Sudden Cardiac Death
Interface Between Pathophysiology and Epidemiology

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KEYWORDS

• Sudden cardiac death • Cardiac arrest • Coronary heart disease • Population risk • Epidemiology • Ventricular tachyarrhythmias • Asystole • Pulseless electrical activity

KEY POINTS

- Sudden cardiac death (SCD) accounts for 50% of all cardiovascular deaths; approximately 50% of all SCDs are first cardiac events; sudden cardiac arrest (SCA) accounts for up to 50% of heart disease–related years of productive life lost.
- Measures of risk of SCA and SCD can be substrate based or expression based.
- The pathophysiologic cascade for SCA includes modules of atherogenesis, plaque destabilization, onset of ischemia, and arrhythmia.
- Mechanisms of tachyarrhythmias leading to SCA differ for onset of ischemia and reperfusion of ischemic myocardium.

Sudden cardiac arrest (SCA), defined as an event characterized by an abrupt loss of blood flow caused by an unexpected cessation of cardiac mechanical function, followed by the outcome of sudden cardiac death (SCD), is a major public health problem because of its incidence and demographics. Current estimates for out-of-hospital SCDs are in the range of 390,000 per year in the United States[1,2] (**Box 1**). The number of emergency medical system (EMS)–assessed out-of-hospital SCAs (OHCAs) in the United States is estimated at 356,000, among which 347,500 are in adults more than 18 years of age.[1] An additional 200,000 in-hospital SCAs (IHCAs) occur annually.[3] The overall national survival rates following OHCA and IHCA are in the range of 10% and 26%, respectively. A perspective on the impact of SCD is provided by the so-called rule of 50s[2]: SCD accounts for 50% of all cardiovascular deaths[4]; approximately 50% of all SCDs are first (recognized) expressions of a cardiac disorder[5]; and SCA accounts for up to 50% of heart disease–related loss of years of productive life.[6] The loss of years of productive life includes both premature deaths and the consequences of persisting neurologic damage following SCA among survivors. Despite this long-recognized large public health burden attributable to SCA and SCD, prediction of risk at the individual patient level remains very limited.[2] Population studies and clinical trials have identified high-risk subgroups, but individual risk prediction, especially among the general population, awaits the identification of more powerful markers than are currently available. The exceptions are a few very-high-risk subgroups or specific causes in which individual risk prediction is adequate, but most events emerge from other segments of the population.

Four temporal elements contribute to the pathophysiologic bases of risk, expression, and outcomes of SCA: (1) prodromes, (2) onset of symptoms heralding cardiac arrest, (3) the SCA itself, and (4) consequent death versus survival.

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Box 1
Site-specific incidence of sudden cardiac arrest (SCA). Recent incidence figures for sudden cardiac arrest in the United States are provided for out-of-hospital and in-hospital events, with subgroups according to specific sites

Out of hospital	~390,000 annually in United States
Cumulative survival ~10%	
Home/residence	~80% of events; survival 6%
Public venues (general)	~15% to 25% survival
Public venues (specific) (eg, airports, airliners, casinos)	40% to 70% survival
In hospital	~200,000 annually in United States
Cumulative survival ~24%	
SCA during procedures in electrophysiology and cardiac catheterization laboratory	Greater than 95% survival
SCA in coronary care unit or medical intensive care unit	Greater than 90% survival (ACS) Greater than 40% survival (transient factors) Less than 30% survival (heart failure; shock)
General care units	~15% to 20% survival

Because the proximate cause of SCA is an abrupt disturbance in cardiovascular function resulting in loss of consciousness caused by cessation of blood flow, the time definition must recognize the brief interval between onset of the mechanism directly responsible for initiating the cardiac arrest and the consequent loss of blood flow. The arbitrary 1-hour definition primarily refers to the duration of the heralding symptoms, and defines the interval between the onset of symptoms signaling the pathophysiologic disturbance leading to cardiac arrest and the onset of the cardiac arrest. When the pathophysiologic onset is an acute myocardial infarction or abrupt worsening of heart failure, a 1-hour definition (or longer) is appropriate, but when the heralding event is a hemodynamically significant tachyarrhythmia, the interval between onset and cardiac arrest is often a matter of seconds. Once cardiac output ceases, or central systolic blood pressure decreases to less than 60 mm Hg, loss of consciousness occurs rapidly. Human centrifuge studies during the early years of the space program identified an interval between abrupt cessation of carotid blood flow and loss of consciousness of 10 seconds or less.

Prodromes, occurring during the weeks or months before an SCA, if recognized, are general predictors of an impending event, but are not specific for SCA itself. The same premonitory signs and symptoms may be more specific for the imminent cardiac arrest when they begin abruptly. Sudden onset of chest pain, dyspnea, or palpitations and other symptoms of arrhythmias often occur within the 1-hour before the onset of the SCA. In contrast, the fourth element, biological death, may range from minutes in the absence of return of spontaneous circulation (ROSC) to a much longer delay in patients who remain biologically alive for a long period after ROSC because of failure to restore hemodynamic, metabolic, or neurologic function and stability, but ultimately leading to death. In the latter circumstance, the causative pathophysiologic and clinical event is the SCA, because the SCA is the factor responsible for the delayed biological death. Most studies link the SCD (the outcome) to the SCA (the event), rather than to a biological death that occurs during hospitalization after cardiac arrest or within 30 days. Thus, when a consequent death follows an SCA during the days or weeks of a postarrest hospitalization, it should still be defined as an SCD following an SCA. In contrast, unwitnessed deaths use the definition of SCD for persons known to be alive and functional 24 hours prior, assuming other causes, such as neurologic, hemorrhagic, traumatic, or toxicologic causes, are not identified postmortem. Not all sudden deaths that seem to be cardiac are actually cardiac in origin based on subsequent evaluation.[7] A significant proportion are associated with abrupt neurologic events or other noncardiac causes. This point emphasizes the importance of careful adjudication of events when analyzing causation data. Another caution relates to patients with unexplained SCDs, based on negative autopsy findings. Under these circumstances, postmortem genetic studies should be performed in order to identify previously undiagnosed genetic disorders, particularly among persons who are less than or equal to 40 years of age at the time of SCD.[8]

INCIDENCE OF SUDDEN CARDIAC ARREST

The incidence of SCD has long been estimated to be in the range of 1 per 1000 population per year