EDITORIAL COMMENT

Identifying Athletes at Risk for Sudden Death*

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In this issue of the Journal, Corrado et al. (1) have described a prospective cohort study conducted in Veneto Region of Italy from 1979 to 1999 comparing sudden death (SD) in competitive athletes versus non-athletes in the range of 12 to 35 years of age. The study was well powered at approximately 29,000,000 person-years. The prospective cohort design was also optimal in addressing the study question, drawing on a comprehensive sports medicine database and using a small and experienced group of cardiac pathologists to provide a highly accurate final diagnosis. In the unique Veneto database, all participants ages 12 to 35 years in an organized sports program requiring regular training and competition underwent a preparticipation and subsequent yearly history, physical examination, resting and (limited) exercise electrocardiogram, and pulmonary function studies by a registered sports medicine specialist, as required by Italian law (2). The population in this region is predominately white and ethnically homogeneous. After initial postmortem examination at regional medical centers, all cardiac specimens were examined at the Institute of Pathological Anatomy of the University of Padua. The findings were conclusive for the following: 1) young competitive athletes were at significantly increased risk of all types of SD compared with non-athletes (relative risk = 2.5); 2) the increased risk of all types of SD among athletes was observed in both males and females (although not statistically significant in females); and 3) SD tends to be exercise related and attributable to underlying cardiovascular pathology in competitive athletes. Relative risk of cardiovascular SD among athletes compared with non-athletes is 2.8. Again, the increased risk of SD from cardiovascular diseases was observed in both males and females. This study was able to illustrate more definitively than other studies to date that participation in competitive sports is associated with a higher risk of SD in patients with a wide range of asymptomatic cardiac disorders by sorting out the confounding effects of male:female ratio among athletes and non-athletes. Using Poisson regression analysis, no interaction between sports participation and gender was found to be significant. This study benefits from two distinct advantages over previous studies on this subject. First, some form of preparticipation screening has been mandated in Italy for over 50 years and since 1971 has included a yearly comprehensive examination of both competitive and non-competitive athletes. These evaluations are performed by specifically trained physicians who are registered with the Italian Sports Medicine Foundation (3). Thus, universal preparticipation screening is entrenched in the culture, and there is less likelihood for selection bias associated with other cultural or economic variables. Second, the pathologic studies of the heart specimen were performed by a single program with impeccable technique in evaluating coronary anatomy. These lesions may not be detected by the more routine pathologic examination and, without such a rigorous methodology, may be under appreciated as a cause of SD.

The use of person-years as an analytical unit may lead to subtle biases. However, we think these biases may lead to a more conservative estimate of SD risk for athletes and thus not invalidate the authors’ conclusions based on the study. Consider an individual who participated in sports at a highly competitive level in high school and college but had withdrawn from competitive sports because of injury at age 22. This individual will contribute 9 person-years to the athletic subsample and 14 person-years to the non-athletic subsample. Suppose this individual died suddenly at age 35 from a coronary event; the SD event will be counted as non-athlete SD, thus biasing the result. One can conceive of other situations where the bias may occur in the opposite direction. The likelihood of occurrence for each situation will ultimately determine the direction of bias of the final estimate.

Although this is a persuasive study, we believe that its results and conclusions may not be completely generalizable to the scale and diversity of the U.S. population for three reasons. First, this study population is almost homogeneously white, whereas the U.S. athletic pool is racially, ethnically, and culturally diverse. Each racial and ethnic subgroup of athletes may have differential risks for underlying cardiovascular risks and SD risks. For example, the population in Italy has a high incidence of arrhythmogenic right ventricular dysplasia, which is thought to be the cause of death in 15% of the patients in this study. In the U.S., a large number of competitive athletes at the high school and collegiate level are African American. Studies have shown that among U.S. athletes with SD, 52% are white and 44% are African American (4). The most common structural cardiovascular finding attributable to SD in U.S. athletes is hypertrophic cardiomyopathy (HCM), which is disproportionately more prevalent in African American athletes; in fact, recent papers published by Maron et al. (5,6) showed that nearly half of athletes who experienced SD were...
African American. In contrast, HCM is an infrequent attributable cause of SD (1 of 51) of Italian athletes in the current study. Second, the definition of a young competitive athlete may not be consistent between the U.S. and Italy. The study defines young competitive athletes as adolescents and young adults who participated in an organized sports program requiring regular training and competition (according to Italian guidelines for sports medicine). The terms, "organized sports program," "training," and "competition" are somewhat subjective and describe a wide range of intensity and type of exercise, including such activities as tennis, platform diving, fencing, and archery. On the same theme, the competitive structure and training practices around soccer in community settings can be quite different from the competitive structure surrounding collegiate basketball or football. Whereas in the study by Corrado, the most common competitive sport involved in SD was soccer, the most common competitive sports involved in SD for U.S. athletes are basketball and football. Recent findings from Maron et al. (4) showed that about two-thirds of all SDs in the U.S. were related to football or basketball. Third, the genetic predisposition, dietary pattern, and environmental compositions of Italians are distinctly different from those of Americans, even among adolescents and young adults.

Another issue of interest is the apparent uniform quality of the preparticipation screening and protocol required by Italian law in contrast to the U.S., where exercise recommendations to athletes are based largely on the intuition of the individual physician. In the U.S., there is great regional variation in the manner of preparticipation screening compared with the Corrado study, but it must be remembered that the Veneto region of Italy has a population of a little more than four million people, roughly the same as Cook County, Illinois or half the population of North Carolina, a scale that lends itself to more uniformity and coordination.

The American Heart Association recommends that "[S]ome form of preparticipation cardiovascular screening for high school and collegiate athletes is justifiable and compelling, based on ethical, legal, and medical grounds. Noninvasive testing can enhance the diagnostic power of the standard history and physical examination; however, it is not prudent to recommend routine use of such tests as 12-lead ECG, echocardiography, or graded exercise testing for detection of cardiovascular disease in large populations of athletes" (7).

The costs of such a strategy would be difficult to justify, particularly because the accuracy of the echocardiographic diagnosis of arrhythmogenic right ventricular dysplasia, acquired cardiovascular disease, anomalous origin of the coronary artery, and myocardial bridge depends greatly on skill and experience in the performance and evaluation of the echocardiographer. These lesions accounted for 30 of 46 deaths among the male athletes in this study. Furthermore, 5 of 46 deaths among the male athletes were attributed to myocarditis, a condition that would likely occur after a preparticipation evaluation. The economic and emotional costs of universal laboratory screening would be increased by false-positive findings and misinterpretation of the physiologic changes related to training, particularly in discriminating between physiologic increases in left ventricular wall thickness and mass in the elite athlete and HCM. On the other hand, given the higher proportion of HCM found in U.S. athletes with SD, it is likely that a careful family and personal history of cardiac symptoms, followed by echocardiographic evaluation of all suspicious reports and regular follow-up history of symptoms, would bring about an improvement in the detection of individuals at risk for SD with strenuous exercise (7–11). There will always be borderline findings in which there is no meaningful data to support whether or not restriction of such individuals from competitive athletics would reduce their risk for SD. In the absence of an unbiased exploration of this question, clinical reason will have to suffice.

The difference between male and female risk for SD is interesting and fertile soil for future study. There may be differences in the risks for certain conditions, the time course of disease, or the degree of myocardial hypertrophy. Among other possible explanations are sociologic (reluctance to complain of symptoms), economic (greater impact on future wage-earning in high-profile sports), or attentional factors (greater sensitivity to internal environment). Whatever the cause of these differences, it is important to avoid inappropriate applications of findings about one gender to the other.

In light of the information provided by Corrado et al. (1), we as cardiologists should press on with exploration of more reliable and affordable methods of detecting individuals at risk for SD during sports activities. This is a daunting task, considering the wide variability in expertise in diagnosing rare cardiac lesions and the immense economic pressure placed on and by the sports industry in this country. Nevertheless, this study illustrates that sensitive recognition of cardiac abnormalities by preparticipation screening, if followed by exclusion from competitive sports, will reduce mortality from SD. It also demonstrates that the systematic case finding and analysis within a comprehensive and well-organized health care system, when fed back to the practitioner through continuing education, can effect a major improvement in detection of individuals at risk. This knowledge will lead to an improved understanding of the risks involved in athletic competition among individuals with lesions predisposing to SD. The human and economic costs of effective screening will undoubtedly be the subject of studies for years to come. Second, for those individuals considered at risk, the likelihood of SD is truly greater with participation in competitive sports, a finding that must be taken into consideration by individuals, the sports community, educational systems, and health care providers.
REFERENCES