Cardiac arrest describes the loss of mechanical activity of the heart as confirmed by the absence of signs of circulation.¹ Sudden cardiac death is further described as a death from a cardiac cause within 1 hour from the onset of symptoms in a person without any prior condition that would appear fatal.² The World Health Organization proposed an alternate definition based on the recognition that many cardiac arrests are not witnessed: an unexpected, unexplained death within 1 hour of symptom onset for witnessed events, or within 24 hours of last observed alive and symptom-free, for unwitnessed events.³ Sudden cardiac arrest is a term commonly applied to such an event when the patient survives.⁴

Episodes of cardiac arrest have multiple causes. In addition to primary cardiac events, respiratory arrest, pulmonary embolism, trauma, cerebral events, and many other conditions can lead to sudden unexpected death. For the purposes of surveillance, research, and treatment, it would be ideal to reserve sudden cardiac arrest for only primary cardiac events. However, this goal is elusive. Even with a full narrative of the death, experts often disagree on appropriate classification.⁵ In survivors of out-of-hospital cardiac arrest, 12-lead electrocardiogram and history are poor predictors of which patients have “significant” cardiac lesions at the time of emergency catheterization.⁶ Among victims of cardiac arrest who had high-grade coronary stenosis at autopsy, only a small minority were previously known to have coronary heart disease.⁷ Classification of causes of arrest based on information acquired in-hospital is conditioned on survival to hospital, making it susceptible to selection bias. There is significant and important variation in the proportion of patients with cardiac arrest who are treated or transported by emergency medical services (EMS) providers,⁸ so relying on data from this source does not distinguish reliably among causes of cardiac arrest.

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These observations suggest that the cause of arrest can accurately be determined only by conducting a postmortem examination.

Because it would be impractical to perform an autopsy on every fatal arrest, classification must rely on information available to paramedics in the out-of-hospital setting. For the purpose of evaluation of prehospital emergency care of cardiac arrest, a pragmatic alternative definition of sudden cardiac arrest\(^9,10\) includes patients with nontraumatic, out-of-hospital cardiac arrest, who are assessed by EMS personnel and (1) receive attempts at external defibrillation (by lay responders or emergency personnel), or receive chest compressions by organized EMS personnel; or (2) are pulseless but do not receive attempts to defibrillate or CPR by EMS personnel. The latter includes patients with (1) a do not attempt resuscitation directive signed and dated by a physician, (2) extensive history of terminal illness or intractable disease, or (3) request from the patient’s family.

Each of these definitions has inherent limitations. The suddenness (ie, time course) and cause are difficult to assess because only about two-thirds of cases are witnessed and, in most cases, an autopsy is not performed. Consequently, information from other sources is used to assess timeline and cause, including death certificates, EMS reports, medical records, and medical examiner reports. These sources are used independently or in combinations with each other. Information from death certificates tends to exclude patients who are successfully resuscitated and have been found to overestimate death by cardiac cause.\(^11\) Studies limited to patients with cardiac arrest who are treated by EMS take into account patients who are assessed but not treated because of futility (ie, those with late recognition of death), resulting in an underestimation of incidence and overestimation of survival relative to those that include all patients with cardiac arrest who are assessed or treated by EMS. Surveillance using multiple sources is needed to capture all appropriate cases of cardiac arrest.\(^12\)

**INCIDENCE**

Incidence of disease is defined as the occurrence rate per year for the condition within a population at risk. It is calculated by taking a ratio of the number of persons developing a disease each year divided by the population at risk. Given some of the complications with data collection described above, it is difficult to establish an accurate incidence. The incidence of cardiac arrest treated by EMS is greater than 55 per 100,000 person-years in the United States.\(^11\) Combining information from death certificates, EMS reports and hospital record review suggests that the incidence of cardiac arrest is 95 per 100,000 person years,\(^10\) or 8.04 per 100,000 person-years among children and 126.52 per 100,000 person-years among persons older than 20.\(^13\) Another factor that affects incidence rates is that the number of individuals within a given area may fluctuate by time of day and day of week. Large cities that have more people during the working week may seem, falsely, to have a higher rate of cardiac arrest than would be expected based on the corresponding census population.

There is virtually no data available on incidence of cardiac arrest in the developing world.\(^4\)

The incidence of cardiac arrest has markedly declined during the last 30 years (**Fig. 1**).\(^14–16\) This decline is correlated with a decrease in overall cardiovascular mortality.\(^17\) The reasons for this decline are likely multifactorial, but are mostly attributed to improvements in primary and secondary prevention of coronary heart disease.

**SURVIVAL**

Survival is defined as the number of survivors divided by the number of individuals who experienced the event of interest. Survival after cardiac arrest depends, in part, on the
population considered. Among 39 sites worldwide that published their outcomes over time, median survival for all rhythm groups to hospital discharge was 6.4% (interquartile range [IQR], 3.7%–10.3%). Among 10 sites in North American that collated data describing patients with cardiac arrest using similar definitions contemporaneously with each other, survival for all rhythm groups to hospital discharge was median of 8.4% (IQR, 5.4%–10.4%). Experts have attempted to standardize reporting and comparison of outcomes by disseminating the Utstein template for cardiac arrest. Despite this standardization, there is a greater than fivefold regional variation in survival among patients with any initial rhythm, as well as among patients with ventricular fibrillation. This large variation reemphasizes that cardiac arrest is a treatable condition. However, regional variation in outcome after cardiac arrest is not fully explained by the Utstein factors, which include patient factors, such as age, gender, and initial rhythm; and EMS factors, such as time to arrival and time to first defibrillation. Moreover, despite the marked decline in coronary artery disease mortality during the last 30 years, few communities have been able to achieve sustained improvements in survival after cardiac arrest.

NET BURDEN

Out-of-hospital cardiac arrest affects approximately 490,000 individuals in Europe each year and approximately 350,000 individuals in the United States. It is the third leading cause of death in the United States (Fig. 2; extrapolated from and http://www.cdc.gov/nchs/fastats/deaths.htm, accessed March 11, 2011). The related condition of in-hospital cardiac arrest affects approximately 200,000 individuals in the United States (R Merchant, personal communication, March 10, 2011). Thus, reduction of the burden of illness associated with cardiac arrest is a critical public health issue.

NEED FOR PUBLIC HEALTH SURVEILLANCE OF CARDIAC ARREST

The true incidence of out-of-hospital cardiac arrest and survival from cardiac arrest are unknown. Current health surveillance systems cannot accurately determine the burden of out-of-hospital cardiac arrest, nor measure progress toward reducing this
burden. The Cardiac Arrest Registry to Enhance Survival (CARES) collates cases of out-of-hospital cardiac arrest from participating agencies in the United States, but includes only cases of presumed cardiac origin.\(^{26}\) The National EMS Information System (NEMSIS) is an ongoing effort to create a national EMS database.\(^ {27}\) Because NEMSIS relies on self-report, events submitted by states do not necessarily represent all EMS events occurring within a state and states vary in criteria used to determine the types of EMS events submitted to the NEMSIS dataset.\(^ {28}\) Moreover, NEMESIS has a high rate of missing the vital data on functional status at discharge, limiting its ability to assess the comparative effectiveness of resuscitation interventions. The International Resuscitation Network demonstrated that data related to out-of-hospital cardiac arrest can be collated from five different countries, but does not collect data on an ongoing basis.\(^ {29}\) Other registries have focused on assessment of specific resuscitation interventions (eg, European Resuscitation Council Hypothermia Network).\(^ {30}\) Get With the Guidelines-Resuscitation (formerly known as American Heart Association National Registry for Cardiopulmonary Resuscitation) collates cases of in-hospital cardiac or respiratory arrest from institutions that are primarily in the United States,\(^ {31-34}\) but excludes cases of out-of-hospital cardiac arrest. Thus, although there are several prior and existing multicenter electronic clinical databases, none comprehensively assesses the benefits and harms of emergency cardiovascular care interventions in real-world settings on an ongoing basis through the continuum of care from EMS to hospital discharge by using a scalable, sustainable method.

Clinicians and policy makers need improved estimates of incidence to determine the absolute clinical and public health burden of cardiac arrest. Preventive and treatment measures aimed at reducing mortality from cardiac arrest can only derive from a reliable and valid estimate of its incidence and outcome. However, several barriers to effective surveillance of cardiac arrest exist. A common obstacle is that EMS and hospital systems may be reluctant to share outcome data because of concerns about how the data will be used and potential violation of regulations that protect personal health information. Even before the advent of the Health Insurance Portability and Accountability Act (HIPAA), EMS providers, quality assurance staff, and researchers...
often had difficulty ascertaining the functional status at hospital discharge of patients treated by EMS. However, under HIPAA, disclosure of information is permitted under specific circumstances, including public health disease reporting (http://www.hhs.gov/ocr/privacy/, accessed February 24, 2011). This is a strong argument for making cardiac arrest a reportable event.

PATIENT-LEVEL RISK FACTORS

Our understanding of why some individuals experience sudden cardiac arrest while other clinically comparable persons do not is incomplete and contributes to the ongoing public health challenge posed by cardiac arrest. Patient-level risk factors include fixed and modifiable factors. Overall, about 80% of people who suffer cardiac arrest have coronary artery disease (often undiagnosed), 10% to 15% have cardiomyopathy, and 5% to 10% have another problem, such as congenital heart disease or primary arrhythmogenic problem (eg, long QT syndrome or Brugada syndrome).35

**Fixed**

The risk of cardiac arrest increases with age, peaking in people aged 75 to 84 years. Females have a lower incidence of cardiac arrest than males.11 Genetic risk factors for cardiac arrest include polygenetic factors that contribute to atherosclerosis, in addition to relatively rare genetic syndromes that directly cause arrhythmia such as congenital long QT syndrome and Brugada syndrome. However, the marked reduction in the incidence of ventricular fibrillation over the last few decades15 suggests that genetics have a relatively small contribution to population-attributable risk. It remains unclear how to incorporate increased understanding of genetic risk into mass screening of individuals to cardiac arrest.

**Modifiable**

Health behaviors affect cardiac arrest risk. Given that 80% of sudden cardiac arrest is attributable to coronary disease, modification of risk factors, such as hypertension, diabetes, hyperlipidemia, and smoking, logically reduces both sudden and non-sudden cardiac deaths.17 Regular exercise lowers cardiac arrest risk and can decrease mortality in people with established cardiac disease; however, risk is acutely increased during the period of exertion.36 This relationship may reflect the balance between sympathetic and parasympathetic tone.

Cigarette smoking is thought to be the single most important cause of preventable death in the United States. An estimated 443,000 persons in the United States die prematurely each year due to exposure to tobacco smoke.37 The deleterious effects of smoking may be mediated through increased plasma catecholamines, heart rate, and arterial blood pressure, resulting in coronary spasm and increases in myocardial work and oxygen supply. Collectively these effects lower ventricular fibrillation (VF) thresholds. In patients who successfully quit smoking, rates of cardiac arrest return to near normal over time. Of great concern is the effect of “passive smoking,” which has been associated with an increase in smoking-related disease, primarily heart disease.

People who consume a moderate amount of alcohol (2–6 drinks per week) have a lower risk of sudden cardiac arrest when compared with nondrinkers. However, heavy consumption has been associated with increased risk. The interplay between alcohol and cardiac arrest is unclear but its protective effects are thought to be mediated via increased levels of high-density lipoprotein.36,39
A diet that includes fatty fish is rich in n-3 polyunsaturated fatty acids and has been associated with a lower risk of VF.\textsuperscript{40} Research suggests that the acids stabilize action potentials by altering sodium and calcium ion channels in cardiac myocytes.

Diabetes may be a risk factor for cardiac arrest, independent of its contribution to coronary artery disease.\textsuperscript{41,42} A proposed mechanism is abnormal prolongation of the QT interval due to diabetic autonomic dysfunction, although this has not been proved.\textsuperscript{43} Moderate or vigorous, but not lesser, physical exertion is associated with increased risk of cardiac arrest.\textsuperscript{44} Acute\textsuperscript{45} and chronic\textsuperscript{46} mental health conditions are associated with increased risk of cardiac arrest. However, it is difficult to objectively measure characteristics such as anger, anxiety, hostility, and aggressiveness because there are many confounding issues.

**Structural**

Dilated or hypertrophic cardiomyopathy accounts for about 10\% to 15\% of cases of cardiac arrest.\textsuperscript{35} Decreased left ventricular function, regardless of ischemic or non-ischemic cause, is a strong predictor of cardiac arrest.\textsuperscript{47} Despite that severe left ventricular dysfunction is the best available risk predictor for sudden cardiac arrest, it was observed in less than a third of all cases in one community.\textsuperscript{48} Other structural abnormalities, such as congenital malformations, scar from prior myocardial infarction, infiltrative diseases, and myocarditis, also predispose to cardiac arrest.\textsuperscript{49}

**Coronary Ischemia**

Up to 71\% of patients with cardiac arrest have coronary atherosclerosis and nearly half have an acute coronary occlusion.\textsuperscript{6,50,51} Moreover, there is a high incidence (97\%) of coronary artery disease in patients resuscitated from out-of-hospital cardiac arrest who undergo immediate angiography.\textsuperscript{6} Among these, 50\% have acute coronary occlusion. However, the absence of ST elevation on a surface 12-lead ECG after resuscitation from cardiac arrest is not strongly predictive of the absence of coronary occlusion on acute angiography. A case series of patients with unsuccessful field resuscitation suggested that in such patients VF is more likely to be associated with coronary atherosclerosis than asystole or pulseless electric activity.\textsuperscript{52} An autopsy study compared case subjects who died within 6 hours of symptom onset due to ischemic heart disease and who were not seen by a physician within 3 weeks with control subjects who died within 6 hours of symptom onset due to natural or unnatural noncardiac causes. Control subjects were matched to case subjects by age, gender, and socioeconomic status.\textsuperscript{53} Intraluminal thrombosis was observed in 93\% of case subjects versus 4\% of control subjects. Collectively, these studies suggest that patients who are resuscitated from out-of-hospital VF have a high likelihood of having an acute coronary occlusion.

**Medications**

Medications that reduce coronary disease would logically reduce the rate of cardiac arrest. Indeed, statins decrease mortality due to cardiac arrest,\textsuperscript{54,55} most likely acting via anti-ischemic rather than antiarrhythmic mechanisms.\textsuperscript{56} Beta-blockers, aldosterone antagonists, angiotensin-converting enzyme inhibitors, angiotensin receptor-blockers, and omega-3 fatty acids may also contribute to reduced risk of cardiac arrest.\textsuperscript{57} Medications also have the potential to promote cardiac arrest. Medications that prolong the QT interval, including antiarrhythmics, antipsychotics, and many other classes of medications, may cause ventricular arrhythmias and, therefore, cardiac arrest. Hypokalemia and hypomagnesemia may have the same effect. However, it is unknown how much medication-induced or electrolyte-induced arrhythmias contribute to the overall incidence of cardiac arrest.\textsuperscript{58}
Initial Rhythm

The exact mechanism of collapse in an individual patient is often difficult to establish because more than 40% of all cases present without prior warning and are not readily under close observation. Therefore, much of what we understand is hypothesized from information obtained or observed after the event has begun. In the vast majority of cases, individuals who suffer cardiac arrest have evidence of structural heart disease. In general, approximately 80% have coronary atherosclerosis, another 10% to 15% have nonischemic cardiomyopathy, and the remaining 5% to 10% have a congenital disorder or no evidence of structural disease. Usually this underlying structural abnormality predisposes an individual to a fatal or near fatal arrhythmia that is precipitated by an acute trigger, such as an ischemic event or electrolyte imbalance. The rhythm that is first recorded after the onset of cardiac arrest classified into three categories: (1) ventricular tachyarrhythmias, including pulseless ventricular tachycardia and VF (VT/VF); or (2) pulseless electrical activity (PEA); or (3) asystole.

Initial rhythm has a large impact on survival: published rates of survival after treatment of any initial rhythm range from 0% to greater than 20% among those with EMS-treated arrest and 0% to 45% for those with VF arrest. Consistently, survival is greatest in patients with a first-recorded rhythm of VF. VF is characterized by rapid, ineffective, uncoordinated movement of the ventricles that does not produce a pulse. The ECG of VF shows measurable electrical activity with chaotic, irregular ventricular complexes. If untreated, the electrical organization of the ventricular fibrillation signal deteriorates into asystole over minutes. Coronary ischemia is thought to be the primary precipitant of VT/VF, a correlation confirmed in recent studies. The cause of PEA is diverse and related to a variety of factors, including hypoxia, hypovolemia, electrolyte imbalance, tamponade, pneumothorax, and thromboembolism.

Historically, most out-of-hospital cardiac arrest cases documented VT/VF as the first recorded rhythm. The incidence of VF has declined steadily in regions that have tracked EMS data over 10 to 21 years. The decline of VF may be attributed to treatment of cardiac risk factors, increasing rates of ICD placement, and increasing use of beta-blockers. Another possibility is that multisystem organ failure is becoming more common and presenting frequently as non-VF cardiac arrest. This decline is of substantial importance for public health because survival rates are significantly less for PEA compared with VT/VF.

COMMUNITY-LEVEL RISK FACTORS

Socioeconomic and Racial Differences

Disparities in the incidence of and survival from cardiac arrest are observed across socioeconomic gradients and between races. In New York City, for example, a prospective study found that age-adjusted incidence of cardiac arrest was 10.1 per 10,000 for blacks and 5.8 per 10,000 for whites; survival to discharge was 1.4% for blacks and 3.4% for whites. However, after adjustment for socioeconomic factors, prior functional status, initial rhythm, and characteristics of the event, no significant racial differences were found.

Environmental

There is temporal variability in cardiac arrest frequency, with cardiac arrest peaking in the morning and in the winter. Underlying patient, EMS system, and environmental factors need to be explored to offer further insight into these observed patterns. Various physiologic processes have been proposed to explain the diurnal
phenomenon, such as increased clotting or increased parasympathetic instability. Some researchers have suggested that part of the morning peak in cardiac arrest may be due to a reporting artifact (i.e., when patients die during the night but are not discovered until early morning). Potential interventions to reduce periodic variation in unexpected cardiac death include resource allocation of EMS and hospital resources to match anticipated need.

A PUBLIC HEALTH APPROACH TO CARDIAC ARREST

Survival from cardiac arrest varies tremendously across communities. As noted above, this variation is associated with variation in prehospital emergency care. There are many ways to improve the chain of survival after cardiac arrest, including improved communications from citizens to EMS, delivery of care to the patient, delivery of the patient to the hospital, and delivery of cardiac and critical care. Yet few communities have been able to achieve sustained improvements in outcome.

There is only a twofold variation in outcome after care for the related disorder of acute myocardial infarction, but correlates of such variation have been better elucidated. These include geographic region,70–72 hospital volume,73,74 urban location,75 teaching status,72,76 and safety net status.77 Variation in outcome does not seem to associate with large differences in protocols or processes of care, such as rapid response teams, clinical guidelines, use of hospitalists, and medication checks.78 Instead, hospitals in the top or bottom tier of risk-standardized mortality after myocardial infarction differ substantially in terms of their organizational goals and values, senior management involvement, staff presence and expertise in care for patients with acute myocardial infarction, communication and coordination among relevant groups, and problem solving and learning. It has been suggested that such cultural differences are a major factor in regional variation in outcomes after cardiac arrest.79

SUMMARY

A cardiac resuscitation system is an interconnected community, EMS, and hospital response to out-of-hospital cardiac arrest.80 A critical component of such a response is ongoing measurement and improvement of the process and outcome of care. Such regional systems of care have improved provider experience and patient outcome for other time-sensitive conditions, including ST-elevation myocardial infarction and life-threatening traumatic injury. The time has come for us to come together to implement such resuscitation systems of care in our communities. Interested physicians, EMS providers, and members of the lay public have begun this process in Arizona, Minnesota, North Carolina, Pennsylvania, and Washington (www.heartrescueproject.com, accessed March 29, 2011). Ongoing efforts and evaluation are needed in these and other communities to ensure that public health is improved by reducing death and disability due to cardiac arrest.

REFERENCES


