

Sudden Cardiac Arrest in a Young Population: Not So Unpredictable

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“A 6-foot-8, 260-pound forward, Lewis collapsed in the second half of Division II Southern Indiana’s road win over rival Kentucky Wesleyan on January 14, 2010. He died, they would learn later, due to a heart condition he never knew he had.”¹ Highly publicized events such as this promote a common perception that young people who die suddenly tend to be athletes with undiagnosed heart disease. Prior studies have added to this misperception with data suggesting that most victims die of hypertrophic cardiomyopathy. Because study populations often are adolescent athletes, exercise was found to be a major trigger.² Two recent population-based studies of all cardiovascular-related sudden cardiac arrest (SCA) in people 0 to 35 years of age concluded that most events occur during nonathletic activities, and hypertrophic cardiomyopathy was not the most common cause of arrest.^{3,4} A surprising finding was the presence of cardiovascular risk factors (obesity, smoking, hyperlipidemia) in a high percentage of the victims.⁴

In this issue of the *Journal of the American Heart Association (JAHA)*, Allan et al have extended these studies with complete evaluation of all pertinent data from victims aged 2 to 45 years in Toronto (Ontario, Canada), the largest metropolitan area of these 3 studies.³⁻⁵ The data were collected from the Rescu Epistry, a database developed from the Resuscitation Outcomes Consortium Cardiac Epistry and Strategies for Post Arrest Resuscitation Care. Rescu Epistry links emergency medical systems (EMS) data with hospital data and captures all patients for whom a 911 call was made

in a metropolitan area of 6.8 million people. The study population consisted of all out-of-hospital cardiac arrests, aged 2 to 45 years, that were presumed cardiac cause as defined by the Utstein criteria,⁶ as well as drownings and motor vehicle collisions that could have been caused by an SCA. The investigators undertook a comprehensive review of each case, which included EMS and in-hospital data, as well as police reports, death certificates, coroner investigation statements, and autopsies, some of which included toxicology and molecular autopsies. In this jurisdiction, autopsies are performed by a forensic pathologist. When potential cardiac disease is detected, the heart is referred to a cardiovascular pathologist. Furthermore, complete toxicological studies were performed whenever the cause of death was not evident or there was an indication that drugs may be contributory. A coroner, pathologist, and toxicologist participated in the adjudication process if toxicology was positive. A strength of this investigation was autopsy data on 82% of the deceased victims and an analysis of noncardiac diagnoses and medications either prescribed or detected.

The final study population comprised 608 subjects who had a verified cardiac cause. The investigators found that 68% had a previously known cardiac diagnosis or had been prescribed a cardiac medication, 55% had ≥ 1 cardiovascular disease risk factor, and 20% had a psychiatric diagnosis or a prescribed psychotropic medication. The most frequent cardiac diagnosis was coronary heart disease (CHD) (40%), followed by structural disease of the myocardium (29%), whereas 16% were unexplained deaths. Most subjects with CHD were aged >35 years (52%), but of those aged 25 to 34 years, 16% had diagnosable CHD. The events were more common during sedentary activities (73%) and within private residences (72%).

This study greatly broadens our understanding of the epidemiological characteristics of sudden cardiac death in the young. It is the largest complete assessment of the causes and associations related to SCA in the young. The upper age limit was extended to 45 years, instead of 35 years, to maximize the inclusion of inheritable heart disease. The population is skewed to the higher age group and, thus, provides data on an age bracket that is often combined with an older population. The thorough postarrest evaluation,

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including an admirable rate of high-quality postmortem examinations, toxicology studies, and especially the inclusion of prescribed and over-the-counter medications, reveals that previous studies may have overestimated the frequency of undiagnosed heart disease.

Although the range of cardiac diagnoses encountered include those with a recognized risk of SCA in the young (arrhythmic inheritable disease, congenital anomalies, and cardiomyopathies), the most common diagnosis was CHD in 53% of those aged 35 to 45 years and 16% of those aged 25 to 35 years. Both men and women were represented in the CHD group, a finding that is surprising and disturbing. The frequency of cardiovascular disease risk factors was also ominously high and similar to what was observed in Portland, Oregon,⁴ which may predict a growing risk of SCA in middle age, <65 years. Even in the 2 to 24 years age group, 13% had cardiovascular risk factors. The presence of cardiovascular risk factors in childhood tracks into adulthood and predicts coronary artery calcification and atherosclerotic heart disease.⁷ Thus, efforts directed at children and young adults to reduce the prevalence of cardiovascular risk factors may lessen the risk of SCA. Moreover, dietary and exercise interventions have been shown to be safe and effective even in young children.^{8,9}

With growing evidence that many previously unclassified cardiomyopathies have a genetic basis,¹⁰ and a persistent finding of unexplained deaths in autopsy series, the emergence of the molecular autopsy has great potential to enrich the yield of postmortem examinations, explaining ≈30% of autopsy-negative studies. In addition, it is useful in situations of newly diagnosed genetic disease because the likelihood of identifying a causative mutation will be greatest in the deceased person.¹¹ Although molecular autopsies were included in this study, there was no indication of how frequently they were performed, nor how frequently a diagnosis was confirmed. In the United States, molecular autopsies are rarely performed outside of research laboratories because of the cost. However, the American Heart Association suggests genetic analysis be completed when a cause of death cannot be determined.¹² Cascade testing can be lifesaving for family members, where 25% to 50% of first-degree relatives are likely affected, and as well as a substantial percentage of second- and third-degree relatives. As the importance of genetics and personalized medicine increases, the cost of identifying causative mutations should decline.

The prevalence of psychiatric disease with SCA has been previously observed in Scandinavia,^{13,14} but Allan et al are the first to make the observation in North America.⁵ Psychiatric disease, defined herein as a premortem diagnosis or evidence of prescriptions for psychotropic medications, was present in 20% of the victims. Both depression and psychoses were more frequent than in the general Canadian population. Is there a causal relation, as the authors suggest? Schizophrenia is known

to increase the risk of SCA,¹⁵ and psychotropic drugs are well recognized to prolong the QT interval and increase the risk of ventricular arrhythmias, even with therapeutic levels. Adding to the complexity of the analysis is the frequency of polypharmacy, a common occurrence in patients with psychiatric disease and those who experience SCA.¹⁶ However, the relationship among psychiatric disease, the central nervous system, and SCA is likely far more complex and involves more than just autonomic control of heart rate and rhythm.¹⁷ This is a promising area for study, and the authors are commended for the inclusion of these data.

The Utstein criteria for out-of-hospital cardiac arrest⁶ were used by trained data abstractors to make an initial assignment of SCA cause from EMS and in-hospital data. The Utstein criteria have provided a valuable tool for cardiac arrest research, with standardized definitions and a structured framework for data collection for EMS agencies, registries, and clinical trials. Of the 2937 events initially labelled as presumed cardiac, 2167 were adjudicated as other causes after complete review of medical or autopsy records. This illustrates the importance of comprehensive adjudication reviews, such as that of Allan et al,⁵ but also highlights potential shortcomings of using only EMS or registry data to make robust conclusions or recommendations about SCA and cardiopulmonary resuscitation (CPR). An example would be to instruct EMS to provide “personalized CPR” based on their assessment of cardiac versus noncardiac cause. EMS providers must make rapid assessments and cannot be expected to distinguish a definite cardiac event from other causes within the seconds before CPR initiation. Despite these recognized shortcomings, registry data serve as a starting point to understand processes and trends in SCA, as recommended by the 2015 Institute of Medicine report on SCA.¹⁸ A national registry to be inclusive of rural and urban areas, the diversity of ethnic and racial origins in the United States, and the variations with EMS systems will provide a better assessment of SCA throughout the United States and can be used for both quality improvement and research activities.

In this highly coordinated EMS system, the survival rate was 21%, higher than the US national average but still below what we know is achievable. The Institute of Medicine report¹⁸ stressed the role of bystander CPR and the need to develop a “culture of action.” Although CPR courses have been readily accessible to the lay public, many have never taken advantage of these opportunities and the number of trained individuals remains inadequate. We have relied on mass training, such as high school students, mass training events, or individual initiative. However, most SCA events occur in private residences and only family members, often 2 to 4, will be available to provide CPR. The high percentage of patients in this study who had either previously diagnosed CHD or cardiovascular risk factors indicates a likely interaction with a healthcare provider. We miss an excellent

opportunity to protect these patients by not confirming that family members know CPR. Although programs have established that family members can learn CPR,^{19,20} these are primarily hospital based. Training within clinics and physician offices could provide an easy and validated method to train those most likely to witness an SCA event. Physician encouragement of family members would likely increase the training rate and the probability that a person with heart disease is protected by someone trained in CPR. Using the training model of video self-instruction kits, which are inexpensive and can train multiple people on either chest compression only or conventional CPR with rescue breaths (recommended for those aged <18 years), areas in physician offices can be dedicated to this purpose. CPR can be taught, demonstrated, and practiced in a short period, requiring minimal staff time. This could easily be accomplished by family members during the patient testing (echocardiogram).

SCA, once thought to be rare in the young and related to inherited or congenital processes, is far more complex; and in food-rich societies, it is now increasingly related to preventable causes in all age populations. This study identifies populations for whom we need to focus additional energies: along with dietary and exercise recommendations, efforts to encourage CPR training could have a measurable effect on SCA outcomes. Standardized data collection within registries has produced much knowledge about SCA the past 15 years. That, along with the follow-up review and adjudication, as done herein, will continue to expand our knowledge to both prevent and more effectively treat cardiac arrest.

Disclosures

None.

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