Sudden Cardiac Death in Heart Failure

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KEYWORDS

• Heart failure • Implantable cardiac defibrillators • Ischemic heart disease
• Nonischemic cardiomyopathy • Sudden death • Ventricular tachycardia

KEY POINTS

- Sudden cardiac death is common in patients with heart failure and depends on ejection fraction.
- Although several techniques exist for risk stratification, they are imperfect.
- Several pharmacologic strategies exist to prevent sudden death in patients with heart failure.
- Implantable cardioverter-defibrillators, cardiac resynchronization therapy defibrillators, and wearable cardioverter-defibrillators are the most effective tools to prevent sudden death in patients with heart failure and systolic dysfunction.

INTRODUCTION

Heart failure (HF) is a clinical syndrome resulting from structural and functional myocardial abnormalities leading to impaired ability to circulate blood at a rate sufficient to maintain the metabolic needs of internal organs and peripheral tissues. These abnormalities are consequences of long-standing ischemia caused by coronary artery disease or loss of myocardial mass because of prior infarction, myocardial remodeling, and structural damage from long-standing hypertension, valvular disease, or direct toxin exposure (eg, alcohol abuse, illicit substances, chemotherapeutic agents).[1] The prevalence of HF in the United States is around 5.7 million patients, of whom approximately 45% have reduced ejection fraction/systolic dysfunction.[2] There are more than half a million cases of HF newly diagnosed every year and there are more than 1 million hospitalizations yearly with HF as the primary diagnosis.[3] More than 80% of deaths in patients with HF have cardiovascular causes, with most being either sudden cardiac deaths (SCDs) or deaths caused by progressive pump failure.[4]

In general, SCD events are defined as unexpected deaths from cardiovascular causes that are preceded by a witnessed collapse, occur within 1 hour of an acute change in clinical condition, or occur not more than 24 hours after the deceased individuals were known to be in their usual state of health.[5] It is estimated that 350,000 to 380,000 SCD cases occur every year in the adult population in the United States, and that most of these individuals have preexisting heart disease.[6] If the American College of Cardiology/American Heart Association stage-based system for the classification of HF were applied, most patients presenting with SCD could be classified as stage A to D (**Fig. 1**). This classification adds a useful dimension to the understanding of the magnitude of SCD in HF by recognizing that there

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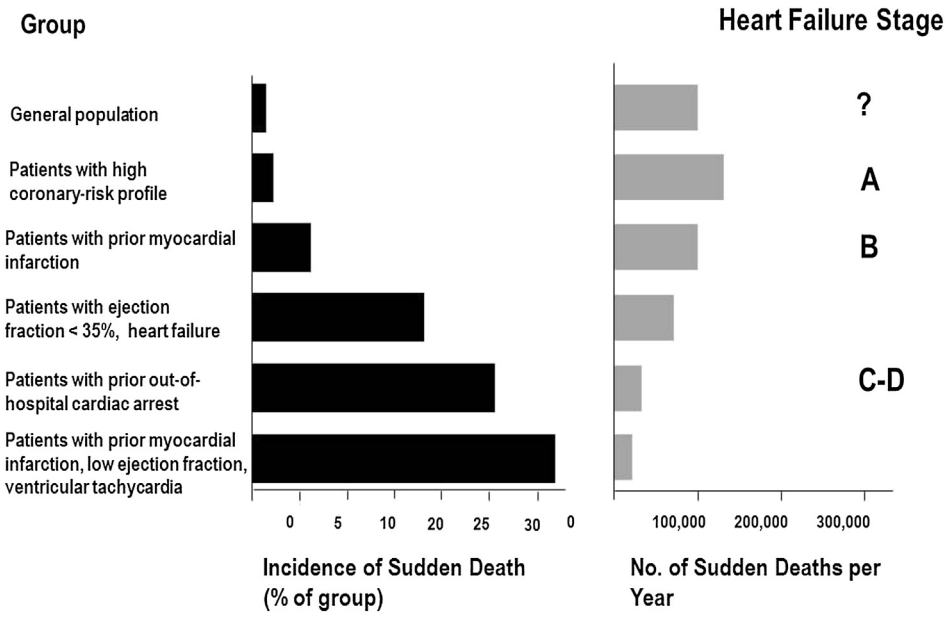

Fig. 1. Relation between incidence of sudden death and heart failure stages. (*Modified from* Huikuri HV, Castellanos A, Myerburg RJ. Sudden death due to cardiac arrhythmias. N Engl J Med 2001;345:1474; with permission.)

are established risk factors and structural prerequisites for the development of SCD and that therapeutic interventions used early after the development of left ventricular dysfunction can prevent the occurrence of SCD.

PATHOPHYSIOLOGY

The mechanisms of SCD in patients with HF are complex and require the chance interaction between a transient event and underlying pathologic substrate. In arrhythmic SCD, the process induces electrical instability and ventricular arrhythmias followed by hemodynamic collapse and death. This event happens more frequently in patients with ischemic cardiomyopathy, and can occur in 2 settings: (1) acute myocardial ischemia (with or without infarction), and (2) structural alterations (scar formation) secondary to prior myocardial infarction or chronic myocardial ischemia. In the setting of acute myocardial ischemia, the electrical instability generates ventricular fibrillation that degenerates to asystole over the course of several minutes. Thus, most SCD cases show asystole or pulseless electric activity when first examined by the emergency medical response teams. In cases in which there has been a short time between collapse and the initial rhythm determination, the proportion with documented ventricular tachycardia/fibrillation increases to 75% to 80%.[7] After experiencing an acute coronary event, women and men have a 4-fold and 10-fold higher risk of SCD, respectively.[8] Although the absolute rate of SCD is highest in the first 30 days after the event and decreases gradually with time,[9] rates are still high in certain subsets of postinfarction patients, and the degree of left ventricular systolic dysfunction and symptoms (New York Heart Association [NYHA] class) are powerful predictors for SCD in these patients.[10] In the chronic stage of ischemic cardiomyopathy (months and years after the initial infarction), the presumed mechanism of SCD is an electrical event caused by ventricular arrhythmias often originating from areas of prior infarcted myocardium that are adjacent to dense scar that has formed over time. Residual endomyocardial fibers survive, probably because of perfusion from the ventricular cavity or retrograde perfusion through sinusoidal channels. These surviving myocytes become embedded within regions of fibrosis that constitute substrate for abnormal nonuniform anisotropy with conduction block and propagation barrier that promote reentry and the ensuing ventricular arrhythmias.

In patients with systolic dysfunction after a myocardial infarction, nonarrhythmic SCD occurs frequently during the first 4 to 6 weeks. Within hours of infarction, extracellular matrix is digested and results in wall thinning and infarct expansion that may result in ventricular rupture that can manifest as SCD.[11] In addition, autopsy data from Optimal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan (OPTIMAAL), Assessment of Treatment with Lisinopril and Survival