**TABLE 317-1 Distinction Between Cardiovascular Collapse, Cardiac Arrest, and Death**

| TERM | DEFINITION | QUALIFIERS | MECHANISMS |
|---|---|---|---|
| Cardiovascular collapse | Sudden loss of effective circulation due to cardiac and/or peripheral vascular factors that may reverse spontaneously (e.g., neurocardiogenic syncope transient hypotension) or require interventions (e.g., hypovolemia, tamponade, ventricular fibrillation). | Broad term that includes cardiac arrest as well as transient events that characteristically revert spontaneously presenting as syncope. | Same as cardiac arrest, plus neurocardiogenic syncope or other causes of transient loss of blood flow. |
| Cardiac arrest | Abrupt cessation of cardiac function resulting in loss of effective circulation that may be reversible by prompt emergency medical intervention. | Rare spontaneous reversions; likelihood of successful intervention relates to mechanism of arrest, clinical setting, availability of emergency medical services, and prompt return of circulation. | Ventricular fibrillation, ventricular tachycardia, asystole, bradycardia, pulseless electrical activity, noncardiac mechanical factors (e.g., pulmonary embolism). |
| Sudden cardiac death | Sudden unexpected death attributed to cardiac arrest, which occurs within 1 hour of symptom onset. | In unwitnessed cases, the definition is often expanded to include unexpected deaths where the subject was documented to be well within the preceding 24 hours. | Same as cardiac arrest. |



and other predisposing conditions also increases. Although absolute SCD rates increase with age, the proportion of deaths that are due to SCD decreases as other causes of death increase.

Women have a lower incidence of SCD and SCA than men, and women are more likely to present with pulseless electrical activity (PEA) and to have their SCD occur at home as compared with men. Possibly related to these factors, the SCD rate has not declined as much for younger women compared to men in recent years. Black as opposed to white Americans have higher rates of SCD, are more likely to have unwitnessed arrests and to be found with PEA, and have lower rates of survival. Socioeconomic disparities, with resuscitation being less likely in low-income neighborhoods, are contributing factors but do not appear to account for the entirety of the elevated SCD rate in blacks. Alternatively, individuals of Hispanic ethnicity appear to have lower rates of SCD, despite having a higher prevalence of cardiac risk factors. It appears that the incidence of SCD may be relatively low among Asian populations as well, both within the United States and globally. These gender and racial differences in SCD/SCA incidence and survival are poorly understood and warrant further research.

### RISK FACTORS (SEE FIG. 317-1)

The presence of overt structural heart disease and/or certain types of inherited arrhythmia syndromes markedly elevates SCD risk (see Chaps. 261 and 262). Preexisting CHD and HF are the most prevalent predisposing cardiac conditions and are associated with a four- to tenfold increase in SCD risk. Correspondingly, SCD shares many of the same risk factors with CHD and heart failure (HF), including hypertension, diabetes, hypercholesterolemia, obesity, and smoking. Diabetes is a particularly strong risk factor for SCD even in patients with established CHD. Hypertension and resultant left ventricular hypertrophy (LVH) appear to be particularly important markers of SCD risk in blacks, in whom the prevalence of these conditions is greater. Smoking markedly elevates risk, and smoking cessation lowers risk particularly among individuals who have not yet developed overt CHD. Serum cholesterol appears to be more strongly related to SCD at younger ages, and the benefits of cholesterol lowering on SCD incidence have not been firmly established. There also appears to be a genetic component to SCD risk that is distinct from that associated with other manifestations of atherosclerosis. A history of SCD in a first-degree relative is associated with an increased risk for SCD, and with the occurrence of ventricular fibrillation (VF) during acute MI, but is not associated with an increased risk for acute MI. These data suggest that genetic factors may predispose to fatal ventricular arrhythmia in the setting of ischemia, rather than to CHD in general.

Obstructive sleep apnea and seizure disorders are also associated with increased SCD risk; the underlying mechanism is not clear but may be due to hypoxia-induced cardiac arrest. Atrial fibrillation also appears to be associated with an increased risk of SCD, which is partly, but not entirely, accounted for by its association with underlying heart disease. Patients with chronic kidney disease are also at higher SCD risk with annualized SCD rates approaching 5.5% in patients undergoing dialysis. Electrolyte shifts and LVH, which are common in this population, have been suggested to play a role. There are also potential dietary influences on SCD risk. Individuals with higher intakes of polyunsaturated fatty acids, particularly n-3 fatty acids, and other components of a Mediterranean-style diet have lower SCD risks in observational studies, possibly due to antiarrhythmic effects of dietary components. Low levels of alcohol intake may be beneficial, but heavy intake (>3 drinks/day) appears to elevate risk.

### PRECIPITATING FACTORS

SCD/SCA occurs with higher frequency at certain times, locations, and in association with certain activities and exposures. Although not consistently observed across all studies, there do appear to be circadian variations in the incidence of SCD and cardiac arrest, with peaks in incidence in the morning hours and again in the later afternoon. There is also seasonal variability in SCD rates, which may be related to temperature and light exposure. Rates are highest during winter in the northern hemisphere and summer in the southern hemisphere. SCD rates also acutely peak during disasters such as earthquakes and terrorist attacks. SCA arrests are more likely to occur in certain locations as well, with notable clustering around train stations, airports, and other public places where there is significant population transit. SCD rates tend to be higher in urban areas, and individuals who live near major roadways are at elevated SCD risk. There is also a well-recognized acute elevation in SCD risk that occurs during or shortly after bouts of vigorous exertion, and men appear to be more susceptible. Habitual exercise and training lower this acute risk but do not eliminate it entirely. Exertion-associated SCDs are particularly tragic and highly publicized when they occur in highly trained athletes; however, the majority of such deaths actually occur in the general population. The common thread among these precipitating factors is likely heightened autonomic tone, which can promote ischemia and has direct proarrhythmia and electrophysiologic actions that lower the threshold for sustained VF.

## CAUSES OF SUDDEN CARDIAC DEATH

### UNDERLYING HEART DISEASE (FIG. 317-1)

Our understanding regarding the diseases that contribute to SCD is derived primarily from autopsy series and cardiac evaluations in cardiac arrest survivors, which are highly variable in level of detail. Despite the limitations of these data, it is generally accepted that sudden death due to cardiac causes is most commonly due to CAD, although the proportion with CAD varies markedly by age, race, and sex. It is estimated that ~70% of SCDs in white men are due to CAD, as compared with only 40–50% in women and blacks. The proportion of SCDs with underlying CAD may be even lower in Asian ethnicities. Recent data suggest that the proportion of SCDs with CAD on autopsy may be declining in some parts of Europe and the United States, and,

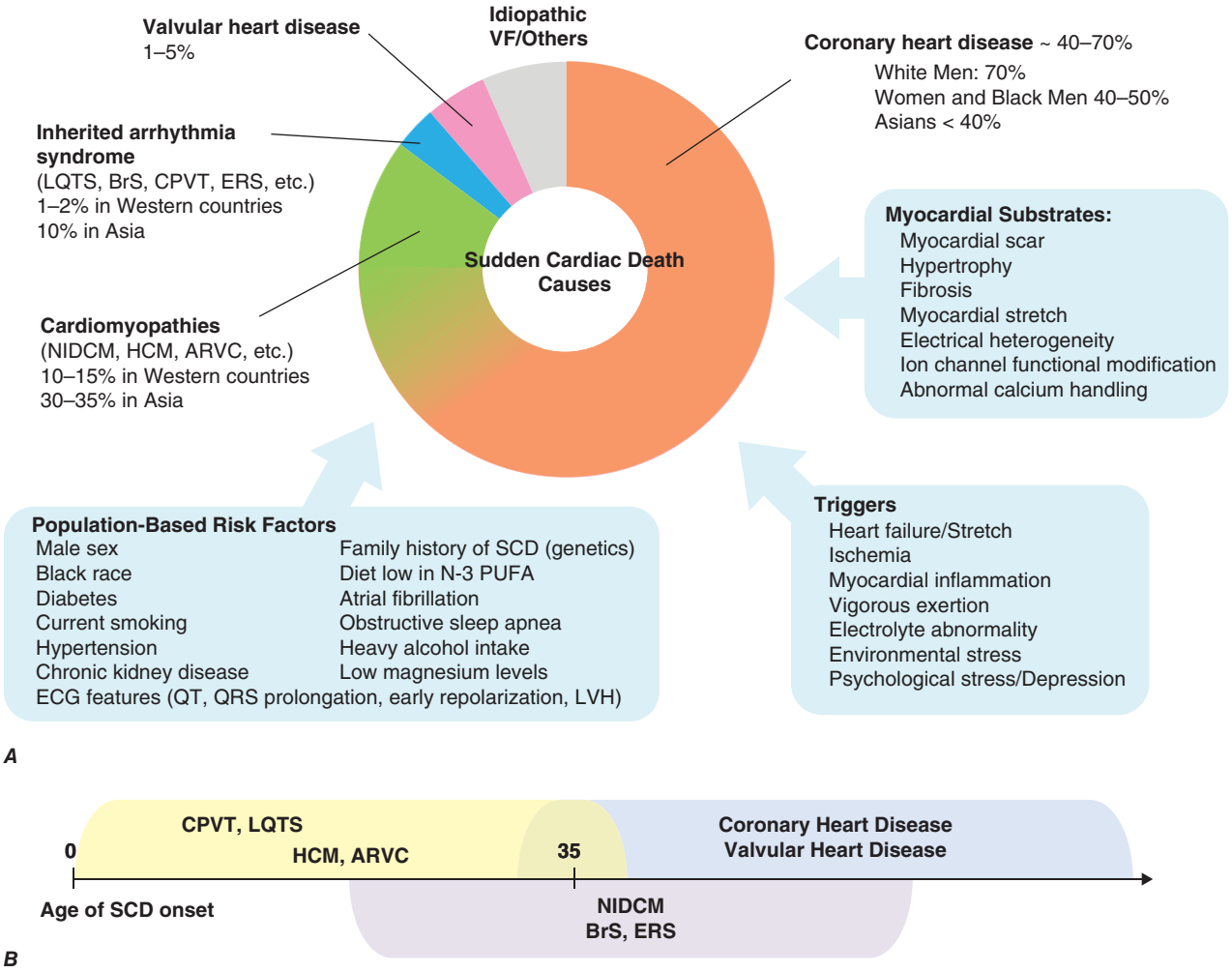



**FIGURE 317-1** ***A.*** Proportionate causes, substrates, risk factors, and triggers of sudden cardiac death (SCD). ***B.*** Variation of causes by age of onset. ARVC, arrhythmogenic right ventricular cardiomyopathy; BrS, Brugada syndrome; CPVT, catecholaminergic ventricular tachycardia; ECG, electrocardiogram; ERS, early repolarization syndrome; HCM, hypertrophic cardiomyopathy; LQTS, long QT syndrome; LVH, left ventricular hypertrophy; NICDM, nonischemic cardiomyopathy; PUFA, polyunsaturated fatty acid; SCD, sudden cardiac death; VF, ventricular fibrillation. *(Reproduced with permission from M Hayashi et al: The spectrum of epidemiology underlying sudden cardiac death. Circ Res 116:1887, 2015.)*

at the same time, increasing in parts of Japan and other parts of Asia. Beyond CAD, nonischemic cardiomyopathies (hypertrophic, dilated, and infiltrative) are the second most frequent cause of SCD in the United States and European countries. Other less common causes include valvular heart disease, myocarditis, myocardial hypertrophy (often from hypertension), and rare primary electrical heart diseases such as long QT and Brugada syndromes. On average, 5–10% of SCA victims do not have a significant cardiac abnormality at the time of autopsy or after extensive premortem cardiac evaluation, and this also varies by gender and race. Before 35 years of age, atherosclerotic CAD accounts for a much smaller proportion of deaths, with hypertrophic cardiomyopathy (HCM), coronary artery anomalies, myocarditis, arrhythmogenic right ventricular cardiomyopathy, and primary ion channelopathies accounting for a significant number of these deaths.

## CARDIAC RHYTHMS AND SUDDEN DEATH

The initial rhythm found when EMS arrive at the scene of an out-of-hospital cardiac arrest is an important indication of the potential cause of the arrest and of the prognosis. In the early days of EMS systems, over half of victims were found in VF, giving rise to the hypothesis that ischemic VF or ventricular tachycardia (VT) degenerating to VF was the most common event. The proportion of cardiac arrests found in VF has decreased markedly since the 1970s, to only 20–25% in more recent studies, and PEA and asystole are now the most common scenarios. However, the vast majority of cardiac arrests are not monitored at the time of collapse, and since arrhythmias are inherently unstable once hemodynamic collapse occurs, the rhythm at the time of EMS arrival may not reflect the rhythm that initially precipitated the SCA because VF and primary bradycardias can degenerate into asystole. Nonetheless, VF as an initial rhythm still predominates in public locations or in other situations when there is a short time frame between witnessed arrest and arrival of EMS, suggesting that VF remains a common initial precipitating rhythm. However, there are also data to support an absolute decrease in VF incidence. Proposed explanations include decreases in underlying CHD incidence, increased use of beta blockers in CHD, and implantable cardioverter defibrillators (ICD) in high-risk patients. There also appears to be an increase in PEA incidence over the past several years, suggesting that the proportion of SCD due to abrupt hemodynamic collapse in the absence of preceding fatal arrhythmia may be increasing. Proposed explanations for these proportional changes in PEA versus VF include the aging of the population and the increased prevalence of end-stage cardiovascular disease and other severe comorbidities. These older, sicker patients may be more likely to have arrests in the home and to have acute precipitants leading to PEA (i.e., respiratory, metabolic, vascular) and/or be less likely to sustain VF up to the point of EMS arrival.

## DISEASE-SPECIFIC MECHANISMS

CAD can cause SCD through several mechanisms **(Table 317-2)**. The most common cause is acute MI or transient myocardial ischemia that leads to polymorphic VT and VF **(see Chap. 262)**. Other primary mechanisms include severe bradyarrhythmias such as heart block with a slow escape rhythm, or PEA due to a massive MI or associated myocardial rupture. Areas of ventricular scar from prior infarcts increase

**TABLE 317-2 Causes of Cardiovascular Collapse and Sudden Cardiac Arrest**

| CAUSE | PATHOPHYSIOLOGIC SUBSTRATE | RHYTHM PRESENTATION |
|---|---|---|
| **Cardiac Causes** | | |
| Coronary artery disease<br>Atherosclerotic, coronary spasm, congenital anomalies | Acute myocardial ischemia/infarction, ventricular rupture, tamponade<br>Ventricular scar from healed infarction | Polymorphic VT/VF<br>Bradyarrhythmia<br>Pulseless electrical activity<br>VT<br>VF |
| Cardiomyopathies<br>Dilated, hypertrophic, ARVC, infiltrative disease, valvular disease with LV failure | Ventricular scar<br>Ventricular hypertrophy<br>Pump failure | VT<br>Polymorphic VT/VF<br>Pulseless electrical activity<br>Bradyarrhythmia |
| Congenital heart disease<br>(Tetralogy of Fallot, VSD, others) | Ventricular scar from surgical repair<br>Hypertrophy | VT<br>Bradyarrhythmias<br>Polymorphic VT/VF |
| Aortic stenosis | Obstruction to aortic outflow<br>Ventricular hypertrophy | Bradyarrhythmia<br>Pulseless electrical activity<br>Bradyarrhythmia<br>Polymorphic VT/VF |
| Mitral valve prolapse/mitral regurgitation | Pump failure<br>Ventricular scar | Polymorphic VT/VF |
| Arrhythmia syndromes without structural heart disease:<br>Genetic:<br>Long QT<br>Brugada<br>CPVT<br>Idiopathic VF, early repolarization<br>Drug toxicities (acquired long QT, others)<br>Electrolyte abnormalities (severe hypokalemia) | Abnormal cellular electrophysiology | Polymorphic VT/VF |
| Wolff-Parkinson-White syndrome | Accessory atrioventricular connection | Pre-excited AF/VF |
| Commotio cordis | Blunt precordial impact | Polymorphic VT/VF |
| **Noncardiac Causes of Cardiovascular Collapse** | | |
| Pulmonary embolism | | PEA |
| Stroke | | PEA, bradyarrhythmia |
| Aortic dissection | | PEA, VF |
| Exsanguination/hypovolemia | | PEA |
| Tension pneumothorax | | PEA |
| Sepsis | | PEA |
| Neurogenic | | PEA, bradyarrhythmia |
| Drug overdose | | PEA, bradyarrhythmia |

*Abbreviations:* AF, atrial fibrillation; ARVC, arrhythmogenic right ventricular cardiomyopathy; CPVT, catecholaminergic polymorphic ventricular tachycardia; LV, left ventricle; PEA, pulseless electrical activity; VF, ventricular fibrillation; VSD, ventricular septal defect; VT, ventricular tachycardia.

the predisposition to reentrant VT, which often degenerates to VF. Once patients have suffered an MI, their risk of SCD elevates up to 10-fold, with the highest absolute rates in the first 30 days after MI. The mechanisms underlying SCD vary at different time points after MI, with nonarrhythmic causes such as myocardial rupture and/or extensive reinfarction predominating early, within the first 1–2 months, and ischemic polymorphic VT and/or scar-related ventricular arrhythmias prevailing later. VT and sudden death can, and often do, occur years after an initial MI.

**Cardiomyopathies and Other Forms of Structural Heart Disease** Scar-mediated reentrant VT can also occur in a host of nonischemic cardiomyopathies in which replacement fibrosis and/or inflammatory ventricular infiltrates occur (Chap. 261). In congenital heart disease, surgical scars created during corrective surgery, such as those performed to correct ventricular septal defects in tetralogy of Fallot, can also serve as the substrate for ventricular reentry. Other common predisposing processes such as LVH, ventricular stretch due to fluid overload, and cardiomyocyte dysfunction can result in electrical heterogeneity and other electrophysiologic changes that predispose to ventricular arrhythmias, including ion channel alterations that prolong action potential duration, impair cellular calcium handling, and diminish cellular coupling. These processes occur in a wide variety of diseases associated with depressed ventricular function and/or hypertrophy, including CAD, valvular heart disease, myocarditis, and nonischemic cardiomyopathies.

**Absence of Structural Heart Disease** In the absence of structural heart disease, VF can be due to an inherited ion channel abnormality, as in long QT and Brugada syndromes (Chap. 262), rapid atrial fibrillation associated with Wolff-Parkinson-White syndrome (Chap. 256), or drug toxicities, such as polymorphic VT due to drugs that prolong the QT interval (Chap. 263). Blunt, nonpenetrating precordial impact over the (left) chest wall can lead to commotio cordis and is a rare cause of SCD in otherwise healthy individuals. PEA can result from pulmonary emboli, exsanguination, or the terminal phase of respiratory arrest.

## MANAGEMENT OF CARDIAC ARREST

As the ability to predict SCA in the population is very limited, community approaches to reduce death focus on the rapid identification of victims and implementation of resuscitation measures by those

who first encounter the victim, most likely the lay public, who ideally summon EMS and initiate basic life-support measures with chest compressions. The approach is codified in the "out-of-hospital chain of survival," which includes: (1) initial evaluation and recognition of the SCA and activation of the emergency response system; (2) rapid initiation of cardiopulmonary resuscitation (CPR) with an emphasis on chest compressions; (3) defibrillation as quickly as possible usually with an automatic external defibrillation applied by the lay rescuer or emergency medical technician (EMT); (4) advanced life support; (5) postcardiac arrest care; and (6) recovery from cardiac arrest. There have been major advances in each of these areas, and survival rates to hospital discharge for out-of-hospital cardiac arrest have increased, particularly for patients found in VT or VF, where survival rates can approach 30% in some regions. Overall survival rates for out-of-hospital cardiac arrest are also higher for patients receiving CPR, with recent studies in Europe reporting survival rates of 16%. Multiple studies have pointed to socioeconomic disparities in the administration of CPR and application of automatic external defibrillators (AEDs) contributing to reduced survival rates from out-of-hospital cardiac arrest in black and Hispanic populations in the United States.

The initial goal of resuscitation is to achieve the return of spontaneous circulation (ROSC). Success is strongly related to the time between collapse and initiation of resuscitation, decreasing markedly after 5 min, and the rhythm at the time of EMT arrival, being best for VT, worse for VF, and poor for PEA and asystole. Outcomes are also determined by the age, clinical state, and comorbidities of the victim prior to the arrest.



## INITIAL EVALUATION AND INITIATION OF CPR

The rescuer should check for a response from the victim, shout for help, and call or ask someone else to call their local emergency number (e.g., 911), ideally on a cell phone that can be placed on speaker mode at the patient's side such that the responding dispatcher can provide instructions and queries to the rescuer. Consideration of aspiration or airway obstruction is important, and if suspected, a Heimlich maneuver may dislodge the obstructing body. A trained health care provider would also check for a pulse (taking no longer than 10 seconds so as not to delay initiation of chest compressions) and assess breathing. Gasping respirations and brief seizure activity are common during SCA and may be misinterpreted as breathing and responsiveness. Chest compressions should be initiated without delay and administered at a rate of 100–120/min depressing the sternum by 5 cm (2 in.) and allowing full chest recoil between compressions. Chest compressions generate forward cardiac output with sequential filling and emptying of the cardiac chambers, with competent valves maintaining forward direction of flow. Interruption of chest compressions should be minimized to reduce end-organ ischemia. Ventilation may be administered with two breaths for every 30 compressions if a trained rescuer is present, but for lay rescuers without training, chest compressions alone ("hands-only CPR") are more likely to be effectively applied and of similar benefit. If a second rescuer is present, they should be sent to seek out an AED, which are now widely available in many public areas.

## RHYTHM-BASED MANAGEMENT (SEE FIG. 317-2)

The rapidity with which defibrillation/cardioversion is achieved is an important predictor of outcome. A defibrillator, most often an AED, should be applied as soon as available. AEDs are easily used by lay rescuers and trained first responders, such as police officers and trained security guards. When the arrest is witnessed, the use of AEDs by lay responders can improve cardiac arrest survival rates. Once patches are applied to the chest, a brief pause in chest compressions is required to allow the AED to record the rhythm. An AED will advise delivery of a shock if the recorded rhythm meets criteria for VF or VT. Chest compressions are continued while the defibrillator is being charged. As soon as a diagnosis of VF or VT is established, a 200-J biphasic waveform shock should be delivered. Chest compressions are resumed immediately and continue for 2 min until the next rhythm check. If VT/VF is still present, a second maximal energy shock is delivered. This sequence is continued until personnel to administer advanced life support are available or ROSC is achieved. Electrocardiogram (ECG) rhythm strips produced by the AED should be retrieved, as the initial rhythm can be an important consideration in determining the cause of the arrest and to guide further therapy and evaluation if resuscitation is successful.

When advanced cardiac life support is available, an intravenous line is established for administration of medication and consideration given to placement of an advanced airway (endotracheal tube or supraglottic airway device). Intraosseous access may be considered if attempts at intravenous access are not successful or are not feasible. Epinephrine 1 mg every 3–5 min may be administered intravenously or intraosseously. If circulation is not restored or the patient is less than fully conscious despite return of circulation, confirmation that acidosis and hypoxia are adequately addressed should be assessed with arterial blood gas analysis. If metabolic acidosis persists after successful defibrillation and with adequate ventilation, 1 mEq/kg $NaHCO_3$ may be administered.

The cardiac rhythm guides resuscitation when monitoring is available. VT is treated with external shocks synchronized to the QRS when VT is monomorphic, and asynchronous shocks for polymorphic VT or VF. If VT/VF recurs after one or more shocks, amiodarone 300 mg can be administered as a bolus via intravenous or intraosseous route in the hope that arrhythmia recurrence will be prevented after the next shock, followed by a 150-mg bolus if the arrhythmia recurs. If amiodarone fails, lidocaine can be administered.

Consideration of etiology should also guide therapy (Chaps. 261 and 262). Commonly encountered causes of recurrent VT/VF may be due to ongoing myocardial ischemia or infarction that would benefit from emergent coronary angiography and revascularization, or QT prolongation causing the polymorphic VT torsades des pointes that may respond to administration of magnesium. Hyperkalemia should respond to administration of calcium, while other measures are implemented to reduce serum potassium.

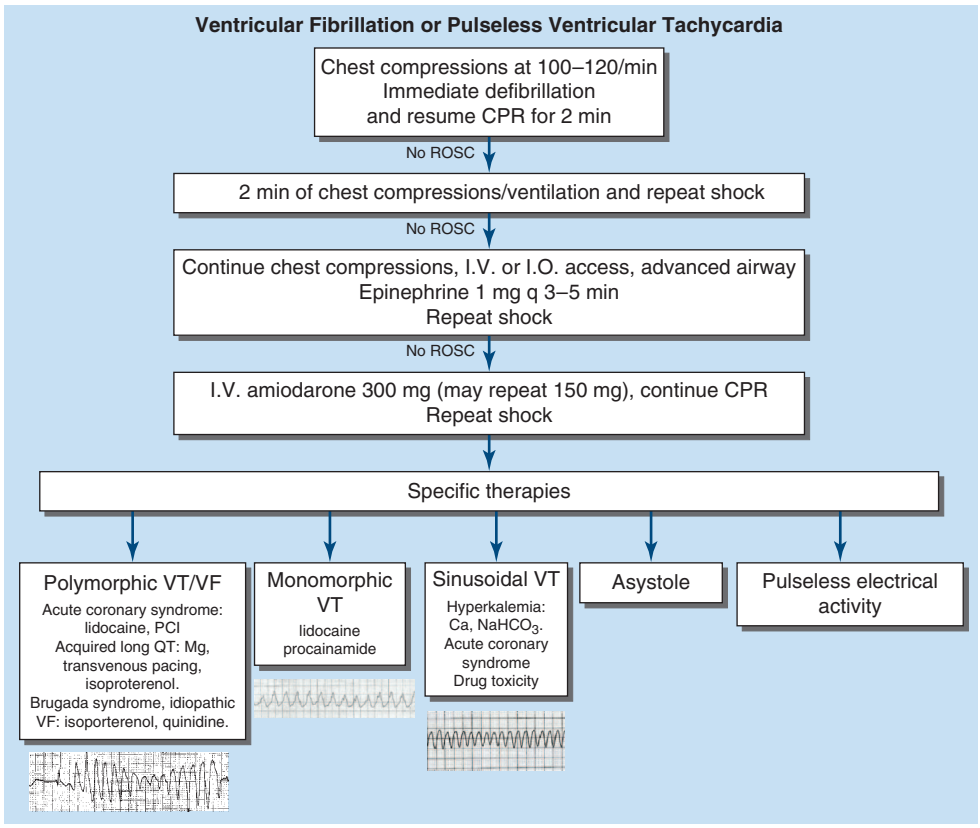
PEA/asystole should be managed with CPR, ventilation, and administration of epinephrine. Causes of PEA/asystole that require specific therapy should be considered including airway obstruction, hypoxia, hypovolemia, acidosis, hyperkalemia, hypothermia, toxins, cardiac tamponade, tension pneumothorax, pulmonary embolism, and MI. Naloxone should be administered if opiate overdose is suspected.

## POSTCARDIAC ARREST ACUTE MANAGEMENT

Following restoration of effective circulation, the possibility of acute MI should be immediately assessed. The majority of patients who have ST elevation consistent with acute MI will be found to have a culprit coronary stenosis/occlusion and emergent coronary angiography with percutaneous angioplasty, and stenting is recommended. Emergent angiography may also be considered if cardiogenic shock, electrical instability, signs of significant myocardial damage, or ongoing ischemia is present. Emergent or early angiography has not been found to result in better outcomes compared to delayed angiography in patients presenting with out-of-hospital cardiac arrest due to a VT/VF with no ECG evidence of ST-segment elevation. Thus, decisions regarding which patients without ST-segment elevation should undergo urgent angiography are complex, and factors such as hemodynamic or electrical instability and evidence of ongoing ischemia are taken into consideration.

Hemodynamic instability is often present following resuscitation, and further ischemic end-organ damage is a major consideration. Optimizing ventilation with consideration of acidosis, hypoxemia, and electrolyte abnormalities is important. Maintaining systolic blood pressure at >90 mmHg and mean blood pressure >65 mmHg is desirable and may require administration of vasopressors and adjustment of volume status. Potentially treatable reversible causes, including hyperkalemia, severe hypokalemia, and drug toxicity with QT prolongation causing torsades des pointes, should be identified and treated (Chap. 262).

After stable spontaneous circulation is achieved, brain injury due to ischemia and reperfusion is a major determinant of survival and accounts for over two-thirds of deaths. The probability of successful

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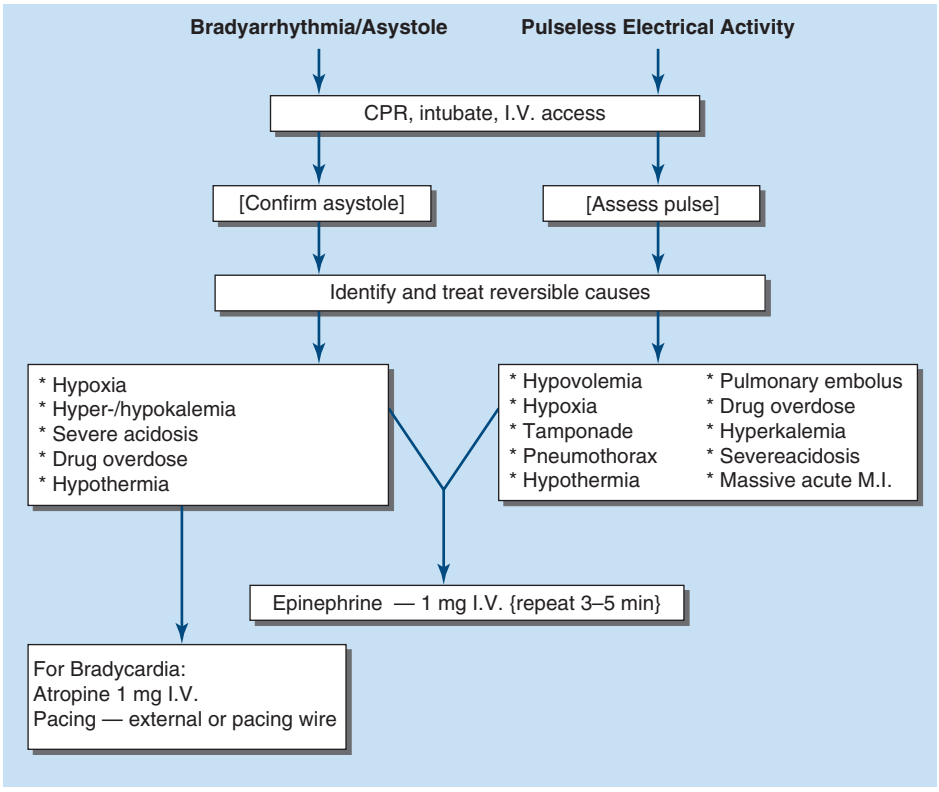


*B*

**FIGURE 317-2 Algorithm for approach to cardiac arrest due to ventricular tachycardia (VT) or ventricular fibrillation (VF; shockable rhythm).** ***A.*** Chest compressions with ventilation and defibrillation or cardioversion should be initiated as soon as possible. Defibrillation should be repeated with minimal interruption of chest compressions. Once an intravenous or intraosseous access is established, administration of epinephrine defibrillation and amiodarone and defibrillation are performed. Further therapy can be guided by possible causes as suggested by the initial or recurrent cardiac rhythm as shown. CPR, cardiopulmonary resuscitation; I.O., intraosseous; I.V., intravenous; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation. ***B.*** Algorithm for approach to cardiac arrest due to bradyarrhythmias/asystole and pulseless electrical activity. Chest compressions with ventilation (and intubation) should be initiated as soon as possible, and intravenous access should be obtained. Once an intravenous or intraosseous access is established, administration of epinephrine is performed. At the same time, an investigation for potential reversible causes should be made and any such causes should be treated if present. For bradycardic rhythms, atropine 1 mg administered intravenously and external subcutaneous or transvenous pacing are also performed. Defibrillation should be repeated with minimal interruption of chest compressions. Further therapy can be guided by possible causes. CPR, cardiopulmonary resuscitation; I.O., intraosseous; I.V., intravenous; M.I., myocardial infarction.

neurologic recovery decreases rapidly with time from collapse to ROSC and is <30% at 5 min in the absence of bystander CPR. The time between collapse and restoration of circulation is generally imprecise, and some patients have a period of hypotensive VT prior to complete collapse, such that a reported long period before the arrival of rescuers does not always preclude good neurologic recovery. Therapeutic hypothermia (targeted temperature management) has been shown to improve the likelihood of survival and neurologic recovery in patients who present with shockable (VT or VF) rhythms and is recommended for all cardiac arrest patients who remain comatose, regardless of presenting rhythm, who have lack of purposeful response to verbal commands following ROSC. A constant target temperature of 32–37.5°C for at least 24 h is recommended, although a recent trial failed to demonstrate benefit compared with a strategy of targeted normothermia with early and aggressive treatment of fever. Shivering suppression with analgesics and sedatives may be needed. Induction of hypothermia should be started in the hospital, as no benefit was shown for implementation before hospital arrival, and administration of large volumes of cold saline for this purpose increased the risk of pulmonary edema. Brain injury is often accompanied by seizures and status epilepticus that may have further deleterious effects, warranting periodic or continuous electroencephalography (EEG) monitoring. Treatment of clinically apparent seizures is indicated and may also be reasonable in those with EEG patterns on the ictal-interictal continuum on monitoring. Several other therapies hoped to improve postarrest outcomes have been assessed but have not been shown to be beneficial, including administration of corticosteroids, hemofiltration, and efforts to tightly control blood glucose.

Hypothermia and sedation preclude reliable prognostication for neurologic recovery. Functional neurologic assessment for neurologic recovery is generally deferred for at least 72 hours after return to normothermia, typically 4–5 days after the cardiac arrest. Features that predict poor outcome include the absence of pupillary reflex to light, status myoclonus, absence of EEG reactivity to external stimuli, and persistent burst suppression on EEG.

### LONG-TERM MANAGEMENT AFTER SURVIVAL OF OUT-OF-HOSPITAL CARDIAC ARREST

For patients who survive cardiac arrest and have neurologic recovery, the likely underlying cause of the arrest guides further treatment. For arrests not due to an obvious noncardiac cause, a full evaluation for the forms of structural heart disease outlined in Fig. 317-1 and Table 317-2 should be performed including an assessment for underlying CAD and ischemia as well as echocardiography and/or cardiac magnetic resonance imaging (MRI) to look for evidence of prior MI, valvular disease, and nonischemic cardiomyopathies, and to provide an assessment of left ventricular ejection fraction (LVEF). If the initial evaluation is not definitive or is suggestive of an inflammatory cardiomyopathy (i.e., sarcoidosis, myocarditis), a cardiac positron emission tomography (PET) scan and/or endomyocardial biopsy may also be performed. Patients without obvious structural abnormalities should undergo an evaluation for primary electrical disease (long QT syndrome [LQTS], Brugada syndrome, early repolarization syndrome, or Wolff-Parkinson-White syndrome). In cases where a heritable syndrome is suspected, further genetic evaluation should be considered. Diagnostic electrophysiology studies are warranted in selected patients to assess inducible arrhythmias, or provocative testing, such as with epinephrine challenge for LQTS, or sodium channel blocker (e.g., procainamide) challenge for Brugada syndrome.

Patients with shockable rhythms at arrest (VF and VT) that are not deemed to have been due to a transient reversible cause and have reasonable life expectancy should undergo insertion of an ICD for secondary prevention of SCA/SCD. Most of these patients will be found to have CAD. Patients with a VF arrest that occurs within the first 48 h of a documented acute MI generally do not require an ICD because they have a similar risk of sudden death over the next 5 years as infarct survivors who did not have a cardiac arrest. However, patients who have a large infarction with acutely depressed LVEF (e.g., <35%) have an increased risk for future development of life-threatening ventricular arrhythmias related to reentry in the infarct scar **(Chap. 259)**. The percentage of patients with such large infarcts has been declining due to improved revascularization strategies for acute MI. Implantation of an ICD early after MI in these patients does not, however, improve overall survival, in part because a significant number of sudden deaths in the first 3 months are due to recurrent myocardial ischemia or myocardial rupture, rather than cardiac arrhythmias. For patients with large infarcts, a wearable defibrillator that will treat VT/VF if it occurs may be used while left ventricular remodeling is taking place, followed by reevaluation of arrhythmia risk after the infarct is healed to determine if an ICD is warranted. Patients who experience VF in the hospital >48 h after MI or in the setting of myocardial ischemia without infarction may be at risk for recurrent VT/VF. These patients should be evaluated and optimally treated for ischemia. If there is evidence that clearly implicates ischemia immediately preceding the onset of VF without evidence of a prior MI, coronary revascularization may be adequate therapy. Others may warrant ICD implantation. When the cardiac arrest is due to sustained monomorphic VT, a prior infarct scar is often present, and the recurrence rate is significant regardless of whether the arrest occurred in association with elevated serum troponin. In this circumstance, even when revascularization is performed for ischemia, an ICD is usually warranted owing to the risk of recurrence of scar-related VT.

Patients who have cardiac arrest due to a treatable reversible cause, such as hyperkalemia or drug toxicity with QT prolongation causing torsades des pointes **(Chap. 262)**, which can be adequately addressed and prevented by other means, do not usually need an ICD. An ICD is usually recommended for cardiac arrest due to VT or VF without a clearly reversible cause, particularly when structural heart disease, such as hypertrophic or dilated cardiomyopathy, arrhythmogenic cardiomyopathy, cardiac sarcoidosis, or a cardiac syndrome associated with sudden death, including Brugada syndrome, or LQTS is present **(Chaps. 261 and 262)**. In patients with structural heart disease, it is important to recognize that life-threatening arrhythmias can be an indication of terminal, end-stage heart disease with minimal prospect for meaningful survival despite successful resuscitation, and ICDs will not alter the course of these patients and should not be implanted in this situation unless there is a prospect for cardiac replacement therapy with future cardiac transplantation or a ventricular assist device.

Finally, the psychological needs of both the SCA survivor and family members need to be assessed and addressed. Comprehensive rehabilitation and treatment plans for physical, neurologic, cardiopulmonary, and cognitive impairments of the SCA survivor should be formulated before hospital discharge.

## PREVENTION OF SCD

Although advances in CPR and postresuscitation care have improved survival rates after cardiac arrest, 90% of patients will not survive to be discharged from the hospital. Of those who do survive, a proportion (~20%) are left with severe neurologic and/or physical disability. The majority of cardiac arrests do not occur in public places where AEDs and rapid defibrillation have the greatest impact. Patients who suffer an arrest at home also have longer EMS response times and are much less likely to be found in VF. Finally, 50% of cardiac arrests are not witnessed, precluding effective resuscitation efforts. Thus, preventive efforts are critical to reducing mortality from cardiac arrest.

### SCD RISK STRATIFICATION

The presence of overt structural heart disease and/or primary electrical heart disease is associated with an increased risk of SCD that varies with the severity and type of disease. For patients with structural heart disease, depressed left ventricular function is the best validated marker for risk, and clinical HF elevates risk further. After MI, SCD risk increases gradually as the LVEF decreases to 40% and then exponentially thereafter. In addition to LVEF and congestive heart failure, other potential markers of increased SCD risk in the setting of structural heart disease include unexplained syncope, sustained VT induced at electrophysiologic study (EP study), left ventricular scar size and heterogeneity on cardiac magnetic resonance, markers of altered

autonomic function and altered repolarization, and QRS prolongation. The majority of these tests, with the exception of the EP study in post-MI patients, broadly predict death from cardiovascular causes and are not able to discriminate between patients who will die suddenly from an arrhythmia and those who will die of other cardiac causes. For example, patients with the greatest degree of systolic HF and/or lowest LVEF, although at elevated risk for SCD, are more likely to die from pump failure. Although sustained VT at EP study does identify individuals at a higher risk of SCA versus non-SCA in certain subsets of patients, the sensitivity of the test is generally inadequate when LV function is significantly reduced.

## PREVENTIVE THERAPIES FOR SCD IN HIGH-RISK POPULATIONS

Therapy with beta-adrenergic blockers has been demonstrated to reduce SCD risk in a multitude of settings, including after MI, among patients with ischemic and nonischemic cardiomyopathy, and in LQTS. Angiotensin-converting enzyme inhibitors, aldosterone antagonists, and more recently angiotensin receptor/neprilysin inhibitors and sodium-glucose cotransporter 2 inhibitors (SGLT2i) have been associated with reductions in SCD in subsets of patients with structural heart disease, primarily ischemic and nonischemic cardiomyopathy accompanied by HF. Coronary artery bypass grafting has also been associated with reductions in SCD risk, and revascularization may lower SCD risk through reduction in ischemic events and resultant improvements in left ventricular systolic function by reducing areas of hibernating myocardium.

For patients whose disease continues to confer a substantial risk of sustained VT or VF on optimal medical therapy, an ICD is recommended **(Table 317-3)**. The ICD indication in these patients is referred to as "primary prevention of sudden death." The indications for primary prevention ICDs vary depending on the type of underlying structural heart disease and its severity, and the strength of evidence varies by indication. In some cases, there are slight differences in the



**TABLE 317-3 Implantable Cardioverter Defibrillator (ICD) Indications**

| | ESC GUIDELINES | AHA/ACC/HRS GUIDELINES | LEVEL OF EVIDENCE |
|---|---|---|---|
| **Secondary Prevention** | | | |
| *All Disease States with VT or VF* | | | |
| Cardiac arrest due to VF or hemodynamically unstable sustained VT after evaluation to define the cause of the event and to exclude any completely reversible causes | Class I | Class I | A |
| Structural heart disease and spontaneous hemodynamically stable sustained VT | Class IIa | Class I | B |
| Structural heart disease and spontaneous hemodynamically not-tolerated sustained VT | Class I | Class I | B |
| Sustained VT and normal or near-normal ventricular function | – | Class IIa | C |
| *Syncope* | | | |
| Patients with syncope and inducible VT or VF at EP study | – | Class I | B |
| Patients with syncope and structural heart disease in whom invasive and noninvasive studies have failed to determine a cause | – | Class IIb | C |
| **Primary Prevention** | | | |
| *Coronary Artery Disease* | | | |
| LVEF ≤35% + NYHA functional class II–III | Class I | Class I | A |
| LVEF ≤35% (ESC) + NYHA functional class I | Class IIa | – | B |
| LVEF ≤30% (AHA) + NYHA functional class I | – | Class I | A |
| LVEF ≤40% + NSVT + inducible monomorphic VT | Class IIa | Class I | B |
| LVEF ≤40% + unexplained syncope + inducible monomorphic VT | Class IIa | Class I | B |
| *Nonischemic Cardiomyopathy* | | | |
| LVEF ≤35% + NYHA functional class II–II | Class IIa | Class I | A |
| LVEF ≤35% + NYHA functional class I | – | Class IIb | B |
| Pathogenic mutation in *LMNA* gene + 2 or more risk factors (NSVT, LVEF <45%, nonmissense mutation, male sex) | – | Class IIa | C |
| *LMNA* mutation with estimated 5-year risk of VA ≥10% + NSVT or LVEF <50% or AV conduction delay | Class IIa | – | C |
| LVEF >35% and ≥ 2 risk factors (syncope, LGE on CMR, inducible VT at PES, pathogenic mutations in *PLN*, *FLNC*, and *RBM20* genes) | Class IIa | – | C |
| *NYHA Functional Class IV Candidates for Advanced Heart Failure Therapy* | | | |
| Awaiting cardiac transplant | Class IIa | Class IIa | C |
| With destination LVAD and sustained VT | Class IIa | – | B |
| With destination LVAD | – | Class IIa | B |
| *Arrhythmogenic Right Ventricular Cardiomyopathy* | | | |
| Arrhythmic syncope | Class IIa | Class IIa | B |
| Moderate right (<40%) or left (<45%) ventricular dysfunction and NSVT or inducible monomorphic VT | Class IIa | – | C |
| Significant right ventricular dysfunction with LVEF ≤35% | – | Class I | B |
| Significant right ventricular dysfunction with RVEF ≤35% | Class IIa | Class I | C |
| *Hypertrophic Cardiomyopathy* | | | |
| Maximum left ventricular wall thickness >30 mm | – | Class IIa | B |
| SCD in first-degree relative presumably due to HCM | – | Class IIa | B |
| Unexplained syncope | – | Class IIa | B |
| NSVT or abnormal blood pressure response during exercise + additional SCD risk modifiers or high-risk features | – | Class IIa | C |

(*Continued*)

**TABLE 317-3 Implantable Cardioverter Defibrillator (ICD) Indications (Continued)**

| | ESC GUIDELINES | AHA/ACC/HRS GUIDELINES | LEVEL OF EVIDENCE |
|---|---|---|---|
| NSVT or abnormal blood pressure response during exercise without additional SCD risk modifiers or high-risk features | – | Class IIb | C |
| Estimated 5-year risk of sudden death based on the HCM Risk–SCD Calculator ≥6% | Class IIa | – | B |
| Estimated 5-year risk of sudden death based on HCM Risk–SCD Calculator (≥4 to <6%) AND | Class IIa | – | B |
| Significant LGE on CMR or | | | |
| LVEF <50% or | | | |
| Abnormal blood pressure during exercise test or | | | |
| Left ventricular apical aneurysm or | | | |
| Presence of sarcomeric pathogenic mutation | | | |
| Estimated 5-year risk of sudden death based on the HCM Risk–SCD Calculator ≥4 to <6% | Class IIb | – | B |
| Estimated 5-year risk of sudden death based on the HCM Risk–SCD Calculator <4% AND | Class IIb | – | B |
| Significant LGE on CMR or | | | |
| LVEF <50% or | | | |
| Left ventricular apical aneurysm | | | |
| *Congenital Long QT Syndrome* | | | |
| Symptomatic high-risk patients + ineffectiveness or intolerance of β-blocker therapy (high risk: QTc >500 ms, genotypes LQTS 2 and LQTS 3, LQTS 2 females, age <40 years, onset of symptoms <10 years, recurrent syncope) | – | Class I | B |
| Unexplained syncope during β-blocker and genotype-specific therapy | Class I | – | B |
| Symptomatic patients + intolerance or contraindication of β-blocker and genotype-specific therapy | Class IIa | – | B |
| Asymptomatic patients with QTc >500 ms during β-blocker treatment | – | Class IIb | B |
| Asymptomatic patients with high-risk profile according to 1-2-3- LQTS-Risk calculator | Class IIb | – | |
| *Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)* | | | |
| Syncope during β-blocker treatment | – | Class I | C |
| Syncope during combined β-blocker and flecainide treatment | Class IIa | – | C |
| *Brugada Syndrome* | | | |
| Spontaneous type 1 Brugada ECG + recent history of syncope presumed due to ventricular arrhythmia | Class IIa | Class I | C |
| Asymptomatic patients with type 1 Brugada ECG and inducible ventricular fibrillation | Class IIb | – | C |
| *Cardiac Sarcoidosis* | | | |
| Cardiac sarcoidosis with 1 or more risk factors for SCD | – | Class IIa | C |
| Indication for permanent pacemaker implantation regardless of LVEF | Class IIa | – | C |
| LVEF >35% and significant LGE on CMR after resolution of acute inflammation | Class IIa | – | C |
| LVEF 35–50% and inducible VT at PES | Class IIa | – | C |
| *Familial Cardiomyopathy* | | | |
| Patients with familial cardiomyopathy associated with SCD | – | Class IIb | C |
| *Left Ventricular Noncompaction* | | | |
| Patients with left ventricular noncompaction | – | Class IIb | C |

*Abbreviations:* ACC, American College of Cardiology; AHA, American Heart Association; AV, atrioventricular; CMR, cardiac magnetic resonance; ECG, electrocardiogram; EP, electrophysiologic; ESC, European Society of Cardiology; HCM, hypertrophic cardiomyopathy; HRS, Heart Rhythm Society; LGE, late gadolinium enhancement; LQTS, long QT syndrome; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; NSVT, nonsustained ventricular tachycardia; NYHA, New York Heart Association; PES, programmed electrical stimulation; RVEF, right ventricular ejection fraction; SCD, sudden cardiac death; VA, ventricular arrhythmia; VF, ventricular fibrillation; VT, ventricular tachycardia.



strength of recommendation among professional societies in Europe and America for implantation of an ICD, but overall, there is agreement on ICD implantation for the highest-risk patients. In patients with a history of MI >40 days ago, primary prevention ICDs are indicated for those with class II–III New York Heart Association (NYHA) HF and LVEF <35% and those who are NYHA functional class I with LVEF <30%. Although ICDs have not been found to be beneficial when implanted within 40 days of an MI, those with recent or old MI, nonsustained VT, LVEF <40%, and inducible sustained VT at EP study also warrant an ICD. In general, these criteria are not applied to patients who are within 90 days of myocardial revascularization, since some will experience improvement in ventricular function and older trial data suggested there was no benefit with ICDs in these patients. High-risk patients with low LVEFs may be considered for a wearable defibrillator with later reassessment of ventricular function and ICD placement.

ICDs for primary prevention of sudden death are also recommended for patients with diseases other than CAD that put them at risk for SCD. Primary prevention ICDs are currently indicated in select high-risk patients with HCM, arrhythmogenic right ventricular dysplasia, cardiac sarcoidosis, Brugada syndrome, and congenital LQTS. ICDs are currently also recommended for those with nonischemic dilated cardiomyopathy (DCM) who have an LVEF ≤35% and who have NYHA functional class II or III symptoms on guideline-directed medical therapy. In addition to invasive electrophysiologic testing, new risk stratification methods for certain conditions have emerged, including genetic findings and the presence of late gadolinium enhancement (LGE) on MRI. For example, the European guidelines account for pathogenic mutations associated with a high risk of ventricular arrhythmias in patients with nonischemic cardiomyopathy, hypertrophic cardiomyopathy, and long QT syndrome. The presence of LGE has been shown to be a risk factor for sudden death in patients with cardiac sarcoidosis and hypertrophic cardiomyopathy, and thus, this imaging finding has been incorporated into ICD implantation guidelines.

**TABLE 317-4 Implantable Cardioverter Defibrillator (ICD) Not Indicated**

| |
|---|
| Patients who do not have a reasonable expectation of survival with an acceptable functional status for at least 1 year, even if they meet ICD implantation criteria. |
| Patients with incessant VT or VF. |
| Patients with significant psychiatric illnesses that may be aggravated by device implantation or that may preclude systematic follow-up. |
| Patients with drug-refractory New York Heart Association class IV congestive heart failure who are not candidates for cardiac transplantation or cardiac resynchronization therapy. |
| Syncope of undetermined cause in a patient without inducible ventricular tachyarrhythmias and without structural heart disease. |
| VF or VT is amenable to surgical or catheter ablation in patients without other disease predisposing to sudden cardiac arrest (e.g., atrial arrhythmias associated with Wolff-Parkinson-White syndrome, RV or LV outflow tract VT, idiopathic VT, or fascicular VT in the absence of structural heart disease). |
| Patients with ventricular tachyarrhythmias due to a completely reversible disorder in the absence of structural heart disease (e.g., electrolyte imbalance, drugs, or trauma). |

*Abbreviations:* LV, left ventricular; RV, right ventricular; VF, ventricular fibrillation; VT, ventricular tachycardia.

*Source:* Adapted from H Könemann et al: Management of ventricular arrhythmias worldwide: comparison of the latest ESC, AHA/ACC/HRS, and CCS/CHRS guidelines. JACC Clin Electrophysiol 9:715, 2023.

Although the ICD is very effective for treatment of arrhythmic sudden death, competing causes of mortality must be considered in patients with severe cardiomyopathy. Data from a recent randomized trial, the Danish Study to Assess the Efficacy of ICDs in Patients with Non-ischemic Systolic Heart Failure on Mortality (DANISH), performed in patients with nonischemic DCM and LVEF ≤35%, who also had elevated N-terminal pro-B-type natriuretic peptide levels and NYHA class II–IV HF, have resulted in some debate regarding the utility of ICDs in this population. This trial did not demonstrate an overall mortality benefit of the ICD despite a reduction in the incidence of SCD. In subgroup analyses, mortality benefits were observed in younger patients in whom the competing risk of dying from other causes of death was lower. These data underscore the importance of considering competing risks for other causes of mortality when deciding to implant a primary prevention ICD. Patients who are likely to die from other causes are unlikely to benefit from an ICD. Patients who do not have a reasonable expectation of survival with an acceptable functional status for at least 1 year should not undergo ICD placement. There are also other circumstances where an ICD is not indicated even if there is a significant sudden death risk (Table 317-4).

## THE CHALLENGE OF SCD PREVENTION (FIG. 317-3)

**The Greatest Number of Sudden Deaths Occur in "Low-Risk" Patients** While patients with reduced left ventricular

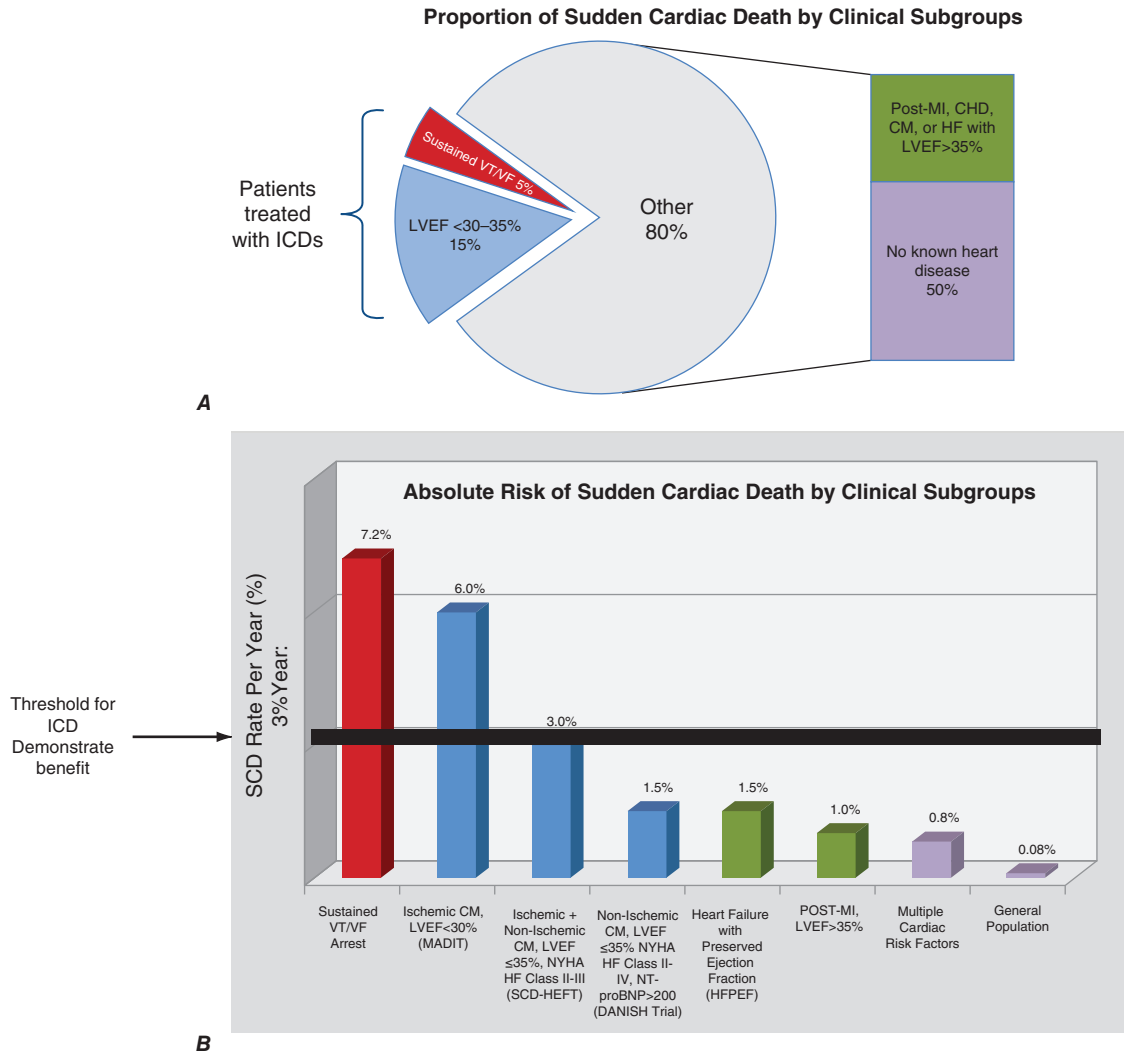


**FIGURE 317-3** ***A.*** Proportion of sudden cardiac deaths that occur in clinical subgroups of the population treated and not treated with implantable cardioverter defibrillators (ICDs). ***B.*** Absolute risk of sudden cardiac death within clinical subgroups in comparison to the threshold of risk where ICDs demonstrated benefit.

function and HF are at substantially elevated SCD risk, only ~20% of all SCDs occur in patients with poor left ventricular function. Most SCDs occur in individuals with preserved ventricular function who would not qualify for a primary prevention ICD. Although SCD rates are elevated compared to the general population, the absolute SCD risk in patients with CHD or HF who have an LVEF >35% is not high enough to warrant consideration of ICD therapy. While the incidence of SCD is lower in patients with preserved LVEF, SCD accounts for a greater proportion of cardiac deaths, and active efforts are being made to advance SCD risk stratification in this segment of the population. However, at present, SCD prevention primarily involves cardiac risk factor modification and standard medical therapy for the underlying condition.

**Preventing Sudden Death in the General Population** Only about one-half of men and one-third of women who suffer SCA are recognized to have heart disease prior to the event, and only half have warning symptoms prior to the event. SCD often occurs without warning as the first manifestation of cardiac disease. In order to prevent these SCDs, preventive interventions would need to be employed broadly to the general population. Although several risk scores have recently been developed with the intent to stratify SCD risk in low-risk populations, the clinical utility to date is limited by the low absolute incidence of SCD, which is estimated to be only 50–90 per 100,000 in the general adult population. Therefore, current efforts aimed at preventing SCD in general populations primarily focus on modification of the SCD risk factors outlined previously. Individuals who adhere to a low-risk, healthy lifestyle that includes avoidance of smoking, maintaining a healthy body weight, participating in moderate exercise, and a Mediterranean-type dietary pattern have markedly lower rates of SCD. A substantial number of SCDs are likely to be preventable through lifestyle modifications and treatment of risk factors.

## FURTHER READING


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# Section 3 Neurologic Critical Care

# 318 Nervous System Disorders in Critical Care

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Life-threatening neurologic illness may be caused by a primary disorder affecting any region of the neuraxis or may occur as a consequence of a systemic disorder such as hepatic failure, multisystem organ failure, or cardiac arrest **(Table 318-1)**. Neurologic critical care focuses on preservation of neurologic tissue and prevention of secondary brain injury caused by ischemia, hemorrhage, edema, herniation, and elevated intracranial pressure (ICP). Encephalopathy is a general term describing brain dysfunction that is diffuse, global, or multifocal. Severe acute encephalopathies represent a group of various disorders due to different neurologic or systemic etiologies but that share the common themes of primary and secondary brain injury.

## PATHOPHYSIOLOGY

**Brain Edema** Swelling, or edema, of brain tissue occurs with many types of brain injury. The two principal types of edema are vasogenic and cytotoxic. *Vasogenic edema* refers to the influx of fluid and solutes into the brain through an incompetent blood-brain barrier (BBB). In the normal cerebral vasculature, endothelial tight junctions associated with astrocytes create an impermeable barrier (the BBB), through which access into the brain interstitium is dependent upon specific transport mechanisms. The BBB may be compromised in ischemia, trauma, infection, and metabolic derangements, and typically develops rapidly following injury. *Cytotoxic edema* results from cellular swelling, membrane breakdown, and ultimately cell death. Clinically significant brain edema usually represents a combination of vasogenic and cytotoxic components. Edema can lead to increased ICP as well as tissue shifts and brain displacement or herniation from focal processes **(Chap. 30)**. These tissue shifts can cause injury by mechanical distention and compression in addition to the ischemia of impaired perfusion consequent to the elevated ICP.

**Ischemic Cascade and Cellular Injury** When delivery of substrates, principally oxygen and glucose, is inadequate to sustain cellular function, a series of interrelated biochemical reactions known as the *ischemic cascade* is initiated **(see Fig. 437-2)**. The release of excitatory amino acids, especially glutamate, leads to influx of calcium and sodium ions, which disrupt cellular homeostasis. An increased intracellular calcium concentration may activate proteases and lipases, which then lead to lipid peroxidation and free radical–mediated cell membrane injury. Cytotoxic edema ensues, and ultimately necrotic cell death and tissue infarction occur. This pathway to irreversible cell death is common to ischemic stroke, global cerebral ischemia, and traumatic brain injury.

*Penumbra* refers to areas of ischemic brain tissue that have not yet undergone irreversible infarction, implying that these regions are potentially salvageable if ischemia can be reversed. Factors that may exacerbate ischemic brain injury include systemic hypotension and hypoxia, which further reduce substrate delivery to vulnerable brain tissue, and fever, seizures, and hyperglycemia, which can increase cellular metabolism, outstripping compensatory processes. Clinically, these events are known as *secondary brain insults* because they lead to exacerbation of the primary brain injury. Prevention, identification, and treatment of secondary brain insults are fundamental goals of management.

An alternative pathway of cellular injury is *apoptosis*. This process implies programmed cell death, which may occur in the setting of ischemic stroke, global cerebral ischemia, traumatic brain injury, and