

Sudden Cardiac Death in the Young

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Abstract—Although the occurrence of sudden cardiac death (SCD) in a young person is a rare event, it is traumatic and often widely publicized. In recent years, SCD in this population has been increasingly seen as a public health and safety issue. This review presents current knowledge relevant to the epidemiology of SCD and to strategies for prevention, resuscitation, and identification of those at greatest risk. Areas of active research and controversy include the development of best practices in screening, risk stratification approaches and postmortem evaluation, and identification of modifiable barriers to providing better outcomes after resuscitation of young SCD patients. Institution of a national registry of SCD in the young will provide data that will help to answer these questions. (*Circulation*. 2016;133:1006-1026. DOI: 10.1161/CIRCULATIONAHA.115.020254.)

Key Words: congenital heart disease ■ death, sudden, cardiac ■ heart arrest ■ pediatrics ■ resuscitation

Few medical events are more traumatic than the sudden, unanticipated death of a young person. Sudden cardiac death (SCD) is statistically uncommon in the young, but its dramatic presentation and cascading effects in the family and community make it a newsworthy event. Widely publicized cases of SCD in athletes personify the metaphor of hidden vulnerability lurking in the body of a vigorous, healthy young person. There is a high degree of concern regarding the risk of SCD in children and teenagers among the lay public, in comparison with other much more prevalent deadly risks of childhood, such as accident, injury, suicide, and violence (Figure 1). Nonetheless, it is fair to consider SCD in the young as a public health issue, and to develop strategies based on evidence and expert consensus to mitigate it.

This review will examine the current state of knowledge and practice regarding SCD in the young. This will include the pathophysiology of SCD, the disease processes that predispose to it – especially among asymptomatic youth – and strategies for resuscitation and identification of those at risk. Because many major etiologies of SCD in the young are genetically determined, the sudden death of a young person must often be studied within the context of the family. Advances in cardiovascular genetics have added both molecular insight and new levels of complexity and ambiguity to our understanding of affected families. Both pre-mortem and post-mortem genetic testing now promise disease-specific risk assessment and therapy for the surviving relatives of the SCD patient. Finally, SCD in the young is an event that affects the community. These events demand public health policy responses to provide rational and effective strategies to protect our youth against rare but dramatic events. Such strategies might include programs of cardiovascular screening, innovations in the deployment

of public access defibrillation, the development of standards for postmortem investigation of SCD, and the institution of regional and national registries of SCD in the young.

Given such a broad scope, this review will be limited in depth, in general, and, in particular, with respect to the various SCD-predisposing cardiac etiologies (including congenital heart disease). An exception to this will occur in the sections on the science, epidemiology, and outcomes of resuscitation. These will focus on the phenomena around out-of-hospital cardiac arrest, and will be drawn from and more widely applicable to the larger topic of pediatric sudden death in the community. Conversely, the basic knowledge of cardiac etiologies associated with SCD in the young is widely available and will be reviewed succinctly. Pathophysiology and prevention of Sudden Infant Death Syndrome, defined as an infant death unexplained after a thorough case investigation,¹ is also outside the scope of this review, although it includes some deaths attributable to cardiac causes such as channelopathies.² Finally, it is not the intention of this review to repeat or summarize expert consensus recommendations relevant to this broad topic that have been published in several recently published guideline documents. These guideline statements include cardiopulmonary resuscitation,³⁻⁶ implantable cardioverter-defibrillator (ICD) implantation,⁷ evaluation and management of cardiomyopathies^{8,9} and channelopathies,^{10,11} stimulant medication use,^{12,13} screening,^{14,15} and sports eligibility.^{10,16-19}

Epidemiology and Etiologies of SCD in the Young

Epidemiology

SCD is uncommon in children, and, in general, it requires carefully designed, regional, or multicenter studies to generate

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accurate statistics regarding incidence and risk factors. Table 1 presents the incidence of SCD in a variety of younger populations and settings. This highlights the variation inherent in these estimates, and also clearly indicates that the rate of SCD in children is 1 to 2 orders of magnitude less than that seen in the adult population, with incidence ranging from <1 to 10 deaths/100 000 population per year (with exclusion of infants and persons >18 years of age, <1–4 deaths/100 000 population per year). The burden of SCD in terms of lost life-years is disproportionately larger for children because of their greater life expectancy. These statistics are necessary to formulate useful public health policy for the early detection, prevention, and delivery of therapies. Relevant factors include age, sex, presence of comorbid disease, geographic region, and participation in athletic activity.

Population-based studies with a large, well-defined denominator are the gold standard for determining SCD incidence. Because SCD is infrequent in the young, such studies must survey national or regional populations over extended periods. Most have been based on retrospective analyses of administrative databases, use of emergency medical services (EMS) databases, or ad hoc means such as Internet searches or news media review.²⁰ This introduces ascertainment uncertainty with respect to both over- and underdiagnosis. A prospective analysis of SCD in patients of all ages suggested that ascertainment based on death certificates tended to overestimate SCD events.²¹ Case series of SCD allow excellent ascertainment of affected cases and are useful for defining etiology and mechanisms. They also provide an estimate of the absolute magnitude of the problem, but they cannot reliably quantify the denominator population.

Recently, voluntary prospective registries have been developed to monitor the occurrence of SCD in the young over an extended period in stable populations. This approach addresses some of the specific weaknesses of previous techniques by using a prospective and problem-specific approach to ensure relative accuracy and completeness of data available for review. A national registry is in development by the National Institutes of Health in conjunction with the Centers for Disease Control and Prevention for sudden unexpected deaths in a young population in a number of regions, an effort likely to be broadened in the future.³⁹ Much of our current knowledge has been generated from local data collection or research registries that are inclusive of all ages and causes.^{37,40–42}

Important demographic characteristics relevant to the occurrence of SCD in young populations can be derived from available data. First, the prevalence of sudden unexpected death, in general, and SCD, in particular, is age dependent. After an initial period of higher risk of unexpected death in early infancy (largely because of noncardiac causes and Sudden Infant Death Syndrome), the prevalence of SCD falls in early childhood and begins to rise again in adolescence. An example of this from 1 large national study identifying 114 cases of SCD in children ages 1 to 18 comprising nearly 8 million patient-years of observation is presented (Figure 2). Similar findings have been observed in comprehensive surveys from Ontario and 10 North American sites making up the Resuscitation Outcomes Consortium.^{36,43}

These studies also confirm that SCD is significantly more prevalent in young males, by a factor of $\approx 2:1$.^{33,35,43} Less clear is whether ethnicity is associated with increased overall risk or differing patterns of age and sex dependence of SCD in the young. Black newborns and infants have an elevated risk of postneonatal mortality associated with a variety of noncardiac causes, including Sudden Infant Death Syndrome,⁴⁴ and race also appears to be a risk factor in SCD in adults⁴⁵ and in National Collegiate Athletic Association (NCAA) athletes.^{46,47} However, etiologies underlying SCD in these other age groups are different from those responsible for SCD in youth. It may thus be incorrect to infer similar ethnic disparities until further population-based research is performed.

SCD Associated With Identifiable Cardiovascular Disorders

Case series methodology has been used effectively to classify cardiovascular diseases that underlie SCD in the young. Knowledge of the relative prevalence of the underlying diseases also allows for estimation of the relative risks of cardiac arrest. General etiologic categories include heritable and acquired cardiomyopathies and arrhythmia syndromes (channelopathies), structural congenital heart diseases, myocarditis, and coronary abnormalities. In any given patient, these underlying diagnoses may be known, or they may be undiagnosed and presymptomatic. The proportion of detected versus undetected risk of SCD varies by diagnosis, as does our ability to mitigate risk of cardiac arrest by prophylactic therapy and other preventative measures. These 2 factors strongly affect the utility of diagnostic screening in asymptomatic individuals, a topic that will later be discussed at greater length in this article.

Heritable and Acquired Cardiomyopathies and Channelopathies

The heritable cardiomyopathies including hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), dilated cardiomyopathy, and left ventricular noncompaction cardiomyopathy and the heritable channelopathies including long QT syndrome (LQTS), short QT syndrome, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia are potentially lethal but highly treatable genetic heart diseases. The estimated

Mortality Rates Among Children Aged 1–14, by Selected Leading Cause and Age, 2010

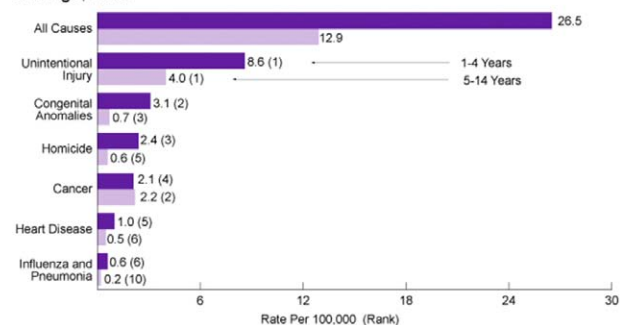


Figure 1. Causes of death in American children. Mortality rates among children 1 to 14 years of age, by selected leading cause and age, 2010.

Table 1. Population-Based Estimates of SCD Incidence in the Young

Study	Patient Group	Age Range, y	SCD Incidence (per 100 000 Patient-Years)	Comments
Molander et al ²²	All unexpected deaths, southern Sweden	1–20	0.7	≈15% SCD
Driscoll et al ²³	Death certificate survey, Olmsted County, Minnesota	1–22	1.3	>50% sudden death cardiac related
Gerein et al ²⁴	Cardiopulmonary arrest patients, Ontario, Canada	<17	1.5 (9.1 all arrests)	16% deemed attributable to cardiac causes
Puranik et al ²⁵	Forensic office review of sudden death, Eastern Sydney, Australia	5–35	1.0	29% autopsy negative
Chugh et al ²⁶	Sudden death survey, Multnomah County, Oregon	1–17	1.7	Same study included infants, accounting for 76% of all events
Park et al ²⁷	Out-of-hospital cardiac arrest, Korea	<19	4.2	Includes ≈25% infants, ≈30% deemed cardiac
Papadakis et al ²⁸	Sudden deaths, England and Wales	1–34	1.8	14% classified as SCD
Hendrix et al ²⁹	Death certificate survey, 12 Dutch provinces	1–40	1.6	Increased rate in patients >30 y
Winkel et al ³⁰	Sudden deaths, Denmark	1–35	1.9–2.8	Dependent on assignment of nonautopsy cases
Margey et al ³¹	Sudden death statistics, Republic of Ireland	15–35	2.9	Sudden unexplained death 27%, hypertrophic cardiomyopathy 15%
Wren et al ³²	All deaths, 1 English health region	1–20	2.5	Half of SCD associated with prior known diagnosis
Winkel et al ³³	All deaths, Denmark	1–18	1.5	No prior medical history in two-thirds of cases
Bardai et al ³⁴	Out-of-hospital, province in the Netherlands	<21	3.2 (9.0 all arrests)	39% cardiac etiology
Meyer et al ³⁵	Out-of-hospital, King County, Washington	<35	2.3	In patients >25 y, coronary artery disease primary cause
Atkins et al ³⁶	Out-of-hospital, multiple US districts	1–11	3.73	Resuscitation Outcomes Consortium
Atkins et al ³⁶	Out-of-hospital, multiple US districts	12–18	6.4	Resuscitation Outcomes Consortium
Kitamura et al ³⁷	Out-of-hospital, Japan	<12	2.4 (female) 3.3 (male)	Nationwide registry of OHCA
Daya et al ³⁸	Out-of-hospital, USA	<18	10.1	Includes infant sudden death

OHCA indicates out-of-hospital arrest; and SCD, sudden cardiac death.

incidence for each of these entities varies, but is thought, for the more common diagnoses, to be ≈1:500 persons for HCM⁴⁸ and ≈1:2000 persons for LQTS.⁴⁹

Structural Congenital Heart Disease

In the United States, ≈40 000 children are born annually with congenital heart disease (CHD). The presence of ventricular

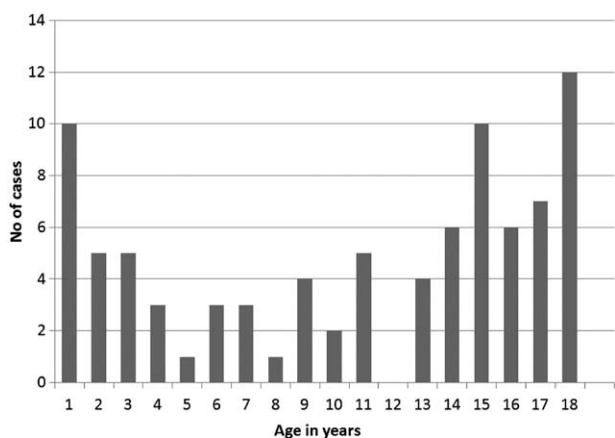


Figure 2. Age distribution of SCD in the Danish population, 2000 to 2006. SCD indicates sudden cardiac death. Reprinted from Winkel et al³³ with permission of the publisher. Copyright © 2014, European Society of Cardiology.

dysfunction in combination with scarring, hypertrophy, and fibrosis increases the likelihood of SCD in many patients with severe and, to a lesser degree, mild forms of CHD.⁵⁰ Patients with CHD have an elevated risk of SCD in comparison with the general population, particularly as they age into early adulthood, and SCD accounts for 15% to 25% of deaths in these patients.^{51,52}

The diversity of CHD makes it a difficult to construct an aggregated risk estimate, but, overall, the incidence of SCD in CHD patients appears much lower than that observed in patients with acquired heart diseases such as dilated or ischemic cardiomyopathy. Patients with tetralogy of Fallot, a form of CHD that is well studied because of its relative prevalence and the availability of long follow-up after surgical palliation, have SCD rates that average 0.1% to 0.2% per year,^{53–57} although there are other lesions and subgroups of patients likely to be at considerably higher risk for SCD (see below). It is likely that ventricular tachycardia, atrial arrhythmia, and heart block with paroxysmal bradycardia all may contribute to some degree, and the prevalence of each of all arrhythmia subtypes increases with age (Figure 3).

SCD in Athletes

Athletes are an important subpopulation of young individuals who have a high public profile, and they have been

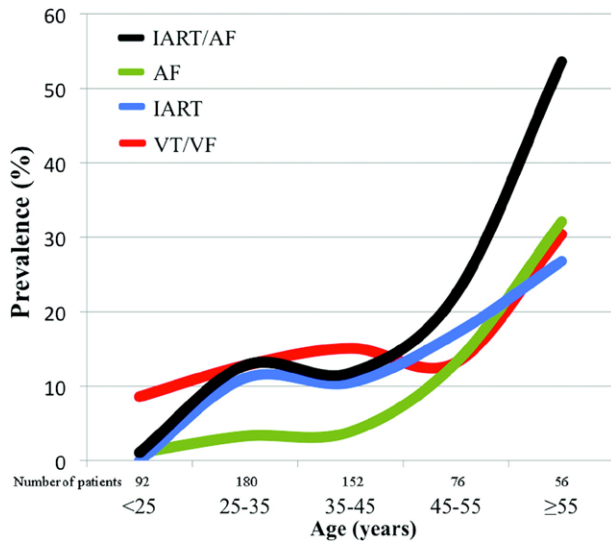


Figure 3. Prevalence of different arrhythmia types as a function of age in patients with tetralogy of Fallot. AF indicates atrial fibrillation; IART, intra-atrial reentrant tachycardia; VF, ventricular fibrillation; and VT, ventricular tachycardia. Reprinted from Khairy et al⁵⁸ with permission of the publisher. Copyright © 2010, the American Heart Association.

studied carefully with respect to the incidence of SCD. In the United States, youth participation in sports is prevalent, with >40 000 000 participants and 7.5 to 8 million teenagers enrolled in organized high school sports.⁵⁹ Occurrence of SCD in young athletes receives media attention, and it is often assumed that sports participation is a direct cause of SCD. Estimates of SCD in athletes varies by >100-fold, ranging from 1:3000/y in NCAA Division 1 male basketball athletes⁴⁷ to 1:917 000/y among high school athletes in Minnesota.⁶⁰ Studies of college athletes have suggested that they have an annual incidence between 1:43 000 and 1:67 000.^{46,61} This risk is 2 to 3 times greater than that cited above for the general population, but this difference may in part be related to demographic factors correlated with sports participation (sex, age, ethnicity).⁴⁷

Etiologies of SCD in the Young Athlete

An early article investigating the etiology of SCD in the young athlete was a case series published from Italy identifying ARVC in 22 young athletes who experienced SCD.⁶² A more extensive autopsy study of young adult athletes from this region showed that ARVC and coronary artery disease accounted for more than half of the nearly 200 cases studied that had identifiable heart disease, with valvular heart disease, nonatherosclerotic coronary artery malformations, myocarditis, and abnormalities of the conduction system accounting for most of the rest.⁶³

Case studies of SCD in the athlete performed in the United States suggested a more prominent role for HCM as the principal pathology underlying this event.^{64,65} A registry of 1866 episodes of SCD in athletes maintained over >25 years revealed that 1049 were attributable to cardiovascular causes. Of these episodes, the majority could be assigned a specific diagnosis. In this study, HCM and congenital abnormalities of the coronary arteries were identified most frequently (Figure 4),⁶⁶ but other series have identified autopsy negative sudden death as the most frequent finding.⁶⁷

Noncardiac causes of sudden death are also frequent in athletes, including heat stroke and traumatic injury. A recent review of all deaths occurring in college athletes in the United States (both on and off the field) revealed the most common cause of death to be accidental (typically motor vehicle), accounting for 50% of all deaths, with noncardiac medical causes such as homicide, suicide, cancer, and drug and alcohol overdose accounting for another 26%.⁶⁸ An important feature of all studies investigating the etiology of SCD in young athletes is the variability in the findings obtained by different investigators, which likely reflects a mix of ascertainment bias, regional variation in forensic practice, and some element of true clinical variation among populations living in different regions of the world (Figure 5).^{28,69–73}

The significant role of sport in society has generated interest in prophylactic identification of individuals at risk, institution of policies intended to protect those individuals, and investment of community resources to respond promptly to cardiac arrests occurring at athletic events. Comprehensive recommendations have been put forward in several revisions by American and European professional societies (the Bethesda Guidelines and the European Society of Cardiology Consensus Recommendations).^{74,75} These documents are based on review of available current and historical data, but differ in certain respects and have resulted in a wide variety of public-mandated and voluntary policies for cardiovascular screening of athletes and recommendations regarding competitive eligibility. New guidelines addressing these issues were released in late 2015.¹⁰ These guidelines largely reiterate the recommendations from a decade ago, although a significant change has occurred with respect to the cardiac channelopathies. In contrast to the previous stance that resulted in de facto disqualification in most sports, it is now acknowledged that there may be shared decision making and respect for patient/family autonomy and well-informed decisions to compete. This is also consistent with 2013 guidelines for management of LQTS which identify as a class I recommendation that athletes with LQTS who desired to compete should see an expert.¹¹

Recent reports highlight difficulties in the application of these guidelines to individuals designated at increased risk for SCD and therefore proscribed from certain athletic activities. Anecdotal evidence exists that many patients with increased risk of SCD compete in both recreational and competitive sports that are formally proscribed by these guidelines. High-profile legal cases have been tried regarding the right of athletes to compete despite disqualification because of medical diagnosis.⁷⁶ Prospective review is now underway regarding the consequences of allowing patients with ICDs and diseases like LQTS, HCM, and ARVC to participate in competitive activities currently proscribed by guidelines.^{77,78} National Institutes of Health–funded prospective studies (Lifestyle and Exercise in Patients with HCM or LIVE-HCM and Lifestyle and Exercise in Patients with LQTS or LIVE-LQTS) began patient enrollment in early 2015 (National Institutes of Health Clinical Trial NCT02549664). The goal is to test the hypothesis that those patients with LQTS or HCM who are the most active will have a higher quality of life than those who are least active without making their disease substrate more arrhythmic.

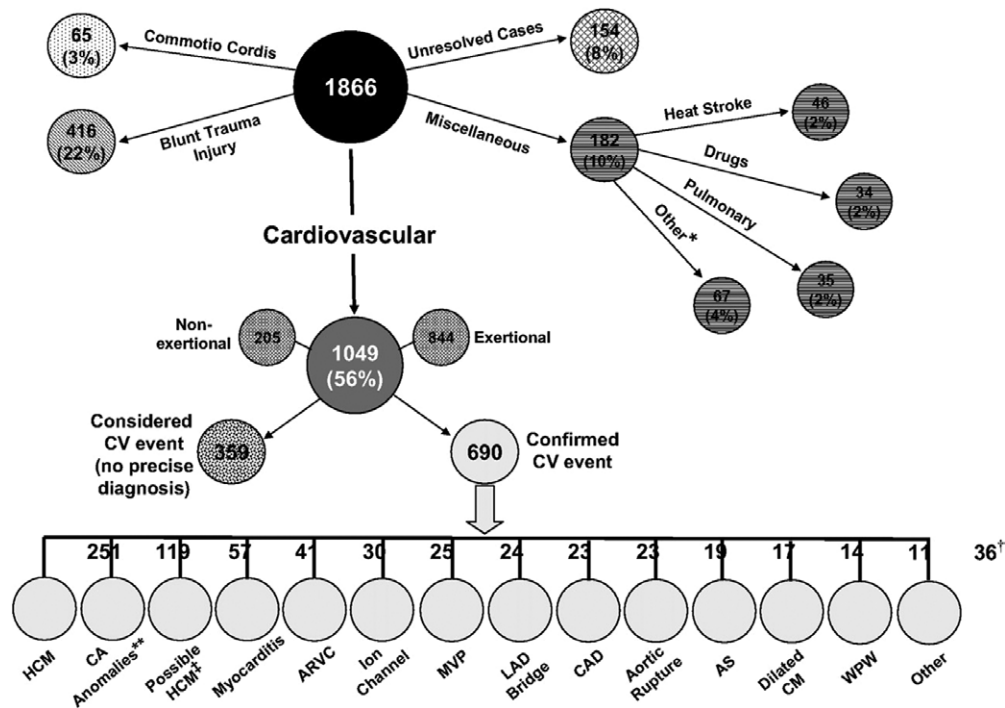


Figure 4. Distribution of causes of death among young US athletes. ARVC indicates arrhythmogenic right ventricular cardiomyopathy; AS, aortic stenosis; CA, coronary artery; CAD, coronary artery disease; CM, cardiomyopathy; CV, cardiovascular; HCM, hypertrophic cardiomyopathy; LAD, left anterior descending coronary artery; MVP, mitral valve prolapse; and WPW, Wolff-Parkinson-White. Reprinted from Maron et al⁶⁶ with permission of the publisher. Copyright © 2006, the American Heart Association.

It is unclear whether sports participation is a modifiable risk factor for SCD. Adrenergic stimulation associated with athletic activity may plausibly act as a proximate cause for cardiac events in patients with HCM,⁷⁹ LQTS,⁸⁰ ARVC,⁸¹ and anatomic abnormalities of the coronary artery.⁸² The epidemiology of SCD in young people indirectly suggests that active participation in sports itself is a cause of SCD.⁸³ However, noncompetitive athletes with similar conditions appear to be at similar risk,⁸⁴ and SCD is as likely to occur during periods of recreational play (which may be as vigorous as competitive activity in young patients),^{85,86} and in quiet time and sleep, as well.⁸⁷ Historical epidemiological studies are inconclusive: an Italian study identified a beneficial effect of national policy mandating cardiovascular screening of athletes in reducing SCD,⁸⁸ whereas studies from Israel, Denmark, and the United States have failed to support that finding.^{69,89,90} No well-designed studies have demonstrated that sports proscription reduces the incidence of SCD. This raises the question as to whether athletes are singled out for cardiovascular scrutiny and intervention, while possibly having neither a higher risk of SCD nor a clearly effective intervention.

SCD Associated With Chest Trauma

SCD is also rarely associated in the normal juvenile heart with blunt chest trauma, a condition referred to as commotio cordis. The frequency of this event is difficult to determine, but studies of SCD at intercollegiate NCAA events indicate that autopsy negative SCD is a relatively frequent finding,⁷¹ and some can clearly be related as trauma-related by history.⁹¹ Animal studies have identified a putative mechanism of commotio cordis, related to serendipitously timed precordial chest trauma that affects the ventricle during a vulnerable

repolarization interval.⁹² Certain sports are more likely to experience these events, both in competitive and in recreational settings (baseball and cricket, lacrosse, soccer, hockey, football, and martial arts).^{91,93,94}

SCD Associated With Use of Medications

In contrast to the debate surrounding the management of SCD risk in athletes, concerns regarding the effects of stimulant medications on SCD risk in the young have largely been settled by recent population-based studies. In 2003, 2.5 million children in the United States were treated with stimulant medications for attention deficit and hyperactivity disorder and similar disorders of school and social function.⁹⁵ Many of these medicines have sympathomimetic effects of small but measurable degree.^{96,97} An apparent cluster of SCD events in patients receiving stimulants for attention deficit and hyperactivity disorder led to the suspension of one such drug (a methylphenidate preparation) in Canada, release of a public health advisory, and a so-called black box warning regarding the use of stimulant drugs by the US Food and Drug Administration, and recommendation for pretreatment electrocardiographic evaluation before starting therapy.¹² Subsequently, however, several epidemiological studies conducted using large administrative databases clearly show that such medications have no effect, and possibly even a negative, healthy-user effect of these medications on SCD prevalence.^{98,99}

Counterbalancing these findings are specific, recent data developed from a large LQTS registry relating to the use of stimulant medications in patients with LQTS, which suggest that the use of these medications was associated with increased risk of cardiac events, particularly in males.¹⁰⁰ A concurrent,

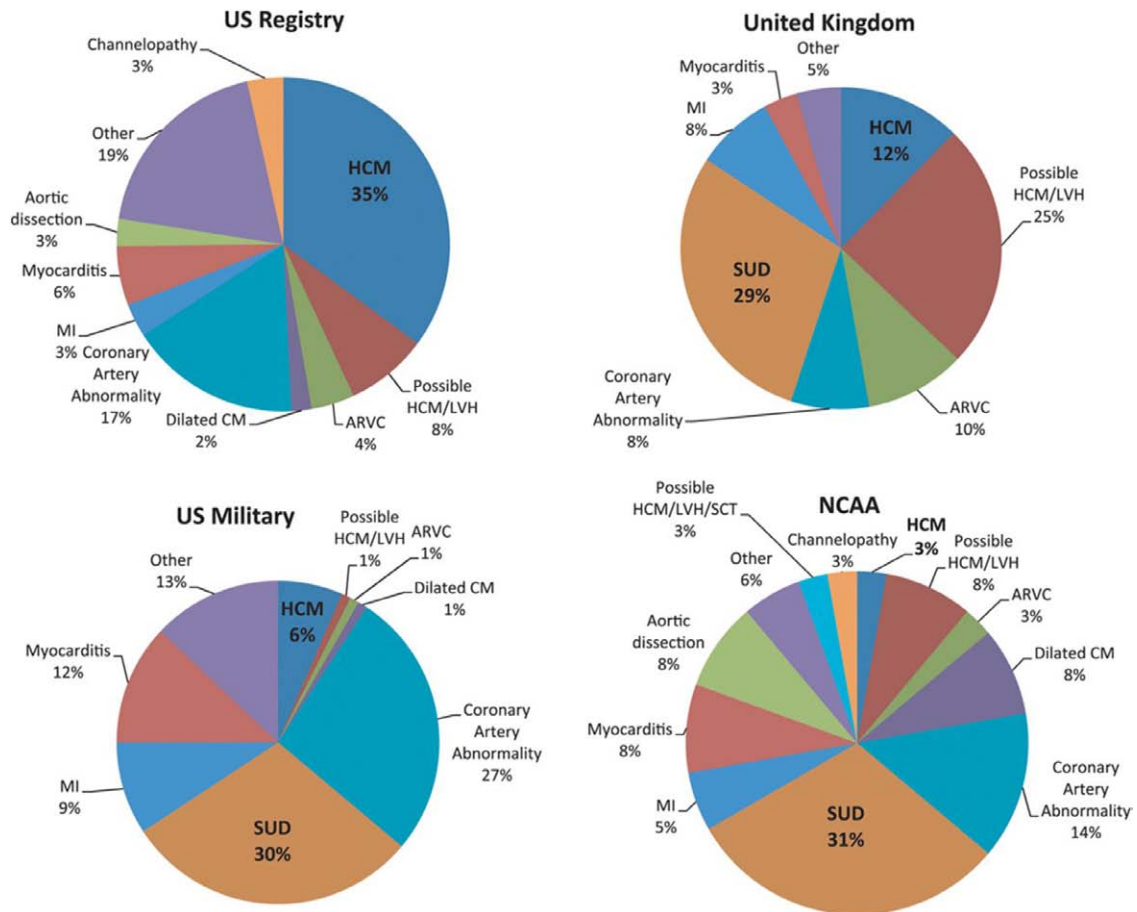


Figure 5. Comparison of 4 studies of SCD etiology. ARVC indicates arrhythmogenic cardiomyopathy; CM, cardiomyopathy; HCM, hypertrophic cardiomyopathy; LVH, left ventricular hypertrophy; MI, myocardial infarction; NCAA, National Collegiate Athletic Association; SCD, sudden cardiac death; SCT, sickle cell trait; and SUD, sudden unexplained death. Reprinted from Harmon et al⁷¹ with permission of the publisher. Copyright © 2014, the American Heart Association.

smaller retrospective study found no such effect,¹⁰¹ indicating that in LQTS consensus regarding the safety of stimulant medication has not yet been reached.

Identification of Young Patients at Risk for SCD Prodromal Signs and Screening

Prodromal Symptoms/Signs/Events – Value of Warning Signs

Certain prodromal symptoms and clinical events identify groups of patients at increased risk for SCD. Their specific predictive power can be incorporated into calculations regarding the desirability of interventions such as diagnostic screening or, in the case of known disease, primary prevention by medical therapy or ICD implantation.

The most reliable presenting symptom that specifically indicates both the likely presence of a primary cardiac diagnosis is aborted or resuscitated sudden cardiac arrest. The likelihood of recurrent episodes of cardiac arrest in these patients is so well-recognized that it constitutes a significant fraction of ICD implantations performed in young patients,¹⁰² even in cases for which a specific diagnosis may not be established and the patient receives the default classification of idiopathic ventricular fibrillation.

Other prodromal symptoms commonly associated with the risk of SCD are those of nonsustained arrhythmia: palpitations, chest pain, syncope, and seizure, representing transient fluctuations in pulse and blood pressure caused by brief arrhythmic episodes. Studies of unexpected SCD in apparently healthy children suggest that a significant fraction, perhaps one-fourth to one-half, may have experienced an antecedent symptom, frequently syncope or seizure.³³ However, palpitation, chest pain, and syncope are prevalent in healthy children,¹⁰³ and thus of limited diagnostic value as an isolated finding. An exception to this may be exertional syncope, which is associated with considerably greater likelihood of cardiac disease.¹⁰⁴ When taken in combination with other findings of cardiac disease, however, any of these symptoms may be indicative of increased risk.

Screening for SCD in the Young

Many have proposed screening programs for SCD, either on a societal basis or for subpopulations (like athletes) perceived to be at high risk. This has been the recent subject of study by a working group at the National Heart, Lung, and Blood Institute.¹⁰⁵ This topic can be approached by applying general principles used to determine whether a screening test is clinically useful. First, the test must be diagnostically sensitive for the target disease. The disease should not be exceedingly rare,

and should pose a risk of a life-threatening manifestation as a first event. The cost of the test and the potential costs of a false-positive diagnosis should be low. Finally, effective therapies should be available.^{106,107} The utility of a screening test is measured in relation to threshold values that are societally accepted (\$50 000–\$100 000 for each life-year saved in the United States).

Various cardiovascular screening strategies have been proposed, including ECG, history and physical examination, and echocardiogram, singly and in combination.^{108–112} The sensitivity, specificity, and positive and negative predictive values of tests used for cardiac screening depend on the disease in question and its prevalence in the screened population. Analyses of differing screening approaches have been published in community populations,¹¹³ and in age-defined populations (eg, in neonates for the diagnosis of LQTS)⁴⁹ and those identified by athletic participation^{114,115} or by the use of stimulant medications.^{116,117} This literature suggests that the ECG is a sensitive and efficient screening test for most diagnoses that cause SCD in young people and may be prophylactically treated, including LQTS, Wolff-Parkinson-White, HCM, and Brugada syndrome.¹¹⁸ Various coding systems have been developed in efforts to optimize the utility of the ECG in this screening function.^{119,120}

Cost-effectiveness studies of screening in asymptomatic youth have been performed, with selected results presented below (Table 2). All such studies are sensitive to underlying assumptions and provide a range of possible findings on sensitivity analysis. However, they suggest that ECG screening in most settings is cost-ineffective, or marginally cost-effective, with sensitivity to initial assumptions regarding baseline disease prevalence and efficacy of available therapies. Cost-effectiveness could be increased by targeting groups that have a particularly high risk of SCD (eg, NCAA Division 1 athletes⁴⁷) if effective measures could be taken to mitigate those risks, or groups that may stand to gain significant additional protection by early identification of arrhythmic disease (eg, screening for LQTS in infancy^{49,121}).

There is widespread community-based interest in cardiac screening, often based on the application of existing guidelines^{12,14,15} by self-organized advocacy groups. Many such groups have demonstrated a high level of proficiency in structuring these programs. Although cardiovascular screening has been adopted as public policy and met with widespread acceptance in some countries,^{49,88,129} practical concerns have limited enthusiasm for mandated screening in the United States and elsewhere.¹³⁰ Chief among these are (1) the impact of false-positive findings, which include unnecessary workup, prescription from sport or other desired, healthful or necessary activity, and possible creation of psychological harms^{115,116}; (2) the effect of inaccuracy in diagnosis to discount the potential value of cardiovascular screening in actual use^{131–133}; and (3) the willingness of patients with positive screening tests to pursue further diagnosis and management.¹¹⁴

The effective yield of screening tests can be increased by limiting testing to relatives of disease probands. For heritable arrhythmias, this markedly increases the pretest probability regarding the potential prevalence (ie, 50%) of disease in the

tested population, enhancing the positive predictive value. This approach, termed cascade screening, is useful in families with known disease-causing mutations and phenotypes,^{134,135} such as LQTS, and in cases of sudden unexplained death, as well,^{135–139} using electrocardiographic, genetic, or other techniques as appropriate. In 1 study using a national registry, an average of 2.1 new cases were identified per each LQTS proband,¹³⁴ and observational studies have noted a high diagnostic yield of affected family members of patients with SCD and unexplained cardiac arrest,¹³⁷ although this has not been a uniform finding.¹⁴⁰

SCD in the Young and the Affected Family

Several challenges relevant to the health of surviving family members must be confronted immediately following an event of SCD in the young. First, the occurrence and quality of a postmortem evaluation (ie, autopsy) hinges on the specific state, county, and city in which the SCD occurred, because there is a wide range of competency with respect to postmortem cardiac diagnosis, and the availability of specialized cardiac examination, as well.¹⁴¹ Second, the scope of cardiac evaluations among first-degree relatives following an SCD event is not standardized. In the absence of a standard of care for clinical investigation of families affected by SCD, the response of physicians confronted with this presentation may range from simple inquiry as to symptoms, to obtaining a broad range of noninvasive and, in some cases, invasive cardiac testing on each individual, and then repeating such testing at frequent intervals. Third, the occurrence and quality of postmortem genetic testing (also referred to as the molecular autopsy) is unsettled at the present time, with the emergence of new genetic technology and increasingly subtle understanding of the significance of different genetic markers and point mutations, and thus also varies tremendously.^{142–146} Application of genetic testing of the SCD patient, a potentially valuable and specific tool for clinical investigation when performed within the construct of wider familial investigations, is also often confronted by challenges with reimbursement for tests performed on deceased individuals.

As a consequence, the ability of the clinician to provide useful diagnostic information to families of young SCD patients is at present in a state of transition. In the best case scenario, phenotypic and in some cases genotypic information obtained both from the affected individual and close relations will be considered together to provide both a specific diagnosis, identification of other family members at risk, and actionable clinical information of value to the survivors.

Presently, there are no consensus guidelines/recommendations as to what a comprehensive postmortem investigation of a youthful SCD patient must entail and what the minimum premortem investigation of the surviving first-degree relatives ought to include. At minimum, standard operating procedures from medical examiner's offices need to include obtaining so-called DNA friendly tissue (blood in EDTA, frozen nucleated tissue, or blood spot cards) to permit postmortem genetic testing if indicated.^{147,148} For the surviving first-degree relatives, cardiological testing should be tailored according to the autopsy findings of the decedent, but a 12-lead ECG,

Table 2. Cost-Effectiveness Studies on ECG-Based Cardiovascular Screening in Young

Study	Patient Group	Age Range, y	Cost per Life-Year Saved	Comments
Fuller et al ¹²²	Preparticipation sports screening	Teenagers	Hx and physical: \$84 000 ECG: \$44 000 Echocardiogram: \$200 000	Designed as means to compare different screening modalities
Zupancic et al ¹²³	LQTS screening in newborns	Newborns	\$28 400–\$118 900	Assumes that most SIDS not preventable by LQTS treatment, and identification of high-risk population
Quaglioni et al ¹²⁴	LQTS screening in newborns	Newborns	€11 700	Includes identification of other cardiac diseases and assumes high treatment effect on LQTS
Denchev et al ¹²⁵	Screening for ADHD medications use	School-aged children	Incremental cost of adding ECG to Hx and physical: \$27 200–\$39 300	Cost of total strategy not modeled, most of benefit based on assumption of restriction from sports activity, not ADHD medications
Wheeler et al ¹²⁶	Preparticipation sports screening	Teenagers and college students	Incremental cost of adding ECG to Hx and physical: \$21 200–\$71 300 Total cost: \$62 000–\$130 000	ECG/history and physical Sensitive to effective of intervention and cost of screening
Schoenbaum et al ¹²⁷	Preparticipation sports screening	Teenagers	Incremental cost of adding ECG to Hx and physical: \$37 300–\$68 800	Cost of total strategy not modeled, with most of cost driven by evaluation of false-positive findings
Leslie et al ¹¹⁷	Screening for ADHD medications use Preparticipation sports screening	School-aged children and adolescents	\$91 000–\$204 000	ECG only Sensitive of prevalence, mortality and effectiveness of interventions
Halkin et al ¹²⁸	20-y ECG screening model at Medicare reimbursement rates	High school and college athletes	\$10 600 000–\$14 400 000 per life saved (cost/life-year not calculated)	Modeled according to Italian screening program using US statistics

ADHD indicates attention deficit and hyperactivity disorder; Hx, history; LQTS, long QT syndrome; and SIDS, sudden infant death syndrome.

24-hour Holter monitor, treadmill stress test, and an echocardiogram make up a reasonable set of initial tests. It remains to be determined whether such postmortem investigations of the decedent and premortem investigations of the living should be pursued in parallel or whether a sequential investigation starting with a molecular autopsy of the decedent may be more cost-effective.

Risk Stratification in Specific Individual Diseases

A small but significant fraction (12%–18%) of young patients experiencing SCD has a previous known cardiac diagnosis.^{33,43} Once a specific high-risk diagnosis has been established, the presence of arrhythmia symptoms or other findings can be used to identify subpopulations at increased risk of SCD. Risk stratification is limited to conditions that are prevalent and well-studied in multiple independent groups of patients; this criterion is met perhaps most notably the case for patients diagnosed with HCM and certain channelopathies such as long QT syndrome, for whom explicit guidelines have been written.^{8,11} However, the studies available to inform risk stratification strategies specific to young populations in this and other SCD-predisposing diseases are generally retrospective in design, and many variables identified as associating with patients at increased risk are also associated with one another. Thus, risk stratification schema for SCD in the young are less explicitly prescriptive than many of the validated risk assessment tools used in adult cardiology, and risk factor assessment must be applied cautiously, and in conjunction with individualized clinical assessment and judgment.

Prophylaxis and Secondary Therapy of SCD in the Young

Primary Prevention and SCD

For patients who have been identified as being at high risk for SCD, it may be appropriate to consider placement of an ICD for primary prevention. This is a principal that has long been widely accepted in adult populations, based on studies of ischemic cardiomyopathy and left ventricular dysfunction in which the benefits of ICD implantation are clearly demonstrated.^{149–151} In children with SCD-predisposing diseases and syndromes, the risk-to-benefit relationship that pertains to ICD use is less clearly developed. From the point of view of risk of ICD, children clearly have a relatively high rate of complications associated with devices, including frequency of inappropriate shocks, lead malfunctions, and difficulties in ICD placement related to intracardiac anatomy and small size.^{152,153} Conversely, from the point of view of potential benefits associated with primary prophylaxis, children may stand to gain relatively less from ICD implantation. In particular, the known rate of sudden death associated with CHD and a variety of arrhythmic cardiomyopathies is considerably lower than that observed in adult populations in whom ICD is seen to be useful (eg, as mentioned above for adults with tetralogy of Fallot, in whom these rates range from 0.1% to 0.2% per year). Guidelines relating to indications for implantation of ICDs for the purpose of primary prevention in children and young people with CHD and other SCD-predisposing illnesses are written with considerable latitude in comparison with those used in adults with acquired heart disease.⁷ However, recognizing the difficulties associated with ICDs in

this population, clinicians specializing in pediatric patients at risk for SCD have generally applied conservative algorithms to the decision-making process regarding whether or not to implant these devices.

Resuscitation of SCD

Relation Between Resuscitation and SCD

It is unfortunate that the epidemiology and clinical diagnosis of SCD-predisposing conditions are not typically addressed in conjunction with the science and practice of resuscitation. For this reason, the literature and knowledge base in these 2 fields is, to a great extent, nonoverlapping, although they are well connected around the shared topic of defibrillation. Given the dismal rates of survival of out-of-hospital cardiac arrest (OHCA), all components of resuscitation science can legitimately be considered as relevant to an integrated approach to the prophylaxis and management of SCD in the young. An understanding of clinical characteristics of SCD in the young informs resuscitation strategies and deployment of services in the community. Conversely, continuous improvement and measurement of the efficacy and availability of effective bystander and EMS response to SCD improves survival and changes the risk-to-benefit calculations useful in planning for individual clinical decisions in patients known to have an SCD-predisposing condition.

Definition of Sudden Cardiac Arrest

From the perspective of resuscitation, the concept of sudden cardiac arrest (SCA) is more useful than SCD by virtue of its specificity. SCA is defined as “malfunction or cessation of the electric and mechanical activity of the heart, resulting in almost instantaneous loss of consciousness and collapse.”¹⁵⁴ This definition focuses on primary cardiovascular causes and does not specify an outcome. Previous definitions such as “nontraumatic death occurring instantaneously or within ... 24 hours of the onset of acute symptoms”²³ are better termed sudden unexpected death, because the underlying etiology is broader and the defined outcome is death.

Pathophysiology of SCA and Principles of Management

Rhythms in young people experiencing OHCA include asystole, pulseless electric activity, and ventricular fibrillation (VF). In epidemiological studies of OHCA in youth, asystole is more common than ventricular arrhythmias.^{36,155} However, these studies include patients with comorbidities, intercurrent illness, drowning, and suffocation. In SCA in the population discussed here, the primary arrhythmia is often VF.³⁵

The pathophysiology of SCA induced by pulseless ventricular tachycardia and VF is time dependent, with 3 phases distinguished by cardiac rhythm and metabolic consequences of low flow and hypoxia. These phases define appropriate therapies and predict the probability of survival and neurological disability.¹⁵⁶ The initial electric phase lasts \approx 4 minutes and is defined by the presence of shockable rhythms. During this period, the heart is responsive to defibrillation, as established by outcomes of ICD implantation and deployment of public-access defibrillation program studies.^{157–159}

The circulatory phase is characterized by the onset of tissue hypoxemia and emergence of asystole. Cardiopulmonary

resuscitation (CPR) to provide oxygen delivery is crucial during this phase.¹⁶⁰ Defibrillation is less effective, but may be enhanced by preshock epinephrine administration and effective CPR.^{161–165} The metabolic phase commences \approx 10 minutes after SCA, distinguished by asystole, worsening hypoxia, and circulating metabolic factors resulting in cell death and end organ dysfunction. Survival during the metabolic phase is unlikely and often associated with severe functional disability.

Components of CPR

CPR has 4 components in both children and adults: chest compression, defibrillation, ventilation, and pharmacological agents. Although all are thought to be important, effective chest compression and early defibrillation have been most clearly linked to increased survival.

Chest Compression

Chest compressions generate forward blood flow by causing intrathoracic pressure changes^{166,167} and by direct cardiac compression.¹⁶⁸ Standard CPR produces 30% to 40% of normal cardiac output with variations between vascular beds: cerebral flow may be as high as 60%, but myocardial flow is substantially lower at 10% to 30%.^{166,169} Restoration of cerebral function depends on the former,^{170,171} whereas cardiac resuscitation depends on adequate coronary perfusion pressure.^{166,172–174}

Perfusion pressures increase over a period of 5 to 7 compressions during CPR but fall rapidly during pauses. Thus, time for coronary and cerebral perfusion is curtailed during ventilatory pauses.¹⁷⁵ Effective CPR also requires complete chest recoil to allow venous return into the thorax,^{176–179} and excessive compression rates compromise coronary blood flow and compression depth.^{180–182} On balance, compression fractions of $<$ 80% appear associated with decreased survival,^{183–185} and current recommendations emphasize short, infrequent pauses.

Defibrillation

Early defibrillation is a significant determinant of survival from VF arrest. It was hypothesized originally that the electric current terminated fibrillation by depolarization of a critical mass of myocardium.¹⁸⁶ Recently, the importance of preventing reinitiation of fibrillation after defibrillation has been recognized.¹⁸⁷ Determinants of defibrillation success are current delivery, waveform shape, and transthoracic impedance. Biphasic waveforms have a high success rate for VF termination and have replaced monophasic devices in practice.^{188–191}

Airway Management and Ventilation

Assisted ventilation was initially considered essential for successful resuscitation.¹⁹² However, when cardiac arrest is abrupt, oxygen content within the vascular space is adequate to permit a period of compression without ventilation. Positive pressure ventilation increases intrathoracic pressure and may decrease cardiac output and coronary perfusion pressure.^{176,193} Optimal compression:ventilation ratios have not been determined, but recent guidelines trended toward a greater emphasis on chest compression.¹⁹⁴

Pharmacological Agents

Vasopressive and antiarrhythmic agents are widely used in resuscitation, but no drug has been shown in prospective

trials to improve long-term survival after cardiac arrest.¹⁹⁵ Administration of epinephrine during cardiac arrest has been accepted as a standard of care, but its use remains controversial; although epinephrine has been shown to improve return of spontaneous circulation, no improvement in long-term survival has yet been demonstrated.¹⁹⁶ Vasopressin has been used as an alternative, but trials comparing epinephrine with either vasopressin or placebo have failed to show superiority to hospital discharge or long-term survival.^{194,197,198} Further clinical trials are needed on this topic, because all studies to date have been underpowered to draw conclusions with respect to survival outcomes.¹⁹⁹

Similarly, limited evidence is available to guide the use of antiarrhythmic agents during cardiac arrest. In 1 randomized out-of-hospital trial, amiodarone improved survival to hospital admission in comparison with placebo,²⁰⁰ and this drug has been recommended for treatment of shock-resistant or recurrent pulseless ventricular tachycardia/VF since 2005. However, no randomized trial testing the efficacy of amiodarone or lidocaine for OHCA has demonstrated improved survival to discharge.²⁰¹ An study in hospitalized young patients showed that survival to hospital discharge is improved with lidocaine in comparison with amiodarone²⁰² and guided the 2015 American Heart Association (AHA) recommendations to downgrade amiodarone during cardiac arrest in children.⁴ The Resuscitation Outcomes Consortium is currently conducting a study of antiarrhythmic use during CPR.²⁰³

High-Quality CPR

It has become apparent that high-quality CPR is a major determinant of survival.^{4,160,184,204,205} In practice, CPR performance is often suboptimal by both EMS and hospital providers.^{181,206,207} Metrics of the quality of CPR include maintenance of appropriate chest compression rate and depth, adequacy of chest recoil, fraction of time during CPR that chest compressions are being performed, and maintenance of appropriate ventilation rate. Multiple studies have shown the positive effect on outcomes when these parameters are measured and monitored.^{183,208–210}

Major emphasis is now placed on chest compression, and animal and human studies^{172,174,211–215} have shown equivalent survival with chest compression only. In 2008, the AHA recommended chest compression only CPR for bystanders who witnessed the sudden collapse of a patient,²¹⁶ and, in 2010, the AHA revised the ABC (Airway–Breathing–Chest Compression) of CPR to CAB (Chest Compression–Airway–Breathing).²¹⁷ This recommendation was made based on the data that demonstrate the effectiveness and the need to increase the frequency and quality of bystander CPR and to reduce obstacles to laypersons performing CPR.^{36,218–220} In practice studies, delay of intubation until after 4 cycles of chest compression, defibrillation, and administration of epinephrine by EMS providers has resulted in the doubling of survival in patients with witnessed arrest and shockable rhythms and OHCA survival increased by 40%.¹⁶⁷ A recent, population-based study from Japan suggests that broad dissemination of chest compression–only CPR for bystanders was associated with a substantial increase in neurologically favorable survival.²²¹

CPR Techniques for Young Children

The basic physiological principles of CPR apply to babies and children, but there are differences in technique to accommodate age-related differences in body size, elasticity of the chest wall, and differing primary causes of arrest. Thus, the AHA guidelines recommend different compression-ventilation ratios and less compression depth for infants.^{3,194} Current guidelines also do not recommend chest compression–only CPR for young children, based on 2 Japanese studies in which children who received chest compression–only had worse neurological outcomes. However, chest compression–only CPR was as effective as conventional CPR in children presumed to have arrest from a cardiac etiology.²²²

Chain of Survival

Survival after cardiac arrest depends on the immediate initiation of treatment, with the likelihood of survival decreasing 10% with every minute delay in the initiation of CPR.²²³ The Chain of Survival construct has guided practical deployment of resuscitation principles in the field.

Wide disparities exist in survival of OHCA in the United States. Data from 10 North American sites revealed survival rates ranging from 7.7% to 39.9%.²⁰⁴ Although differences in patient demographics, education, and health status account for some of this difference, it is likely that community and healthcare system factors accounted for much of this variability.²²⁴ Several communities have undertaken to improve their survival statistics, including the Seattle/King County, Arizona, Denver, and Wake County, North Carolina.^{225–231} Each has observed a doubling or tripling of survival from OHCA, and their experiences have provided direction for system improvement in other communities. Critical factors include strong leadership, robust community engagement, an efficient, well-supported EMS system, and hospitals capable of providing excellent postarrest care.

Leadership

Leadership in the high-performing communities has established a culture of excellence, with continuous data collection, analysis and reporting, so that the progress associated with the implementation of new strategies could be measured.^{225–232} Examples of successful new approaches have included changing CPR protocols to minimize chest compression pauses during defibrillation, continuous chest compression for several minutes and delayed ventilations and intubation, and use of the impedance threshold devices.

Community Engagement

The first 3 links of the chain (early EMS activation, early CPR, and early defibrillation) require community response and acceptance of civic duty to respond and deliver basic life support. Bystander CPR improves the response of the heart to defibrillation²³³ and can double or triple survival to hospital discharge and improve neurological outcome.^{234–240} However, only 4% of the US population has received any CPR training,²⁴¹ and of the 15% to 20% of OHCA, only 20% to 30% receive bystander CPR or defibrillation.^{242–245}

CPR training has been supported by the AHA and the American Red Cross for decades, but CPR courses are an inefficient and expensive method to train large numbers of

responders, with rural areas and communities with a high proportion of Hispanic and black residents particularly difficult to reach. Alternative methods to provide training to all members of society include school-based training, or as a prerequisite for civil activity such as obtaining a driver's license. School-based training has been endorsed by the World Health Organization²⁴⁶ and the AHA.²⁴⁷ Legislatures in 27 states have enacted legislation to require or support CPR training as a graduation requirement.

A Danish program to expand public CPR response included mandatory training in schools and before receipt of a driver's license, distribution of CPR self-instruction kits, improved dispatch CPR training, and an increased number of automated external defibrillators (AEDs).²⁴⁸ Bystander CPR rates increased from <20% to 40% to 70% and survival from OHCA increased from 2.9% to 10.2%. In the United States, the Take Heart America Program also increased bystander CPR rates and hospital discharge.²⁴⁹ Targeting family members of persons at high risk for training (eg, those with inherited arrhythmia syndromes or CHD) also has merit, with instruction shown to improve self-confidence to perform CPR and increase the number of trained personnel by inclusion of other family members, caregivers, and friends.^{250–253}

Public Access Defibrillation

The development of AEDs, which allow minimally trained persons to use a defibrillator, has led to the establishment of Public Access Defibrillation sites over the past 20 years. Outcome improvements have been demonstrated in selected sites, such as government buildings, airports and transportation centers, and casinos.²²⁴ The Public Access Defibrillation Trial demonstrated a 2-fold improvement in adult survival with good neurological function when patients were resuscitated with CPR and AEDs in comparison with only CPR.¹⁵⁹

Public Access Defibrillation sites require an organizational structure to maintain effectiveness.²⁵⁴ Public Access Defibrillation programs that have appropriate leadership, with AEDs placed in locations of highest risk with ongoing maintenance, have a cost per quality-adjusted life-year of \$30 000 to \$100 000.^{255–257} However, in programs where ≥ 1 of these elements is absent, the cost per QALY can be substantially higher.^{258,259} Practical problems encountered with Public Access Defibrillation programs include expired disposable equipment, limited access to the AED, and poorly marked locations.²⁶⁰ School-based AED programs have strong support because of the social prominence of sports events in that setting and concern for prevention of sudden death in athletes.^{261,262} Despite the rarity of an event, school programs appear to be effective.^{263,264}

Because the many cardiac arrests occur in the home, home AEDs could be potentially useful. Successful AED use has been reported for young children,^{265,266} but randomized trials placing AEDs in homes of older high-risk individuals have not shown benefit,²⁶⁷ possibly because of the low proportion of witnessed events and low use of the AED despite its availability.

Hospitals and Postarrest Care

The final link in the chain of survival is early postresuscitation care in hospitals. Post-cardiac arrest syndrome is recognized

as a complex clinical condition encompassing several pathophysiologic processes.^{268,269} Myocardial dysfunction, neurological injury, systemic ischemic injury, and reperfusion injury dictate both rapid assessment and therapeutic needs to stabilize a patient and prevent further injury. Patients may develop systemic inflammatory and septic shock syndromes that further affect disability-free outcomes.^{270,271} Multidisciplinary care is focused on hemodynamic and ventilatory support, neurological preservation, and prevention of further injury and secondary comorbidities.

Targeted temperature management has been applied with a goal of slowing pathophysiologic events and biochemical systems that cause cellular damage. Early randomized studies used targeted temperatures of 32°C to 34°C and reported improved neurological outcomes for patients with VF arrests.²⁷² However, questions remain about optimal target temperature, specific populations, duration of hypothermia, and methods for induction, maintenance, and reversal. A recent multicenter, randomized trial of targeted temperature management in young OHCA patients observed no difference in neurological outcomes at 1 year.²⁷³ Despite this seemingly negative response, targeted temperature management remains a therapeutic option for patients <18 years, has been rapidly incorporated into standard clinical practice, and is still recommended for patients with shockable rhythms.²⁷⁴ Extracorporeal membrane oxygenation may be of potential use for patients with underlying CHD or where a reversible disease process is present and where existing protocols, personnel, and equipment are established and readily available.^{4,275,276} No data are available for extracorporeal membrane oxygenation for OHCA where institution of cardiovascular support is markedly delayed, although it has been demonstrated to be effective following prolonged CPR after in-hospital cardiac arrest in children.^{277,278}

Conclusions

Over the past decade, there has been a proliferation of data to guide the identification and management of children and young adults who are at risk for SCD. The prevalence of this problem is low, but its consequences are great, and a stepwise approach can be used to identify targets for prophylaxis and therapy. By organizing, and placing into perspective, relevant literature in each of these areas, outstanding deficiencies of knowledge relevant to these topics can be more readily identified. Urgent questions that must be addressed include the following.

- How can we use our knowledge of the epidemiology of SCD in the young to guide the further development of effective clinical and health policy interventions? Should ECG screening be used to identify youth at risk? If so, should screening be universal or should it be focused on subgroups perceived to be at higher risk of SCD?
- How should postmortem evaluation be performed following SCD, both of the patient and of his or her living relatives, and what is the utility of postmortem genetic testing (ie, the molecular autopsy)?

- Is it possible to reduce the prevalence of SCD in the young by prophylactic lifestyle restrictions? Which conditions might benefit from that approach, what types of activities should be restricted, and how could the effects of such interventions be measured?
- Which young patients actually benefit from primary prevention ICDs? Can improvements in ICD design and implant techniques improve the risk-to-benefit ratio in children and make them more useful technology in patients known to be at high risk?
- Are there modifiable barriers to improving resuscitation of the young in the community? How can EMS and postresuscitation care be better organized to improve survival outcomes after OHCA in the young?

Management of SCD in the young includes both preemptive mitigation of its risk and effective response to cardiac arrest by the community. Steps toward these goals may include the informed and appropriate use of screening programs to identify patients at risk, risk stratification for patients with SCD-predisposing diseases, provision of appropriate prophylactic therapy and advice regarding lifestyle, wide deployment of resuscitation expertise and technology, and services for diagnostic evaluation and provision of aftercare to affected families. The institution and use of a national registry of SCD in the young will be a major source of data that will help to answer some of the most pressing questions in this area.

Acknowledgments

We acknowledge and express appreciation for the critical reading of this manuscript and the editorial remarks by Dr Dominic Abrams.

Disclosures

Dr Ackerman is supported in part by the Mayo Clinic Windland Smith Rice Comprehensive Sudden Cardiac Death Program. He is a consultant for Boston Scientific, Gilead Sciences, Medtronic, St. Jude Medical, and Mayo Clinic and he receive sales-based royalties from Transgenomic for their FAMILION-LQTS and FAMILION-CPVT genetic tests. Dr Friedman is supported in part by National Institutes of Health 1U10HL109816. He is a consultant for Biosense Webster. Dr Atkins reports no conflicts.

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Sudden Cardiac Death in the Young

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Circulation. 2016;133:1006-1026

doi: 10.1161/CIRCULATIONAHA.115.020254

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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