Basso C, Schiavon M, Thiene G. Screening for hypertrophic cardiomyopathy in young athletes. *N Engl J Med*. 1994;339:364-369.
12. Maron BJ, Thompson PD, Puffer JC, et al. Cardiovascular preparticipation screening of competitive athletes: a statement for health professionals from the Sudden Death Committee (clinical cardiology) and Congenital Cardiac Defects Committee (cardiovascular disease in the young), American Heart Association. *Circulation*. 1996;94:850-856.
13. Corrado D, Pelliccia A, Bjørnstad HH, et al. Cardiovascular preparticipation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol: Consensus Statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. *Eur Heart J*. 2005;26:516-524.
14. Tutela sanitaria delle attività sportive [Medical protection of athletic activities]. *Gazzetta Ufficiale della Repubblica Italiana*. December 23, 1971:8162-8164.
15. Decree of the Italian Ministry of Health, February 18, 1982. Norme per la tutela sanitaria dell'attività sportiva agonistica [rules concerning the medical protection of athletic activity]. *Gazzetta Ufficiale della Repubblica Italiana*. March 5, 1982:63.
16. Pelliccia A, Maron BJ. Preparticipation cardiovascular evaluation of the competitive athlete: perspectives from the 30-year Italian experience. *Am J Cardiol*. 1995;75:827-829.
17. Thiene G, Pennelli N, Rossi L. Cardiac conduction system abnormalities as a possible cause of sudden death in young athletes. *Hum Pathol*. 1983;14:704-709.
18. Richardson P, McKenna WJ, Bristow M, et al. Report of the 1995 WHO/ISFC Task Force on the definition and classification of cardiomyopathies. *Circulation*. 1996;93:841-842.
19. Mitchell JH, Maron BJ, Epstein SE. 16th Bethesda Conference: cardiovascular abnormalities in the athlete: recommendations regarding eligibility for competition. *J Am Coll Cardiol*. 1985;6:1186-1232.
20. Comitato Organizzativo Cardiologico per l'Idoneità allo Sport (COCIS). Protocolli cardiologici per il giudizio di idoneità allo sport agonistico. *G Ital Cardiol*. 1989;19:250-272.
21. 26th Bethesda Conference: recommendations for determining eligibility for competition in athletes with cardiovascular abnormalities: January 6-7, 1994. *J Am Coll Cardiol*. 1994;24:845-899.
22. Selvin S, ed. Poisson regression analysis. In: *Practical Biostatistical Methods*. Belmont, Calif: Duxbury Press; 1995:455-490.
23. Nistri S, Thiene G, Basso C, et al. Screening for hypertrophic cardiomyopathy in a young male military population. *Am J Cardiol*. 2003;91:1021-1023.
24. Pelliccia A, Di Paolo FM, Corrado D, et al. 2006 Evidence for efficacy of the Italian national preparticipation screening programme for identification of hypertrophic cardiomyopathy in competitive athletes. *Eur Heart J*. 2006;27:2196-2200.
25. Corrado D, Thiene G, Cocco P, Frescura C. Non-atherosclerotic coronary artery disease and sudden death in the young. *Br Heart J*. 1992;68:601-607.
26. Corrado D, Basso C, Poletti A, et al. Sudden death in the young: is coronary thrombosis the major precipitating factor? *Circulation*. 1994;90:2315-2323.
27. Basso C, Frescura C, Corrado D, et al. Congenital heart disease and sudden death in the young. *Hum Pathol*. 1995;26:1065-1072.
28. Basso C, Thiene G, Corrado D, et al. Arrhythmogenic right ventricular cardiomyopathy: dysplasia, dystrophy, or myocarditis? *Circulation*. 1996;94:983-991.
29. Corrado D, Basso C, Thiene G, et al. Spectrum of clinicopathologic manifestations of arrhythmogenic right ventricular cardiomyopathy/dysplasia: a multicenter study. *J Am Coll Cardiol*. 1997;30:1512-1520.
30. Basso C, Maron BJ, Corrado D, Thiene G. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. *J Am Coll Cardiol*. 2000;35:1493-1501.
31. Basso C, Thiene G, Corrado D, et al. Hypertrophic cardiomyopathy: pathologic evidence of ischemic damage in young sudden death victims. *Hum Pathol*. 2000;31:988-998.
32. Basso C, Corrado D, Rossi L, Thiene G. Ventricular preexcitation in children and young adults: atrial myocarditis as a possible trigger of sudden death. *Circulation*. 2001;103:269-275.
33. Corrado D, Basso C, Buja G, et al. Right bundle branch block, right precordial ST-segment elevation, and sudden death in young people. *Circulation*. 2001;103:710-717.
34. Basso C, Calabrese F, Corrado D, Thiene G. Post-mortem diagnosis in sudden cardiac death victims: macroscopic, microscopic and molecular findings. *Cardiovasc Res*. 2001;50:290-300.
35. Corrado D, Basso C, Thiene G. Sudden cardiac death in young people with apparently normal heart. *Cardiovasc Res*. 2001;50:399-408.
36. Teare D. Asymmetrical hypertrophy of the heart in young adults. *Br Heart J*. 1958;20:1-18.
37. Frank S, Braunwald E. Idiopathic hypertrophic subaortic stenosis: clinical analysis of 126 patients with emphasis on the natural history. *Circulation*. 1968;37:759-788.
38. Maron BJ. Hypertrophic cardiomyopathy: a systematic review. *JAMA*. 2002;287:1308-1320.
39. Marcus FI, Fontaine GH, Guiraudon G, et al. Right ventricular dysplasia: a report of 24 adult cases. *Circulation*. 1982;65:384-398.
40. Maron BJ, Zipes DP. Introduction: eligibility recommendations for competitive athletes with cardiovascular abnormalities—general considerations. *J Am Coll Cardiol*. 2005;45:1318-1321.