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Etiology of Sudden Death in Sports

Insights From a United Kingdom Regional Registry

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ABSTRACT

BACKGROUND Accurate knowledge of causes of sudden cardiac death (SCD) in athletes and its precipitating factors is necessary to establish preventative strategies.

OBJECTIVES This study investigated causes of SCD and their association with intensive physical activity in a large cohort of athletes.

METHODS Between 1994 and 2014, 357 consecutive cases of athletes who died suddenly (mean 29 ± 11 years of age, 92% males, 76% Caucasian, 69% competitive) were referred to our cardiac pathology center. All subjects underwent detailed post-mortem evaluation, including histological analysis by an expert cardiac pathologist. Clinical information was obtained from referring coroners.

RESULTS Sudden arrhythmic death syndrome (SADS) was the most prevalent cause of death (n = 149 [42%]). Myocardial disease was detected in 40% of cases, including idiopathic left ventricular hypertrophy (LVH) and/or fibrosis (n = 59, 16%); arrhythmogenic right ventricular cardiomyopathy (ARVC) (13%); and hypertrophic cardiomyopathy (HCM) (6%). Coronary artery anomalies occurred in 5% of cases. SADS and coronary artery anomalies affected predominantly young athletes (≤ 35 years of age), whereas myocardial disease was more common in older individuals. SCD during intense exertion occurred in 61% of cases; ARVC and left ventricular fibrosis most strongly predicted SCD during exertion.

CONCLUSIONS Conditions predisposing to SCD in sports demonstrate a significant age predilection. The strong association of ARVC and left ventricular fibrosis with exercise-induced SCD reinforces the need for early detection and abstinence from intense exercise. However, almost 40% of athletes die at rest, highlighting the need for complementary preventive strategies. (J Am Coll Cardiol 2016;67:2108–15) © 2016 by the American College of Cardiology Foundation.

Sudden cardiac death (SCD) is a tragic event that occasionally affects apparently healthy individuals (1), including young (≤35 years of age) athletes (2–5). A spectrum of cardiac diseases is implicated in SCD, with variable prevalence depending on the age and other demographics of the cohort (6). Many reports regarding the causes of SCD in athletes are limited by the lack of a detailed post-mortem examination performed by an experienced cardiac pathologist. A recent study comparing the interpretation of autopsy findings between a referring pathologist and a specialist cardiac pathologist demonstrated a 40% disparity with respect to actual cause of death (7).

Knowledge of precise causes and precipitating factors of SCD may influence national strategies to

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prevent such events, including pre-participation screening methods and widespread availability of automated external defibrillators (AEDs). Pre-participation screening with electrocardiography (ECG) is useful for detecting quiescent inherited cardiac diseases, particularly inherited cardiomyopathies, and ion-channelopathies but has limited value in detecting athletes with coronary artery disease (CAD). AEDs appear to be more effective in the termination of arrhythmias in athletes with CAD or coronary artery anomalies than in athletes with cardiomyopathy (8,9).

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The objective of this study was to investigate the causes and circumstances of SCD in a large cohort of athletes, as determined by post-mortem examination performed by an expert cardiac pathologist.

METHODS

The Cardiac Risk in the Young (CRY) center for cardiac pathology is located at St. George's University of London. The center is led by an expert cardiac pathologist (M.N.S.) and receives over 400 whole hearts from cases of SCD across the United Kingdom annually. General pathologists are likely to refer to the CRY center when the clinical history is suggestive of inherited cardiac disease, especially when the death affects a young or athletic individual or when the cause of death is uncertain after the initial autopsy.

STUDY POPULATION. We retrospectively reviewed cases from a database of 3,684 cases of SCD referred to the CRY center for cardiac pathology between 1994 and 2014. SCD was defined as death occurring within 12 h of apparent wellbeing. We retrieved a subgroup of 357 cases (9.7%) of individuals who had engaged in regular sport activities, defined as >3 h of organized physical training per week. The majority (84%) of referrals occurred between 2004 and 2014. Competitive athletes were defined as those who were involved in organized sports requiring participation in regular, formal competition. Circumstances of death were subdivided broadly into death occurring during exercise and death during rest or sleep.

POST-MORTEM EXAMINATION. All SCD cases underwent a full post-mortem evaluation by the local pathologist. Following the exclusion of extra-cardiac causes, the heart was sent to our center after written consent of the coroner and the family of the deceased. The local pathologist also performed an initial cardiac autopsy before referring the heart in 58% of cases. A thorough toxicology screen was conducted in all cases in accordance with the usual investigation of sudden and unexpected deaths in the United Kingdom. Comprehensive macroscopic examination of the whole heart and histological analysis were performed in accordance with guidelines on "Autopsy practice for sudden death with likely cardiac pathology" of the Royal College of Pathologists (10) and the Association for European Cardiovascular Pathology (11). All cardiac structures were systematically examined. Heart weight was recorded in grams, and ventricular wall thickness and internal cavity dimensions were measured at mid-ventricular level, excluding the papillary muscles and fat. A minimum of 10 blocks of tissue were taken for histological analysis as reported previously (6,7). Sections of myocardium were fixed in formalin, embedded in paraffin, and stained with hematoxylin and eosin and with elastic Van Gieson stain to highlight myocardial fibrosis.

Criteria for defining specific cardiac pathologies have been previously described (6,12) and are summarized in **Table 1**. Sudden arrhythmic death syndrome (SADS) was a diagnosis of exclusion, defined as a structurally normal heart with no evident abnormality on macroscopic and histological evaluation and a negative result for toxicology screening (13–15).

CLINICAL INFORMATION. The referring coroner and pathologist were asked to complete a questionnaire regarding the demographics of the deceased, medical history, family history, cardiac symptoms, nature and level of physical activity, and exact circumstances of death. Data were derived from a number of sources including: interviews with the family of the deceased, potential witnesses to the SCD, and reports from the deceased's family physician. Data were collected prospectively and stored in an electronic database.

STATISTICAL ANALYSIS. Statistical analysis was performed using PASW version 18.0 software (PASW, Inc., Chicago, Illinois). Results are mean ± SD for continuous variables or numbers of cases and percentages for categorical variables. Comparison of groups was performed using Student *t* test for continuous variables with correction for unequal variance when necessary and chi-square test or Fisher exact test, as appropriate for categorical variables. Univariate and multivariate logistic regression analyses were used to determine the factors associated with death during exertion. Age, sex, and variables that were univariately correlated with the dependent variable were selected and entered into the forward stepwise multiple regression model.

ABBREVIATIONS AND ACRONYMS

AED = automatic external defibrillator

ARVC = arrhythmogenic right ventricular cardiomyopathy

CAD = coronary artery disease

HCM = hypertrophic cardiomyopathy

LV = left ventricular

LVH = left ventricular hypertrophy

SADS = sudden arrhythmic death syndrome

SCD = sudden cardiac death