

# Sudden Cardiac Death From the Perspective of Coronary Artery Disease

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## Abstract

Sudden cardiac death accounts for approximately 50% of all deaths attributed to cardiovascular disease in the United States. It is most commonly associated with coronary artery disease and can be its initial manifestation or may occur in the period after an acute myocardial infarction. Decreasing the rate of sudden cardiac death requires the identification and treatment of at-risk patients through evidence-based pharmacotherapy and interventional strategies aimed at primary and secondary prevention. For this review, we searched PubMed for potentially relevant articles published from January 1, 1970, through March 1, 2014, using the following key search terms: *sudden cardiac death*, *ischemic heart disease*, *coronary artery disease*, *myocardial infarction*, and *cardiac arrest*. Searches were enhanced by scanning bibliographies of identified articles, and those deemed relevant were selected for full-text review. This review outlines various mechanisms for sudden cardiac death in the setting of coronary artery disease, describes risk factors for sudden cardiac death, explores the management of cardiac arrest, and outlines optimal practice for the monitoring and treatment of patients after an acute ST-segment elevation myocardial infarction to decrease the risk of sudden death.

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Sudden cardiac death (SCD) accounts for nearly half of all deaths from cardiovascular disease in the United States.<sup>1</sup> In this review, we discuss the current understanding of SCD mechanisms and risk factors, along with contemporary management and preventive strategies in patients with established coronary artery disease (CAD). We searched PubMed for potentially relevant articles published from January 1, 1970, through March 1, 2014, using the following key search terms: *sudden cardiac death*, *ischemic heart disease*, *coronary artery disease*, *myocardial infarction* (MI), and *cardiac arrest*. Searches were enhanced by scanning bibliographies of identified articles, and articles deemed relevant were selected for full-text review.

## DEFINITION OF SCD

The definition of SCD has been explored many times in the literature. The most recently accepted definition describes it as a natural death due to cardiac causes, heralded by abrupt loss of consciousness and occurring within 1 hour of the onset of symptoms.<sup>2</sup> It may occur in patients with previously documented CAD or may be an initial event. Earlier studies have used less stringent criteria and included patients

who died within 24 hours of the onset of symptoms.<sup>3</sup> Additional criteria for SCD include the absence of trauma as a mechanism and the unexpected timing and mode of death. A population-based study in Maastricht, Netherlands, found that 21% of deaths in men and 14.5% of deaths in women were sudden and unexpected (ie, not preceded by other symptoms).<sup>4</sup> These findings raise the problem of how to characterize such deaths, and in this setting, investigators tend to err on the side of caution and label these events as SCDs, which may overestimate rates and possibly confuse our understanding of the underlying mechanisms involved.

The incidence of SCD ranges from 0.36 to 1.28 per 1000 persons per year,<sup>5-8</sup> with approximately 400,000 deaths annually in the United States alone.<sup>2,9</sup> Using data from the Oregon Sudden Unexpected Death Study, Stecker et al<sup>10</sup> estimated the public health burden of SCD and compared it with death rates for other diseases using national databases such as the US Census Bureau and the National Program of Cancer Registries. The age-adjusted national incidence of SCD was 60 per 100,000 persons. The burden of premature death was greater for men than for women (2.04 million [95% CI, 1.86-2.23 million] vs 1.29 million [95% CI,



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## ARTICLE HIGHLIGHTS

- Sudden cardiac death (SCD) is currently defined as a natural death from cardiac causes occurring within 1 hour of symptom onset and heralded by abrupt loss of consciousness.
- Sudden cardiac death accounts for 400,000 deaths annually in the United States.
- Coronary artery disease is the most common cause of SCD.
- Identifying clinical, angiographic, and electrical variables that confer increased risk of SCD remains an ongoing challenge.
- Prompt management of cardiac arrest with bystander-administered cardiopulmonary resuscitation, appropriate defibrillator shocks, and pharmacotherapy is critical.
- Increases in timely myocardial reperfusion, use of preventive pharmacotherapies, and defibrillator implantation have underpinned the decreased incidence of SCD.

1.13-1.45 million]). Sudden cardiac death accounted for approximately half of all years of potential life lost due to heart disease and exceeded that for all individual cancers and most other leading causes of death, including chronic lower respiratory tract disease and cerebrovascular disease.

#### PATHOLOGIC MECHANISMS RELATED TO CAD

Autopsy studies have found approximately two-thirds of unexpected deaths to be cardiac in origin, with CAD related to atherosclerosis accounting for most of these deaths. For example, Thomas et al<sup>11</sup> reported that 54% (189 of 350) of consecutive cases of “natural” sudden death in adults living in the United Kingdom that occurred within 6 hours of symptom onset were related to ischemic heart disease. Similarly, Leach et al<sup>12</sup> found that 62% (206 of 333) of randomly selected out-of-hospital deaths in the United Kingdom were related to ischemic heart disease. In the same studies, 5% to 10% of sudden deaths occurred with no evidence of CAD or congestive heart failure. In patients who have survived cardiac arrest, 40% to 86% have CAD with more than 75% cross-sectional stenosis.<sup>13</sup> Nonatherosclerotic CAD is unusual and includes causes such as dissection, embolism, and arteritis. Acute coronary lesions including plaque disruption or thrombus have been noted

in more than 50% of SCDs related to CAD and in 46% of hearts with evidence of myocardial scarring in the absence of acute ischemia.<sup>14</sup> Plaque rupture appears to be more common in older women,<sup>15</sup> and the probability of finding an acute coronary lesion appears to be greater with increasing duration of prodromal symptoms.<sup>12,16</sup>

Identification of active coronary lesions at autopsy of patients with SCD is highly variable, with rates ranging from less than 20% to more than 80%.<sup>17,18</sup> Variation in reported rates of CAD are most likely related to differences in the accepted definition of SCD among studies, variability in autopsy practices, and temporal changes in population health such as changes in smoking patterns and treatment of CAD. For example, in Olmsted County, Minnesota, as well as in other places, when smoking was banned in public places, the incidence of SCD substantially decreased within approximately 2 years.<sup>19</sup> Furthermore, improvements in primary and secondary pharmacotherapy have resulted in decreasing mortality rates from CAD in the contemporary era.<sup>20</sup> In addition, several population-based studies have found a 15% to 19% decrease in the incidence of SCD related to CAD since the 1980s.<sup>21</sup>

Stable risk factors that contribute to SCD include anatomic defects, myocardial scarring, CAD, and abnormalities in cardiac nerves.<sup>13</sup> Superimposed on these tangible abnormalities are “transient” factors that precipitate SCD. These factors include changes in local oxygen tension and pH, electrolyte imbalances such as hypokalemia and hypomagnesemia, ischemia and/or reperfusion, hemodynamic changes, and toxins and drugs such as alcohol and negatively inotropic medications.<sup>13</sup> One or several of these transient factors may occur to precipitate electrical instability and thereby a terminal event in isolation. For example, one study found that SCD in the setting of acute thrombotic occlusion of a major coronary vessel in the absence of previous MI was usually due to an arrhythmia.<sup>22</sup>

Indeed, SCD in patients with CAD could result from acute ischemia without infarction, acute infarction, electrical instability due to structural abnormalities induced by CAD, or some other problem entirely, in which CAD is an incidental finding. In one study in which the hearts of 270 persons who died of SCD were examined along with analysis of their clinical data, 14 (5%)

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