EC CARDIOLOGY RESEARCHER'S COLUMN - 2019

Sudden Cardiac Death: What we Need to Know

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COLUMN ARTICLE

Introduction

Despite aggressive primary prevention measures, cardiovascular diseases are responsible for approximately 17 million deaths every year in the world. Sudden Cardiac Arrest (SCA) and its most common consequence, Sudden Cardiac Death (SCD), constitute major public health problems in the current era. It accounts for approximately 50% of all cardiovascular deaths [1]. Although the absolute risk of SCD is greater among high-risk populations, most patients have not been identified as being at risk. At least 25% of SCD patients will present with their first symptomatic cardiac event [2].

Definitions

Sudden Cardiac Arrest is the sudden cessation of cardiac activity such that the victim becomes unresponsive, with either persisting gasping respirations or absence of any respiratory movements and no signs of circulation as manifest by the absence of a perceptible pulse. An arrest is presumed to be of cardiac etiology unless it is known or likely to have been caused by trauma, drowning, respiratory failure or asphyxia, electrocution, drug overdose, or any other non-cardiac cause [3].

Sudden Cardiac Death is defined as the sudden and unexpected death occurring within an hour of the onset of symptoms or occurring in patients found dead within 24h of being asymptomatic and presumably due to a cardiac arrhythmia or hemodynamic catastrophe [3]. The term is also used when a congenital, or acquired, potentially fatal cardiac condition was known to be present during life, or, autopsy has identified a cardiac or vascular anomaly as the probable cause of the event, or, no obvious extra-cardiac causes have been identified by post-mortem examination and therefore an arrhythmic event is a likely cause of death [4].

Epidemiology

The risk of SCD is higher in men than in women and it increases with age due to the higher prevalence of coronary artery disease (CAD) in older age [5]. Accordingly, the SCD rate is estimated to range from 1.40 per 100,000 person-years [95% CI 0.95, 1.98] in women to 6.68 per 100,000 person-years (95% CI 6.24, 7.14) in men [5]. SCD in younger individuals has an estimated incidence of 0.46 - 3.7 events per 100,000 person-years [6], corresponding to a rough estimate of 1100-9000 deaths in Europe and 800 - 6200 deaths in the USA every year.

Mechanisms

Ventricular tachycardia (VT) or ventricular fibrillation (VF) is the likely initiating rhythm in most cases of SCA. If VF is not recognized and treated in time, it leads to asystole or pulseless electrical activity (PEA) as a result of persistent ischemia and hypoxia. A significant proportion of SCA is due to bradyarrhythmias and pump failure as well.

Citation: Kashif Bin Naeem. "Sudden Cardiac Death: What we Need to Know". EC Cardiology RCO.01 (2019): 23-27.

Causes

The etiology of SCD differs in young versus old individuals. While channelopathies, cardiomyopathies, myocarditis and substance use predominate in the young [7], older populations have chronic degenerative diseases like coronary artery disease, valvular heart disease and heart failure. Several challenges exist to determine the exact etiology. As old individuals have multiple chronic cardiovascular conditions, it is difficult to determine which contributed most to SCD. In younger people, the cause might not be evident even after autopsy, as conditions like inherited channelopathies or drug-induced arrhythmias are devoid of structural abnormalities. It is useful to attempt to identify the cause of unexpected death (includes autopsy) to help the family to cope with the tragedy, as well as to determine if the risk of sudden death extends to other family members. Unfortunately, even when an autopsy is performed, a proportion of sudden deaths, ranging from 2 to 54% [7] remain unexplained, likely due to the heterogeneity of the autopsy protocols.

Coronary artery disease

At least 80% of SCD patients have underlying coronary artery disease [8,9]. In survivors of cardiac arrest, 40 - 86% of patients are found to have coronary heart disease with vessels showing more than 75% stenosis, depending on age and sex of the population studied. Autopsy studies have reported a recent occlusive coronary thrombus in 15% to 64% of victims of sudden cardiac death with evidence of plaque fissuring, hemorrhage and thrombosis.

Cardiomyopathies

Cardiomyopathies constitute the second largest group of patients who experience SCD. Hypertrophic cardiomyopathy (HCM) has a prevalence of 2 in 1000 young adults and an incidence of sudden cardiac death of 2% to 4% per year in adults and 4% to 6% per year in children and adolescents [10]. Risk factors for SCD include prior SCA, recurrent syncope, family history of SCD, non-sustained VT, a drop in BP with exercise and septal hypertrophy ≥ 30 mm [10]. Idiopathic dilated cardiomyopathy accounts for ≈10% of SCD in adults. Analysis of 14 studies including 1432 patients, mean mortality rate after a follow-up of 4 years was 42%, with 28% of deaths classified as sudden [11]. Syncope and presence of non-sustained VT comprise high risk patients. Arrhythmogenic right ventricular dysplasia (ARVD) is a rare genetic disorder characterized by fibro-fatty infiltration of the right ventricle. It causes SCD in young individuals and adults with an annual incidence of death is ≈2%.

Channelopathies

These comprise rare disorders where cardiac function is normal but electrophysiology derangements are present that are caused by mutations affecting genes associated with various cardiac membrane channels. Congenital long QT syndrome is an autosomal dominant (usually) familial disease with a prevalence of 1:2000. It is characterized by an abnormally long QT interval leading to early afterdepolarizations and torsades de pointes. It may cause ventricular arrhythmias with exercise especially swimming (LQT1), auditory triggers (LQT2) or during sleep (LQT3). Mortality rate is ≈1% per year. High-risk features include corrected QT interval >500 ms, history of syncope or SCA and LQT2/3 genotype. The opposite variant, short QT syndrome is very rare but carries similar potential to end up in VF. Brugada syndrome is an autosomal dominant disorder characterized by mutations in the gene encoding the cardiac sodium channel, predisposing to polymorphic VT or VF usually at rest or during sleep. Risk of SCA is up to 30% at 3 years in untreated symptomatic patients. Catecholaminergic polymorphic ventricular tachycardia (CPVT) results in bidirectional VT during emotional or physical stress.

Others

Wolff-Parkinson-White syndrome (WPW) is characterized by the presence of rapidly conducting accessory pathways. Risk of sudden cardiac death 1 per 1000 patient-years of follow-up. Up to 10% experience sudden cardiac death as their first manifestation of the disease [12]. High risk patients include atrial fibrillation with R-R interval ≤220 ms that may deteriorate into VF. When no cause of SCA can be found, idiopathic VF is labelled.

Diagnostic and prognostic testing

All survivors of SCA need to be investigated to identify reversible factors, find and treat underlying conditions and

determine the risk of recurrence. Specific cardiac testing includes ECG (resting/ambulatory), echocardiography, coronary angiography, exercise stress testing, cardiac MRI and genetic testing (if available).

ECG is readily available and can provide remarkable evidence of coronary artery disease, WPW syndrome, prolonged QT interval, Brugada pattern, Arrhythmogenic Right Ventricular Dysplasia (ARVD) and Hypertrophic Cardiomyopathy (HCM) (Figure 1). 24-hour ambulatory ECG can detect arrhythmias. Echocardiography is used to assess left ventricular function, valvular disease, cardiomyopathy and hypertrophy. Coronary angiography is needed to exclude coronary artery disease or coronary anomalies. Cardiac MRI is useful to evaluate for ARVD and to investigate left ventricular hypertrophy. Genetic testing for the channelopathies, HCM and ARVD can be useful, however, not readily available.

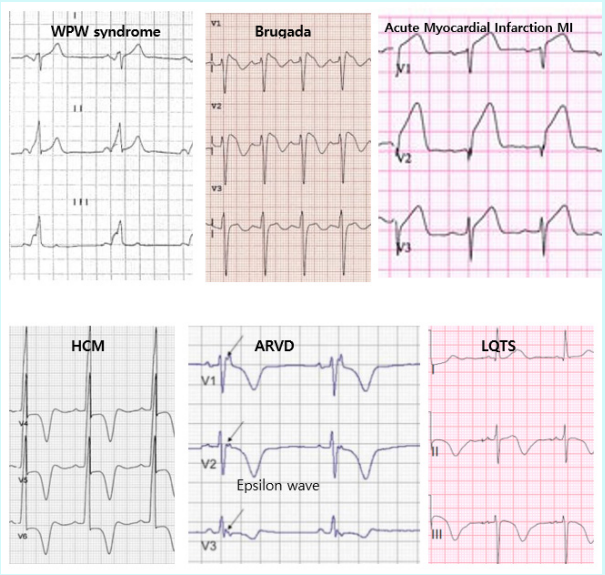

Figure 1: ECG abnormalities indicating various causes of sudden cardiac death.
WPW: Wolff Parkinson White; MI: Myocardial Infarction; HCM: Hypertrophic Cardiomyopathy; ARVD: Arrhythmogenic Right Ventricular Dysplasia; LQTS: Long QT Syndrome.

Screening of family members

The diagnosis of an inheritable arrhythmogenic disorder is established in up to 50% [13] of families with SCD victim, especially channelopathies. The family screening of first-degree relatives of victims of sudden death is needed to identify individuals at risk, advise on available treatment and prevent sudden death. It includes ECG, 2-D echocardiography and genetic testing if available.

Prevention of sudden cardiac death: No test has been identified with sufficient predictive value to accurately predict the risk of SCD. Overall, the most potent predictor of survival has proven to be 'Left Ventricular Ejection Fraction (LVEF). As the majority of episodes of SCD happen in patients with CAD, medicines that reduce myocardial ischemia (beta-blockers) and reduce LV adverse remodelling (ACE-inhibitors and aldosterone antagonists) all prevent SCD. Ventricular ectopics have long been recognized as a risk factor for SCD. However, trials like CAST [14] (class I anti-arrhythmics post-MI) and SWORD [15] (sotalol in MI with poor LV function) showed increased mortality with the use of anti-arrhythmic drugs. The only drug proven to reduce SCD (but not all-cause mortality) is amiodarone (EMIAT, CAMIAT, SCD-HeFT [16-18]). Due to lack of efficacy and potential hazards of anti-arrhythmic drugs, attention has been diverted to the implantation of ICD (Implantable Cardioverter Defibrillator). It prevents SCD in high risk patients with poor LV function, with or without the presence of myocardial ischemia. Several trials have proven reduction in mortality after implantation of ICD in high risk patients. In patients with prior myocardial infarction, MADIT [19] (prior MI, EF ≤35%, non-sustained VT) MADIT-II [20] (prior MI, EF ≤30%) and MUSTT [21] (CAD, EF ≤40%, non-sustained VT) all showed significant reduction in arrhythmic deaths and all-cause mortality. The indication has been extended to patients with non-ischemic cardiomyopathy. DEFINITE [22] (EF ≤35%, non-sustained VT or frequent PVCs) and SCD-HeFT [18] (EF ≤ 35%) trials demonstrated benefit in reducing all-cause mortality. About 30% of patients with advanced heart failure are associated with ventricular conduction delay resulting in a QRS duration of ≥ 120 ms. Such patients benefit from CRT (Cardiac Resynchronisation Therapy) that includes biventricular pac-

ing. CARE-HF [23] and COMPANION [24] randomized trials proved the benefit of CRT in reducing SCD in these patients.

Summary

Sudden Cardiac Death is the sudden and unexpected death occurring within an hour of the onset of symptoms and presumably due to a cardiac arrhythmia or hemodynamic catastrophe. While channelopathies, cardiomyopathies, myocarditis and substance use predominate in the young, older populations have chronic degenerative diseases like coronary artery disease, valvular heart disease and heart failure. All survivors of SCA need to be investigated to identify reversible factors, find and treat underlying conditions and determine the risk of recurrence. Overall, the most potent predictor of survival has proven to be LVEF. The only proven treatment to prevent SCD in high risk patients is the implantation of ICD.

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