Rev Esp Cardiol. 2012;65(11):1039–1052

Update: Arrhythmias (XI)

Sudden Death

Antonio Bayés de Luna[a,*] and Roberto Elosua[b]

[a] Institut Català de Ciències Cardiovasculars, Hospital de Sant Pau, Barcelona, Spain
[b] Grupo de Epidemiología y Geriatría Cardiovascular, IMIM y CIBER de Epidemiología y Salud Pública, Barcelona, Spain

Article history:
Available online 5 September 2012

Keywords:
Physiopathology of sudden death
Genetics and sudden death
Ischemic heart disease and sudden death
Final arrhythmias

ABSTRACT

Sudden death is probably the greatest challenge in modern cardiology. After reviewing its history, we describe the epidemiology of sudden death and its associated diseases. We highlight its physiopathologic aspects, including the factors that act on vulnerable myocardium triggering the final arrhythmia, mainly ventricular fibrillation and, to a lesser extent, bradycardia and sudden death. We emphasize the relevance of acute ischemia, ventricular dysfunction and genetic factors, not only in genetic heart disease, but also as triggers of sudden death in acute and chronic ischemic heart disease. Finally, we describe the best way to identify candidates at risk, discuss how to prevent sudden death, and outline the best approach to managing a patient resuscitated from cardiac arrest.

Muerte súbita

Palabras clave:
Fisiopatología de la muerte súbita
Genética y muerte súbita
Isquemia y muerte súbita
Arritmias finales

RESUMEN

La muerte súbita probablemente sea el desafío más importante de la cardiología moderna. En este artículo, después de realizar una revisión histórica de la muerte súbita, se comentan la epidemiología y las enfermedades asociadas a ella y se hace énfasis en los aspectos fisiopatológicos, especialmente los factores desencadenantes que actuando sobre un miocardio vulnerable precipitan la arritmia final, que en general lleva a la fibrilación ventricular y en menor medida a bradiarritmia y muerte súbita. Se comentan especialmente la importancia de la isquemia aguda y la disfunción ventricular y el papel de la genética, no sólo en las cardiopatías de origen genético, sino también su posible efecto desencadenante en la cardiopatía isquémica aguda y crónica. Por último, se describe cuál es la mejor forma de identificar a los pacientes en riesgo, cómo prevenir la muerte súbita y qué conducta seguir ante un paciente resucitado de una parada cardiaca.

Abbreviations

HF: heart failure
IHD: ischemic heart disease
SD: sudden death
VF: ventricular fibrillation

CONCEPT

Sudden death (SD) is death that occurs unexpectedly within 1 h of the onset of symptoms or when death occurs unwitnessed within 24 h of the deceased being seen alive and in a normal state of health before discovery of the body. Some patients die instantly but most have some prodrome.

HISTORICAL PERSPECTIVE

SD has been known for thousands of years.[1] In ancient Egypt, more than 4000 years ago, SD was already associated with myocardial ischemia. The Ebers papyrus states: "If a patient has pain in the arm and left side of the chest, there is a threat of death." In China 2500 years ago, Chio associated SD with an arrhythmia when he said, "An intermittent pulse is a predictor of imminent death." Around the same time, Hippocrates stated: "Intense chest pain that radiates to the clavicle and back is a sign of poor prognosis." He was the first writer to introduce the concept of risk factors. He wrote: "Obese individuals are more likely to die suddenly than thin ones." These concepts have persisted up to the present. We would note in passing that many publications have drawn attention over the centuries to the shock and fear produced by SD.[2–5] In the 14th century, Count Gaston de Foix died suddenly after returning from a hunt during which he had been in contact with icy water. He felt a tightness in the chest and said: "I am a dead man. May God have mercy on me."[5] (Fig. 1). In the 18th

* Corresponding author: Institut Català de Ciències Cardiovasculars, Avda. S. Antoni M. Claret 167, 08025 Barcelona, Spain.
E-mail address: abayes@csic-iccc.org (A. Bayés de Luna).

1885-5857/$ – see front matter
http://dx.doi.org/10.1016/j.rec.2012.03.025

Figure 1. Death of Count Gaston de Foix.[5]

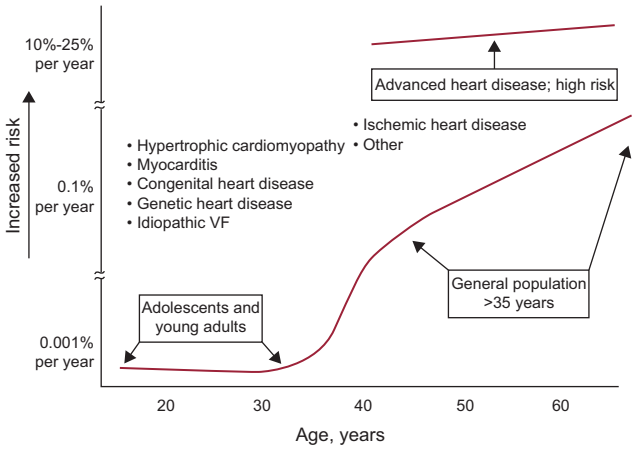

Figure 2. Association between the incidence of sudden death and age. Note that sudden death is associated with various diseases throughout life. VF, ventricular fibrillation. Reprinted with permission from Myerburg et al.[15]

century, a book written by Lancisi[6] on the frequent cases of SD occurring in Rome was published by order of Pope Clement XI. Clinical and autopsy studies showed the association between SD and the presence of chest pain and anatomopathological signs of heart disease. In the late 18th century, Heberden published the first description of "angina pectoris." In the 19th century, Von Bezold showed that experimental occlusion of the coronary arteries caused cardiac arrest. In the 20th century, Herrick[7] described the clinical description of myocardial infarction (MI). Throughout the 20th century, interest in SD increased as its association with coronary disease became clearer,[8] as well as the importance of deterioration in ventricular function (heart failure [HF]) in its presentation, regardless of whether this was associated with ischemia or not.

Finally, in the second half of the 20th century, it was shown that although ischemic heart disease (IHD) continued to be the cause of SD in at least 80% of cases,[9] a group of inherited diseases with structural alterations (cardiomyopathy) or without apparent organic cause (channelopathies) explained many cases of SD in younger people without IHD, whether SD was associated with effort or not.[1]

EPIDEMIOLOGY

SD is probably the greatest challenge in modern cardiology. This is due not only to the immense number of cases (more than 300 000 per year in the United States alone), although its incidence seems to have recently declined and is lower in some Mediterranean countries, such as Spain,[10–13] but also because of its considerable social impact.

Although SD has been observed even in infants, it is rare in the first decades of life due to its association with impaired repolarization, autonomic nervous system abnormalities, and increased vagal tone. During this period, it usually appears during sports activities[14] and in the presence of genetic heart disease (hypertrophic cardiomyopathy, arrhythmogenic right ventricular [RV] dysplasia, arrhythmogenic RV cardiomyopathy, and channelopathies). The incidence of SD gradually increases with age, particularly from 35-40 years onwards, and is particularly high in the acute phase of MI. It is also common in the chronic phase of MI and any heart disease, particularly in the presence of HF (Fig. 2).

ASSOCIATED DISEASES

As mentioned, acute IHD is often associated with SD in adults. However, in the majority of cases of SD, and outside the setting of acute IHD and inherited heart disease (cardiomyopathies and channelopathies) the presence of HF, or at least ventricular dysfunction, can be demonstrated. HF may be associated with idiopathic cardiomyopathy or found in patients with chronic IHD, hypertension, or other cardiomyopathies, etc. Genetic heart disease can cause SD at any age and, although rare, tends to occur between adolescence and ages 50 to 60 years. However, it should be noted that many cases of SD occur before the age of 35 years (Fig. 2). Genetic heart disease manifests more often in men and SD may occur more often during exercise (cardiomyopathies) or while resting or during sleep (channelopathies).

Our group conducted a study within the *Instituto de Salud Carlos III* group network (the EULALIA study), including 204 cases of SD that occurred in the Mediterranean area (Catalonia and Andalusia).[16] This study analyzed the epidemiologic and anatomopathological aspects of diseases associated with SD. Table 1 shows the pathological diagnoses obtained in this group of patients. When compared to a similar study conducted in the United States,[17] it is striking that the incidence of IHD detected at autopsy was lower (80%-90% vs 58%); in these cases the incidence of acute thrombosis (anatomopathological basis of acute MI) was also lower (52% vs 40%) (Fig. 3). This is in line with current evidence-based knowledge[10–13,17,18] that the incidence of IHD in Mediterranean countries is relatively low. This is probably related not only to diet, but also to lifestyle and environmental aspects (Mediterranean culture). In addition, we have noted a greater number of cases of SD involving left ventricular hypertrophy (LVH) (48% vs 20%) in studies conducted in the United States[16,19] (Fig. 3). From the clinical point of view, there were fewer cases of angina pectoris in the SD victims in the EULALIA study than in the Maastricht study[20] (20% vs 37%), which agrees with the low number of cases of IHD found at autopsy. In our series, the incidence of possible associated genetic diseases was 3% of cases (hypertrophic cardiomyopathy, arrhythmogenic RV), and in about 7% there were no findings at autopsy. This suggests that some of the victims presented a channelopathy.