17. Sudden Cardiac Arrest

See Tables 17-1 through 17-3 and Charts 17-1 through 17-3.

Cardiac Arrest (Including VF and Ventricular Flutter)

ICD-9 427.4, 427.5; ICD-10 I46.0, I46.1, I46.9, I49.0

Mortality—16 415. Any-mention mortality—352 089.

Cardiac arrest is defined as the cessation of cardiac mechanical activity, as confirmed by the absence of signs of circulation.[1] Cardiac arrest is traditionally categorized as being of cardiac or noncardiac origin. An arrest is presumed to be of cardiac origin unless it is known or likely to have been caused by trauma, submersion, drug overdose, asphyxia, exsanguination, or any other noncardiac cause as best determined by rescuers.[1] In practice, the accuracy of this classification is difficult, and some data sets do not attempt to make the distinction. Because of fundamental differences in underlying causes and the system of care, epidemiological data for OHCA and IHCA are typically collected and reported separately. For similar reasons, data for adults and children (aged 1–18 years) are commonly reported separately.

There are a number of ongoing challenges to understanding the epidemiology of cardiac arrest in the United States. Despite being a leading cause of death, there are currently no nationwide standards for surveillance to monitor the incidence and outcomes of cardiac arrest. In addition, it is challenging to define what is "unexpected" or "sudden" death. Sudden cardiac death has been defined as unexpected death without an obvious noncardiac cause that occurs within 1 hour of symptom onset (witnessed) or within 24 hours of last being observed in normal health (unwitnessed)[2]; however, this definition is difficult to apply in the real-world setting. OHCA registries and clinical trials typically include patients in cardiac arrest who were either assessed by EMS providers or treated by EMS providers. Regional and cultural differences in EMS system access and decision to treat are potential sources of variability in these data sets. Similar challenges exist related to the epidemiology of IHCA.

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Abbreviations Used in Chapter 17

AED	automated external defibrillator
AF	atrial fibrillation
AV	atrioventricular
BMI	body mass index
BP	blood pressure
CAD	coronary artery disease
CARDIA	Coronary Artery Risk Development in Young Adults
CARES	Cardiac Arrest Registry to Enhance Survival
CI	confidence interval
CPR	cardiopulmonary resuscitation
DCM	dilated cardiomyopathy
ECG	electrocardiogram
EMS	emergency medical services
GWTG	Get With The Guidelines
HCM	hypertrophic cardiomyopathy
HD	heart disease
HF	heart failure
HR	hazard ratio
ICD-9	*International Classification of Diseases, 9th Revision*
ICD-10	*International Classification of Diseases, 10th Revision*
IHCA	in-hospital cardiac arrest
LCL	lower confidence limit
LQTS	long-QT syndrome
LV	left ventricular
MI	myocardial infarction
OHCA	out-of-hospital cardiac arrest
OR	odds ratio
PA	physical activity
PAR	population attributable risk
PVT	polymorphic ventricular tachycardia
ROC	Resuscitation Outcomes Consortium
RR	relative risk
SD	standard deviation
UCL	upper confidence limit
VF	ventricular fibrillation
VT	ventricular tachycardia

Out-of-Hospital Cardiac Arrest

For additional details on OHCA treatment, please refer to Chapter 23, Quality of Care, Tables 23-8 and 23-9.

There are wide variations in the reported incidence of and outcomes for OHCA. These differences are caused in part by differences in definition and ascertainment of cardiac arrest data, as well as differences in treatment after the onset of cardiac arrest.

Children

(See Table 17-1 and Chart 17-1.)

Incidence and Risk Factors

- The incidence of OHCA among individuals <18 years of age in the United States is best characterized by data from the ROC Registry. Extrapolation of the incidence of EMS-assessed OHCA reported by ROC (ROC Investigators, unpublished data, November 23, 2015) suggests that each year, 7037 (quasi CI, 6214–7861) children experience EMS-assessed OHCA in the United States.
- The underlying cause of pediatric OHCA varies by age group. Chart 17-1 illustrates the causes of OHCA by age group based on a retrospective cohort of pediatric OHCA patients treated in King County, WA, between 1980 and 2009.[2]
- The incidence of sudden cardiac death in high school athletes screened every 3 years between 1993 and 2012 with standard preparticipation evaluations during Minnesota State High School League activities was 0.24 per 100 000 athlete-years.[3]
- A longitudinal study of students 17 to 24 years of age participating in National Collegiate Athletic Association sports showed that the incidence of nontraumatic OHCA was 1 per 22 903 athlete participant-years. The incidence

of cardiac arrest tended to be higher among blacks than among whites and among men than among women.[4]
- The most common causes of sudden death in competitive young athletes are hypertrophic cardiomyopathy (26%), commotio cordis (20%), and coronary artery anomalies (14%).[5]

Aftermath

- In the ROC Epistry, survival to hospital discharge in 2014 after EMS-treated nontraumatic cardiac arrest with any first recorded rhythm was 7.2% (95% CI, 4.3%–10.2%) for children (ROC Investigators, unpublished data, June 4, 2015). Survival after bystander-witnessed VF was 71.4% (95% CI, 38.0%–100.0%) for children (ROC Investigators, unpublished data, November 23, 2015).
- In 1 case series, long-term survival of pediatric OHCA patients surviving to hospital discharge was 92% at 1 year, 86% at 5 years, and 77% at 20 years.[6]

Adults

Incidence

(See Tables 17-1 and 17-2 and Charts 17-2 and 17-3.)

- The incidence of EMS-assessed, EMS-treated nontraumatic cardiac arrest and bystander-witnessed VF among individuals of any age during 2014 in the United States is best characterized by an ongoing registry from ROC.
- The total resident population of the United States was 321 716 000 as of September 10, 2015.[7] Extrapolation of the incidence of EMS-assessed OHCA reported by the ROC Investigators (ROC Investigators, unpublished data, November 23, 2015) to the total population of the United States suggests that each year, 110.8 individuals per 100 000 population (95% CI, 108.9–112.6), or 356 500 people of any age (quasi-CI, 350 000–362 000) or 347 000 adults (95% CI, 341 000–353 000), experience EMS-assessed OHCA.
- On the basis of extrapolation of data from the Oregon Sudden Unexpected Death Study, the estimated risk-adjusted incidence of sudden cardiac arrest was 76 per 100 000 per year (≈230 000 per year in the United States) and the estimated risk-adjusted incidence of sudden cardiac death was 69 per 100 000 per year (≈210 000 per year in the United States).[8] This data set excluded cases that were judged to have a noncardiac cause of arrest, which underestimates the overall burden of cardiac arrest. In the same study, the estimated societal burden of premature death was 2 million years of potential life lost for men and 1.3 million years of potential life lost for women.
- Approximately 60% of OHCAs are treated by EMS personnel.[9]
- Twenty-five percent of those with EMS-treated OHCA have no symptoms before the onset of arrest.[10]
- Among EMS-treated patients with OHCA, 23% have an initial rhythm of VF or VT or have a rhythm that is shockable by an automated external defibrillator.[11]
- The incidence of cardiac arrest with an initial rhythm of VF is decreasing over time; however, the incidence of cardiac arrest with any initial rhythm is not decreasing.[12]
- The median age for OHCA is 65 years.[13]
- Cardiac arrest is witnessed by a bystander in 38% of cases and by an EMS provider in 12% of cases and is unwitnessed in 50% of cases.[13]
- The majority of OHCAs occur at a home or residence (70%).[13]
- Among 10.9 million registered participants in 40 marathons and 19 half marathons, the overall incidence of cardiac arrest was 0.54 per 100 000 participants (95% CI, 0.41–0.70).[14] Those with cardiac arrest were more often male and were running a marathon versus a half marathon. Seventy-one percent of those with cardiac arrest died; those who died were younger (mean 39±9 years of age) than those who did not die (mean 49±10 years of age), were more often male, and were more often running a full marathon.

Risk Factors

- Prior HD is a major risk factor for cardiac arrest. A study of 1275 health maintenance organization enrollees 50 to 79 years of age who had cardiac arrest showed that the incidence of OHCA was 6.0 per 1000 person-years in subjects with any clinically recognized HD compared with 0.8 per 1000 person-years in subjects without HD. In subgroups with HD, incidence was 13.6 per 1000 person-years in subjects with prior MI and 21.9 per 1000 person-years in subjects with HF.[15]
- A family history of cardiac arrest in a first-degree relative is associated with an ≈2-fold increase in risk of cardiac arrest.[4,16]
- In a study of 81 722 women in the Nurses' Health Study, the PAR of sudden death associated with 4 lifestyle factors (smoking, PA, diet, and weight) was 81% (95% CI, 52%–93%).[17]
- A study conducted in New York City found the age-adjusted incidence of OHCA per 10 000 adults was 10.1 among blacks, 6.5 among Hispanics, and 5.8 among whites.[18]
- Analysis of 9235 sudden cardiac arrests in the ROC Epistry revealed the incidence of sudden cardiac arrest in the lowest socioeconomic quartile was nearly double that in the highest quartile (incidence rate ratio, 1.9; 95% CI, 1.8–2.0).[19]
- Analysis of data from the CARES registry revealed that patients who had a cardiac arrest in low-income black neighborhoods were less likely to receive bystander-initiated CPR than those who had a cardiac arrest in high-income white neighborhoods (OR, 0.49; 95% CI, 0.41–0.58).[20]

Aftermath

(See Table 17-3 and Chart 17-3.)

- In the ROC Epistry, survival to hospital discharge in 2014 after nontraumatic EMS-treated cardiac arrest with any first recorded rhythm was 12.0% (95% CI, 11.3%–12.7%) for patients of any age (ROC Investigators, unpublished data, November 23, 2015). Survival after bystander-witnessed VF was 38.6% (95% CI, 35.4%–41.8%) for patients of any age. Contemporary survival data will be available on completion of ongoing randomized trials.
- In the ROC Epistry between 2006 and 2010, unadjusted survival to hospital discharge after EMS-treated OHCA increased from 8.2% in 2006 to 10.4% in 2010.[21]
- In CARES, risk-adjusted rates of OHCA survival to hospital discharge increased from 5.7% in 2005 to 2006 to 8.3% in 2012 (adjusted risk ratio, 1.47; 95% CI, 1.26–1.70; $P<0.001$).[22]
- In CARES, 45 501 OHCAs were treated in 2014. Survival to hospital discharge was 10.8%, and survival with good

neurological function (Cerebral Performance Category 1 or 2) was 8.5%. For bystander-witnessed arrest with a shockable rhythm, survival to hospital discharge was 36.1%.[13]

- In a study using the US Nationwide Inpatient Sample data, in-hospital mortality for patients hospitalized after treatment for cardiac arrest declined 11.8%, from 69.6% in 2001 to 57.8% in 2009.[23]
- A study conducted in New York City found the age-adjusted survival to 30 days after discharge was more than twice as poor for blacks as for whites, and survival among Hispanics was also lower than among whites.[18]
- A study in Denmark of 1218 OHCA patients between 2002 and 2010 demonstrated that transport to a non–tertiary care center versus a tertiary care center after return of spontaneous circulation or with ongoing resuscitation was independently associated with increased risk of death (HR, 1.32; 95% CI, 1.09–1.59; *P*=0.004).[24]

In-Hospital Cardiac Arrest

For additional details on in-hospital arrest treatment outcomes, please refer to Chapter 23, Quality of Care.

Children

Aftermath

- Among 1031 children at 12 hospitals in the GWTG-Resuscitation Registry between 2001 and 2009, the initial cardiac arrest rhythm was asystole and pulseless electrical activity in 874 children (84.8%) and VF and pulseless VT in 157 children (15.2%). Risk-adjusted rates of survival to discharge increased from 14.3% in 2000 to 43.4% in 2009 (adjusted rate ratio per year, 1.08; 95% CI, 1.01–1.16; *P* for trend=0.02) without an increased rate of neurological disability among survivors over time (unadjusted *P* for trend=0.32).[25]
- In 2014, the GWTG-Resuscitation Registry reported 566 IHCAs in children 0 to 18 years old, with 241 surviving to hospital discharge (43%; 95% CI, 39%–47%), and 438 IHCAs in neonates 0 to 30 days old, with 187 surviving to hospital discharge (43%; 95% CI, 38%–47%).

Adults

Incidence

- Extrapolation of the incidence of IHCA reported by GWTG-Resuscitation to the total population of hospitalized patients in the United States suggests that each year, 209 000 (quasi-CI, 192 000–211 000) people are treated for IHCA.[26]
- Analysis of the UK National Cardiac Arrest Audit database between 2011 and 2013 (144 acute hospitals and 22 628 patients ≥16 years of age) revealed an incidence of IHCA of 1.6 per 1000 hospital admissions, with a median across hospitals of 1.5 (interquartile range, 1.2–2.2). The overall unadjusted survival rate was 18.4%.[27]

Aftermath

- In 2014, the GWTG-Resuscitation Registry reported 20 873 IHCAs in adults ≥18 years old, with 5168 surviving to hospital discharge (24.8%; 95% CI, 24.2%–25.4%).
- In the UK National Cardiac Arrest Audit database between 2011 and 2013, the overall unadjusted survival rate was 18.4%. Survival was 49% when the initial rhythm was shockable and 10.5% when the initial rhythm was not shockable.[27]
- Chan et al[28] demonstrated that rates of survival to discharge were lower for black patients (25.2%) than for white patients (37.4%) after IHCA. Lower rates of survival to discharge for blacks reflected lower rates of both successful resuscitation (55.8% versus 67.4% for blacks versus whites, respectively) and postresuscitation survival (45.2% versus 55.5%, respectively). Adjustment for the hospital site at which patients received care explained a substantial portion of the racial differences in successful resuscitation (adjusted RR, 0.92; 95% CI, 0.88–0.96; *P*<0.001) and eliminated the racial differences in postresuscitation survival (adjusted RR, 0.99; 95% CI, 0.92–1.06; *P*=0.68).

Inherited Syndromes Associated With Sudden Cardiac Death

Overview

- The majority of OHCA occurs in the general population without an underlying inherited syndrome associated with sudden cardiac death.[29] A large proportion of patients with OHCA have coronary atherosclerosis.[30] Recent data described below aid in the identification of high-risk subsets that contribute to a small proportion of the overall burden of OHCA but significantly increase the risk of affected individuals experiencing OHCA.

Long-QT Syndrome

- The hereditary LQTS is a genetic channelopathy characterized by prolongation of the QT interval (typically >460 ms) and susceptibility to ventricular tachyarrhythmias that lead to syncope and sudden cardiac death. Investigators have identified mutations in 13 genes leading to this phenotype (*LQT1* through *LQT13*). *LQT1* (*KCNQ1*), *LQT2* (*KCNH2*), and *LQT3* (*SCN5A*) mutations account for the majority (≈80%) of the typed mutations.[31,32]
- Prevalence of LQTS is estimated at 1 per 2000 live births from ECG-guided molecular screening of ≈44 000 infants (mostly white) born in Italy.[33] A similar prevalence was found among nearly 8000 Japanese school children screened by use of an ECG-guided molecular screening approach.[34] LQTS has been reported among those of African descent, but its prevalence is not well assessed.[35]
- There is variable penetrance and a sex-time interaction for LQTS symptoms. Risk of cardiac events is higher among boys than girls (21% among boys and 14% among girls by 12 years of age). Risk of events during adolescence is equivalent between sexes (≈25% for both sexes from ages 12–18 years). Conversely, risk of cardiac events in young adulthood is higher among women than men (39% among women from ages 18–40 years and 16% among men).[32]
- The mainstay of therapy and prevention is β-blockade treatment.[36,37] Implantable defibrillators are considered for high-risk individuals.[38]
- Individuals may be risk stratified for increased risk of sudden cardiac death[39] according to their specific long-QT mutation and their response to β-blockers.[37]

- Among 403 patients from the LQTS Registry from birth through age 40 years, multivariate analysis demonstrated that patients with multiple LQTS gene mutations had a 2.3-fold (P=0.015) increased risk for life-threatening cardiac events (comprising aborted cardiac arrest, implantable defibrillator shock, or sudden cardiac death) compared with patients with a single mutation.[40]

Short-QT Syndrome

- Short-QT syndrome is a recently described inherited mendelian condition characterized by shortening of the QT interval (typically QT <320 ms) and predisposition to AF, ventricular tachyarrhythmias, and sudden death. Mutations in 5 ion channel genes have been described (SQT1–SQT5).[41]
- In a population of 41 767 young, predominantly male Swiss transcripts, 0.02% of the population had a QT interval shorter than 320 ms.[42]
- Among 53 patients from the European Short QT Syndrome Registry (75% males, median age 26 years),[43] a familial or personal history of cardiac arrest was present in 89%. Twenty-four patients received an implantable cardioverter-defibrillator, and 12 received long-term prophylaxis with hydroquinidine. During a median follow-up of 64 months, 2 patients received an appropriate implantable cardioverter-defibrillator shock, and 1 patient experienced syncope. Nonsustained PVT was recorded in 3 patients.[43]
- In a cohort of 25 patients with short-QT syndrome ≤21 years of age followed up for 5.9 years, 6 patients had aborted sudden death (24%).[44] Sixteen patients (84%) had a familial or personal history of cardiac arrest. A gene mutation associated with short-QT syndrome was identified in 5 of 21 probands (24%).

Brugada Syndrome

- The Brugada syndrome is an acquired or inherited channelopathy characterized by persistent ST-segment elevation in the precordial leads (V_1–V_3), right bundle-branch block, and susceptibility to ventricular arrhythmias and sudden cardiac death.[45]
- Brugada syndrome is associated with mutations in several ion channel–related genes.[45]
- Prevalence is estimated at 1 to 5 per 10 000 individuals. Prevalence is higher in Southeast Asian countries, including Thailand and the Philippines. There is a strong male predominance (80% male).[45–50]
- Cardiac event rates for Brugada syndrome patients followed up prospectively in northern Europe (31.9 months) and Japan (48.7 months) were similar: 8% to 10% in patients with prior aborted sudden death, 1% to 2% in those with history of syncope, and 0.5% in asymptomatic patients.[51,52] Predictors of poor outcome included family history of sudden death and early repolarization pattern on ECG.[53,54]
- Among patients with spontaneous or drug-induced Brugada syndrome, first-degree AV block, syncope, and spontaneous type 1 ST-segment elevation were independently associated with risk of sudden death or implantable cardioverter-defibrillator–appropriate therapies.[55]

Catecholaminergic PVT

- Catecholaminergic PVT is a familial condition characterized by adrenergically induced ventricular arrhythmias associated with syncope and sudden death. It is associated with frequent ectopy, bidirectional VT, and PVT with exercise or catecholaminergic stimulation (such as emotion, or medicines such as isoproterenol).
- Mutations in genes encoding *RYR2*[57,57] are found in the majority, and mutations in genes encoding *CASQ2*[58,59] are found in a small minority.[51] However, a substantial proportion of individuals with catecholaminergic PVT do not have an identified mutation.
- Statistics regarding catecholaminergic PVT are primarily from case series. Of 101 patients with catecholaminergic PVT, the majority had experienced symptoms before 21 years of age.[51]
- In small series (n=27 to n=101) of patients followed up over a mean of 6.8 to 7.9 years, 27% to 62% experienced cardiac symptoms, and fatal or near-fatal events occurred in 13% to 31%.[51,52,56]
- Risk factors for cardiac events included younger age at diagnosis and absence of β-blocker therapy. A history of aborted cardiac arrest and absence of β-blocker therapy were risk factors for fatal or near-fatal events.[51]

Arrhythmogenic Right Ventricular Cardiomyopathy

- Arrhythmogenic right ventricular cardiomyopathy is a form of genetically inherited structural HD that presents with fibrofatty replacement of the myocardium, with clinical presentation of palpitations, syncope, and sudden death.[57]
- Twelve arrhythmogenic right ventricular cardiomyopathy loci have been described (ARVC1–ARVC12). Disease-causing genes for 8 of these loci have been identified, the majority of which are in desmosomally related proteins.[57]
- Prevalence is estimated at 2 to 10 per 10 000 individuals.[60,61] Of 100 patients reported on from the Johns Hopkins Arrhythmogenic Right Ventricular Dysplasia Registry, 51 were men and 95 were white, with the rest being of black, Hispanic, or Middle Eastern origin. Twenty-two percent of index cases had evidence of the familial form of arrhythmogenic right ventricular cardiomyopathy.[58]
- The most common presenting symptoms were palpitations (27%), syncope (26%), and sudden cardiac death (23%).[58]
- During a median follow-up of 6 years, 47 patients received an implantable cardioverter-defibrillator, 29 of whom received appropriate implantable cardioverter-defibrillator shocks. At the end of follow-up, 66 patients were alive. Twenty-three patients died at study entry, and 11 died during follow-up (91% of deaths were attributable to sudden cardiac arrest).[58] Similarly, the annual mortality rate was 2.3% for 130 patients with arrhythmogenic right ventricular cardiomyopathy from Paris, France, who were followed up for a mean of 8.1 years.[59]

Hypertrophic Cardiomyopathy

(Please refer to Chapter 20, Cardiomyopathy and Heart Failure, for statistics regarding the general epidemiology of HCM.)

- Over a mean follow-up of 8±7 years, 6% of HCM patients experienced sudden cardiac death.[62]

- Among 1866 sudden deaths in athletes between 1980 and 2006, HCM was the most common cause of cardiovascular sudden death (in 251 cases, or 36% of the 690 deaths that could be reliably attributed to a cardiovascular cause).[16]
- The risk of sudden death increases with increasing maximum LV wall thickness,[63,64] and the risk for those with wall thickness ≥30 mm is 18.2 per 1000 patient-years (95% CI, 7.3–37.6),[63] or approximately twice that of those with maximal wall thickness <30 mm.[63,64] Of note, an association between maximum wall thickness and sudden death has not been found in every HCM population.[63]
- Nonsustained VT is a risk factor for sudden death,[61,65] particularly in younger patients. Nonsustained VT in those ≤30 years of age is associated with a 4.35-greater odds of sudden death (95% CI, 1.5–12.3).[61]
- A history of syncope is also a risk factor for sudden death in these patients,[66] particularly if the syncope was recent before the initial evaluation and not attributable to a neurally mediated event.[67]
- The presence of LV outflow tract obstruction ≥30 mm Hg appears to increase the risk of sudden death by ≈2-fold.[68,69] The presence of LV outflow tract obstruction has a low positive predictive value (7%–8%) but a high negative predictive value (92%–95%) for predicting sudden death.[68,70]
- The rate of malignant ventricular arrhythmias detected by implantable cardioverter-defibrillators appears to be similar between those with a family history of sudden death in ≥1 first-degree relative and those with at least 1 of the risk factors described above.[71]
- The risk of sudden death increases with the number of risk factors.[72]

Early Repolarization Syndrome

(See Table 17-1.)

- Early repolarization, observed in ≈4% to 19% of the population[73–76] (more commonly in young men[73,75,77] and in athletes[74]) has conventionally been considered a benign finding.
- A clinically relevant syndrome was initially described in which ≥1-mm positive deflections (sometimes referred to as "J waves") in the S wave of ≥2 consecutive inferior or lateral leads was significantly more common among patients with idiopathic VF than among control subjects.[73,74] Given an estimated risk of idiopathic VF in the general population (among those aged 35–45 years) of 3.4 per 100 000, the positive predictive value of such J-wave findings in a person 35 to 45 years of age increases the chances of having idiopathic VF to 11 of 100 000.[74]
- In an analysis of the Social Insurance Institution's Coronary Disease Study in Finland, J-point elevation was identified in 5.8% of 10 864 people.[75] Those with inferior-lead J-point elevation more often were male and more often were smokers; had a lower resting heart rate, lower BMI, lower BP, shorter corrected QT interval, and longer QRS duration; and were more likely to have ECG evidence of CAD. Those with lateral J-point elevation were more likely to have LV hypertrophy. Before and after multivariable adjustment, subjects with J-point elevation ≥1 mm in the inferior leads (n=384) had a higher risk of cardiac death (adjusted RR, 1.28; 95% CI, 1.04–1.59; *P*=0.03) and arrhythmic death (adjusted RR, 1.43; 95% CI, 1.06–1.94; *P*=0.03); however, these patients did not have a significantly higher rate of all-cause mortality. Before and after multivariable adjustment, subjects with J-point elevation >2 mm (n=36) had an increased risk of cardiac death (adjusted RR, 2.98; 95% CI, 1.85–4.92; *P*=0.03), arrhythmic death (adjusted RR, 3.94; 95% CI, 1.96–7.90; *P*=0.03), and death of any cause (adjusted RR, 1.54; 95% CI, 1.06–2.24; *P*=0.03).
- In CARDIA, 18.6% of 5069 participants had early repolarization restricted to the inferior and lateral leads at baseline; by year 20, only 4.8% exhibited an early repolarization pattern.[76] Younger age, black race, male sex, longer exercise duration and QRS duration, and lower BMI, heart rate, QT index, and Cornell voltage were associated cross-sectionally with the presence of baseline early repolarization. Predictors of maintenance of the ECG pattern from baseline to year 20 were black race (OR, 2.62; 95% CI, 1.61–4.25), BMI (OR, 0.62 per 1 SD; 95% CI, 0.40–0.94), serum triglyceride levels (OR, 0.66 per 1 SD; 95% CI, 0.45–0.98), and QRS duration (OR, 1.68 per 1 SD; 95% CI, 1.37–2.06) at baseline.
- Evidence from families with a high penetrance of the early repolarization syndrome associated with a high risk of sudden death suggests that the syndrome can be inherited in an autosomal dominant fashion.[78] A meta-analysis of genome-wide association studies performed in population-based cohorts failed to identify any genetic variants that met criteria for statistical significance.[79]

Genome-Wide Association Studies

- Genome-wide association studies have been performed directly on cases of arrhythmic death to try to identify novel genetic variants associated with risk of sudden death. These are intended to discover previously unidentified genetic variants and biological pathways that contribute to potentially lethal ventricular arrhythmias. Limitations of these studies are the small number of samples available for analysis and the heterogeneity of case definition. The number of loci identified as having genome-wide significance for sudden cardiac death is much smaller than for other complex diseases. In addition, studies to date have not consistently identified the same variants. A pooled analysis of case-control and cohort studies used genome-wide association studies to identify a rare (1.4% minor allele frequency) novel marker at the BAZ2B locus (bromodomain adjacent zinc finger domain 2B) that was strongly associated with a risk of arrhythmic death (OR, 1.9; 95% CI, 1.6–2.3).[80]

Table 17-1. Incidence of Out-of-Hospital Cardiac Arrest in US Sites of the Resuscitation Outcomes Consortium

		Annual No. of US Cases		
	Incidence per 100 000 (95% CI)	n	95% LCL	95% UCL
EMS assessed				
Any age	110.8 (108.9–112.6)	356 461	350 349	362 252
Adults	140.7 (138.3–143.1))	347 322	341 397	353 246
Children	9.4 (8.3–10.5)	7037	6214	7861
EMS treated				
Any age	57.3 (56.0–58.7)	184 343	180 161	188 847
Adults	73.0 (71.2–74.7)	180 202	175 759	184 399
Children	7.3 (6.3–8.3)	5465	4716	6214
VF*				
Any age	12.1 (11.5–12.7)	38 928	36 997	40 858
Adults	15.8 (15.0–16.6)	39 003	37 028	40 978
Children	0.5 (0.3–0.8)	374	225	599
Bystander-witnessed VF				
Any age	7.0 (6.5–7.5)	22 520	20 912	24 129
Adults	9.2 (8.6–9.8)	22 710	21 229	24 192
Children	0.3 (0.1–0.5)	225	75	374

Assumes total US population is 321 716 000.[7] CI indicates confidence interval; EMS, emergency medical services; LCL, lower confidence limit; UCL, upper confidence limit; and VF, ventricular fibrillation.

*The estimated number of annual VF cases of any age is less than the estimated number of cases in adults alone because of rounding and missing information about patient age.

Source: Resuscitation Outcomes Consortium Investigators, unpublished data, data time frame is June 1, 2014, to May 31, 2015. Population growth of 0.93% per year has now been added from the 2010 population. In 2013, 23.27% of population was <18 years of age. This is used for annual number of case estimates for adults and children.

Table 17-2. Range of Reported Estimates of Burden of Out-of-Hospital Cardiac Arrest in the United States[81]

Patient Population	Incidence per 100 000 Person-Years	Total Incidence per Year*
CARES		
EMS treated	57	179 877
ROC Epistry*		
EMS treated	63.8	201 690
EMS treated and untreated†	124.8	394 529

CARES indicates Cardiac Arrest Registry to Enhance Survival; EMS, emergency medical services; and ROC, Resuscitation Outcomes Consortium.

*ROC Epistry incidence counts all cardiac arrests (with cardiac and noncardiac pathogenesis), whereas CARES incidence includes cardiac arrest of presumed cardiac origin only.

†"Untreated" refers to cases that did not receive resuscitation treatment because patients were either dead on EMS arrival or had existing do-not-resuscitate orders.

Table 17-3. Survival After Out-of-Hospital Cardiac Arrest in US Sites of the Resuscitation Outcomes Consortium

	Survival to Discharge (95% CI), %
EMS assessed	
Any age	6.3 (5.9–6.7)
Adults	6.4 (6.0–6.8)
Children	7.2 (4.3–10.2)
Unknown age	0.5 (0.0–1.3)
EMS treated	
Any age	12.0 (11.3–12.7)
Adults	12.1 (11.3–12.8)
Children	9.8 (5.8–13.7)
Unknown age	6.7 (0.0–19.3)
VF	
Any age	32.6 (30.2–34.9)
Adults	32.5 (30.1–34.8)
Children	40.0 (15.2–64.8)
Bystander-witnessed VF	
Any age	38.6 (35.4-41.8)
Adults	38.2 (35.0–41.4)
Children	71.4 (38.0–100)

CI indicates confidence interval; EMS, emergency medical services; and VF, ventricular fibrillation.

Source: Resuscitation Outcomes Consortium, unpublished data, time frame: June 1, 2014, to May 31, 2015.

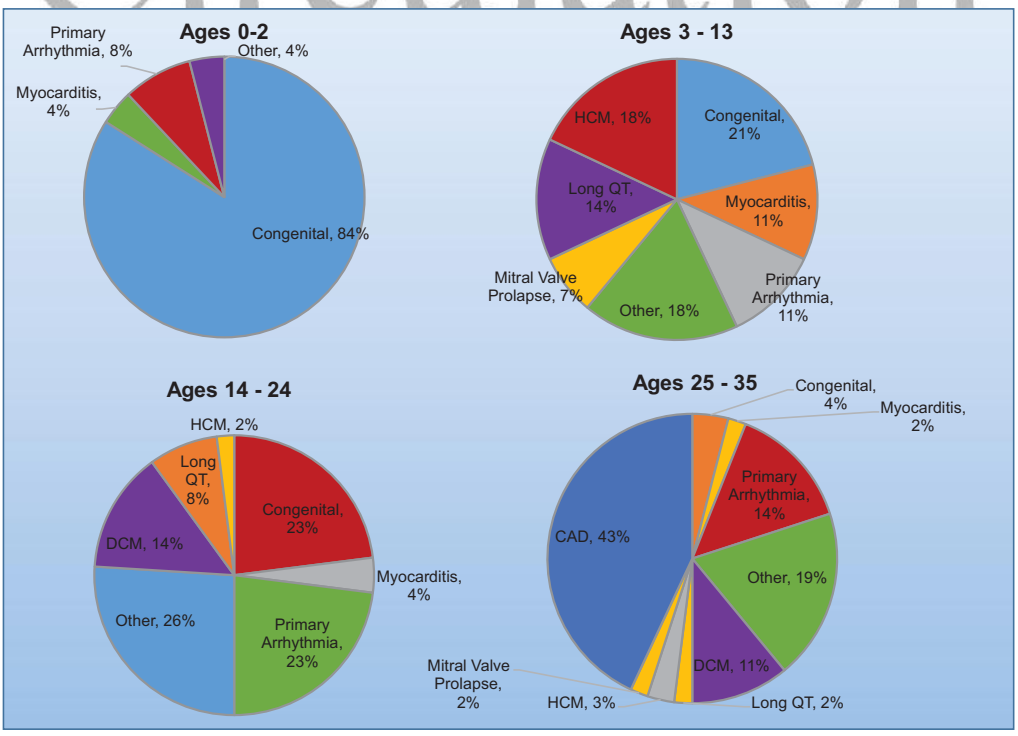

Chart 17-1. Detailed causes of arrest by age group. CAD indicates coronary artery disease; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; and "Other," all other causes. Reprinted from Meyer et al with permission.[2] Copyright © 2012, American Heart Association, Inc.

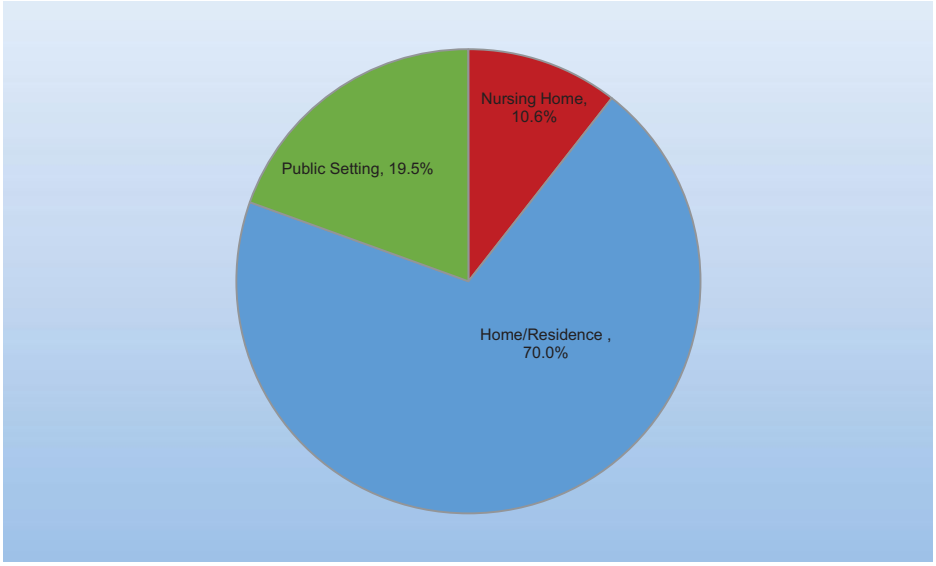

Chart 17-2. Location of out-of-hospital cardiac arrest, 2014. Data derived from 2014 Cardiac Arrest Registry to Enhance Survival (CARES) National Summary Report.[13]

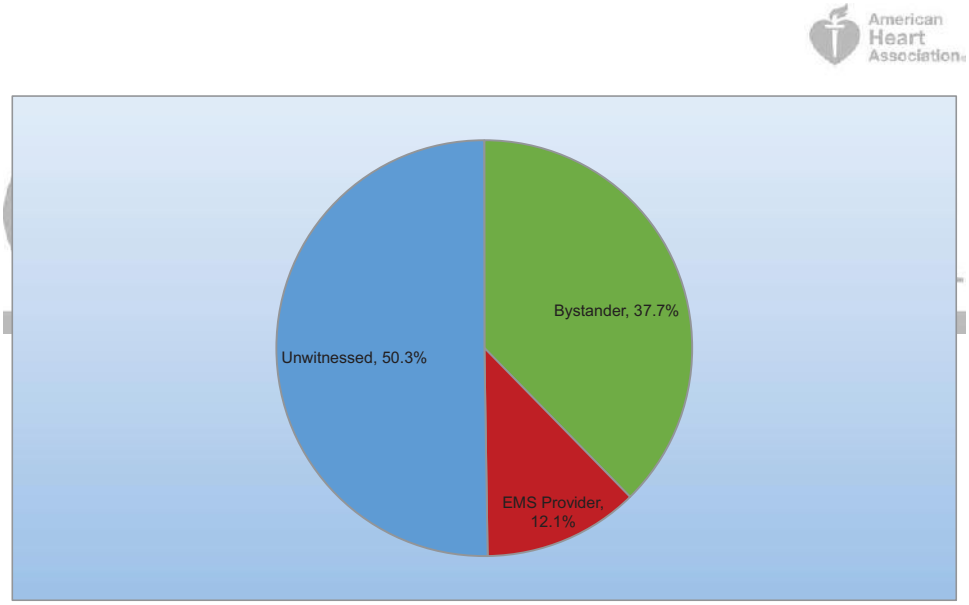

Chart 17-3. Out-of-hospital cardiac arrest witness status, 2014. EMS indicates emergency medical services. Data derived from 2014 Cardiac Arrest Registry to Enhance Survival (CARES) National Summary Report.[13]

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