Review Article

Mechanisms of sudden cardiac death

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Abstract

Worldwide, sudden cardiac death (SCD) is a major problem. It is most frequently caused by ventricular tachyarrhythmias: Monomorphic and polymorphic ventricular tachycardia (VT), torsade de pointes (TdP), and ventricular fibrillation (VF). Beta blockade, ACE inhibition, coronary reperfusion and other treatments have reduced the incidence of VT but pulseless electrical activity (PEA) is increasingly seen, particularly in patients with advanced chronic heart disease. From existing data, bradyarrhythmia in the form of asystole (usually complete heart block without escape rhythm) causes only a minor proportion (10–15%) of SCD. In patients aged 50 years and more, coronary artery disease plays a dominant role causing more than 75% of SCD cases, either by acute ischemia and ventricular fibrillation or by chronic scar formation and reentrant VT. In younger patients, SCD may occur in patients with structurally normal hearts. A number of arrhythmogenic disorders with an increased risk of SCD have been detected and better understood recently, such as long and short QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and the early repolarization syndrome. Most importantly, ECG signs and clinical features indicating high risk for SCD have been identified. Knowledge of the exact electrophysiologic mechanisms of ventricular tachyarrhythmias at the cellular level has been improved and mechanisms such as phase 2 reentry and reflection proposed to better understand why and how SCD occurs.

1. Definition of sudden cardiac death

Sudden cardiac death (SCD) has been defined as “natural death due to cardiac causes, heralded by abrupt loss of consciousness within one hour of the onset of acute symptoms; pre-existing heart disease may have been known to be present, but the time and mode of death are unexpected”. SCD is therefore always non-traumatic and should be unexpected and instantaneous. The delay between onset of symptoms and (sudden) death has been defined differently over time, from “within 24 hours” to “within 6 hours” and “within 1 hour”, which is the currently preferred definition.

The term SCD is usually applied in cases where a patient dies suddenly without any symptoms that indicate an imminent risk of natural death within the next minutes. In fact, 25% of patients treated for out-of-hospital cardiac arrest had literally no symptoms before the abrupt onset of SCD.

It has been argued that in many cases of sudden death, the cause is unknown and SCD due to an arrhythmic event is only assumed, thus overestimating cardiac causes of sudden death. However, autopsy studies in patients with sudden
death showed approximately three quarters of cases due to cardiac disease and only approximately a quarter due to non-cardiac causes, predominantly due to pulmonary embolism (18%) aortic rupture (4%), and intracranial bleeding (3%).

The term “arrhythmic death” has been used instead of SCD, and the Hinkle-Thaler classification distinguishes only arrhythmic and non-arrhythmic cardiac death. However, these terms are not identical with SCD because patients may die non-suddenly due to arrhythmias and not all sudden deaths are due to arrhythmias. The term “sudden death” will be replaced by SCD in this review to clarify that only cardiac mechanisms are considered. In some instances, the term “cardiac arrest” or “aborted SCD” will be used to clarify that survivors of SCD are included.

2. Causes of sudden cardiac death: arrhythmias and underlying pathology
2.1 Underlying arrhythmias

If an ECG documentation is available at the time of sudden loss of consciousness, it shows ventricular fibrillation (VF) in 75%–80%, only rarely (10%–15%) bradyarrhythmia; in 5%–10% the ECG does not show an arrhythmia (Fig. 1.2,6

Bradyarrhythmias lead to sudden death only in rare cases because in most patients, endogenous release of catecholamines generates and sustains an escape rhythm that is sufficient to keep the patient alive. In contrast, endogenous catecholamine release triggered by circulatory collapse due to ventricular tachyarrhythmias rather deteriorates the situation.

In patients with an implantable cardioverter-defibrillator (ICD), up to 80% of all device-treated ventricular tachyarrhythmias are monomorphic ventricular tachycardia (VT). Ventricular tachycardia (VT) is presumed to represent the typical initial arrhythmia in patients with a myocardial scar after infarction. However, monomorphic VT usually does not lead to loss of consciousness or SCD. In 100 patients with stable VT, systolic blood pressure remained at 110 mmHg despite a mean VT duration of 41 minutes at a rate of 188 bpm and the fact that patients had a mean left ventricular ejection fraction of 27%. Monomorphic VT leads to SCD only if other special conditions contribute to an insufficient circulation or if it degenerates into polymorphic VT or ventricular fibrillation (VF).

Polymorphic VT is a very rare finding on Holter tapes (prevalence 0.15%) but caused up to 40% of SCD that occurred in-hospital during rhythm monitoring.10,11 Polymorphic VT was inducible in 15–20% of survivors of SCD who underwent an electrophysiological study.12,13

Polymorphic VT is estimated to be the cause of SCD in approximately 25% of the cases and is particularly frequent in acute myocardial ischemia. Additionally, it is the typical arrhythmia in catecholaminergic polymorphic VT (CPVT), an inherited arrhythmogenic disorder characterized by adrenergically mediated polymorphic ventricular tachyarrhythmias.

Torsade de pointes (TdP) tachycardia is a form of polymorphic VT characterized by a gradual change in the QRS amplitude and twisting of the QRS vector around the isoelectric line. TdP is frequently associated with a prolonged QT interval. It can terminate spontaneously; recur in non-sustained spells, or degenerate into VF. It may be caused by QT-prolonging drugs, ischemia, or may be due to inherited long QT syndromes. It is 2–3 times more frequent in women; advanced age, bradycardia, hypokalemia, hypomagnesemia, left ventricular systolic dysfunction, renal and liver disease (both leading to elevated plasma concentrations of causative drugs) represent risk factors for drug-induced TdP. Patients with advanced heart failure and a history of drug-induced TdP had a significantly higher SCD risk during therapy with amiodarone.

Ventricular flutter and VF are responsible for 23% of out-of-hospital cardiac arrests treated by the emergency medical system.14 VF can result from an initial VT that degenerated into less organized rhythms. However, SCD may also result from primary VF caused by acute myocardial ischemia or due to inherited channelopathies such as Brugada or long QT syndrome.

Pulseless electrical activity (PEA) is usually defined as the presence of spontaneous organized cardiac electric activity in the absence of blood flow sufficient to maintain consciousness and (to distinguish it from e.g. vasovagal syncope) absence of a rapid spontaneous return of adequate organ perfusion and consciousness.15 Clinically, PEA is characterized by the absence of a palpable pulse in an unconscious patient with organized electric activity other than ventricular tachyarrhythmia on the ECG. The definition of PEA does not include the agonal pattern of slow, very wide QRS complexes at the end of a prolonged cardiac arrest. The incidence of PEA as the first documented rhythm in patients with SCD is increasing, potentially due to the ICD therapy, beta blockers and other drugs in heart failure that reduce the risk of VT and VF while not changing the risk of PEA. Additionally, patients with very advanced heart disease may be more likely to develop PEA than VT/VF which is supported by the observation of a higher incidence of PEA in nursing homes compared to public locations.16 Even in patients with PEA who survived

Fig. 1 — Synopsis of the type of arrhythmia documented as the first rhythm at the time of out-of-hospital SCD. The published prevalence ranges widely in different studies and registries. Different forms of VT/VF taken together (four red to orange slices) account for 75% of documented rhythms. Mono VT: monomorphic ventricular tachycardia, PEA: pulseless electrical activity, poly VT: polymorphic ventricular tachycardia, TdP: torsade de pointes, VF: ventricular fibrillation.
to hospital admission, survival rate at hospital discharge was particularly low with approximately 8%. 15

The exact pathophysiology of PEA is not clear. Likely, acute (severe) myocardial ischemia may play a role, and a third of patients with PEA have PCI performed during STEMI. 16 Also hypoxia may play a role since pulmonary disease is a significant independent predictor and three fold more likely to be associated with PEA than with VT/VF in men. 15, 17 Older age is associated with PEA and asystole as SCD mechanism 15, 15 Women have a survival advantage over men for SCD resuscitation outcomes but with a higher risk of PEA. The role of medication in PEA is not clear. A retrospective study (univariate analysis, not adjusted for other parameters) reported that 49% of patients with PEA were on β-blockers compared with 20% of VF patients. 18 Antipsychotic drugs are an independent risk factor for PEA, potentially related to their negative inotropic effects. 15

2.2. Underlying heart disease

SCD can occur at any age, and with or without detectable (“structural”) heart disease. While coronary artery disease and ischemic cardiomyopathy are the predominant cause of SCD in patients aged 50 years and above, a number of more rare diseases can cause SCD in younger populations (Table 1).

Coronary heart disease is the most frequent cause of SCD with acute coronary lesions (ruptured plaque, coronary thrombosis) detected at autopsy in 20–80% cases. 2 It is particularly frequent in patients >65 years of age and more likely as the cause of SCD if symptoms of ischemia are present and the longer (up to 1 hour) they persist before loss of consciousness. Acute myocardial ischemia is considered to be the most important cause of SCD. It is most frequently (~60%) associated with primary VF but also TdP, bradyarrhythmias and monomorphic VT as the primary arrhythmia have been observed. 7 The second mechanism by which coronary artery disease leads to SCD is scar-related VT. Scar formation after myocardial infarction represents an important structural prerequisite for reentry creating unidirectional block and areas of slow conduction. This is reflected in studies with cardiac magnetic resonance imaging where heterogeneity of the scar is a strong predictor of ventricular arrhythmias. 19 The incidence of SCD due to coronary artery disease has been reduced by better revascularization and the use of ACE inhibitors, beta blockers, and statins.

Hypertension predisposes independently to SCD via left ventricular hypertrophy (LVH). Left ventricular hypertrophy determined from ECG or echocardiography predicts an increased risk of SCD. Similar to hypertrophic cardiomyopathy, in severe LVH, loss of parallel orientation of myofibers and a resulting disarray may cause VT or VF. LVH at a late stage may also be eccentric with severely reduced ejection fraction. Hypertension seems to be of particular importance as a cause of SCD in black Africans. This may be due to a greater prevalence of hypertension in black compared with white men or due to a more difficult control of blood pressure resulting in more advanced LVH.

Dilated cardiomyopathy (DCM) is a highly heterogeneous group of non-ischemic diseases that all result in severely reduced left ventricular function. SCD in DCM is most frequently caused by ventricular tachyarrhythmia (approximately 50%), particularly VF, but can also be due to brady-cardia and electromechanical dissociation. The incidence of DCM in DCM has been drastically reduced by treatment with beta blockers, ACE inhibitors and other drugs. Annual mortality in DCM was up to 30% in the era before these drugs were used but as low as 7% at the time that studies such as SCD-HeFT or DEFINITE were performed. 20, 21

If SCD occurs in the absence of coronary artery disease or heart failure, the main causes are hypertrophic (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC). Most data on the incidence of SCD in younger, seemingly healthy patients stem from studies analyzing SCD in athletes. 22, 23

In Minneapolis Heart Institute Foundation Registry, cardiovascular causes of SCD were assessed in 1435 young athletes in the period between 1980 and 2005. HCM was found in 44% of cases of SCD. 22 The second largest cause in this registry was coronary artery anomalies including a tunneled LAD and coronary artery disease (together 23%). ARVC was found as the cause of SCD in 4% of patients, all channelopathies taken together in 3%.

HCM predisposes to SCD due to myocardial hypertrophy, myocyte disarray and fibrosis. Apart from direct proarhythmia, these changes can lead to SCD secondary to myocardial ischemia, diastolic dysfunction, left ventricular outflow obstruction and development of congestive heart failure.

European data from a North Italian registry show a different distribution. 23 In 269 cases of SCD from 1979 to 1996 in persons aged <35 years, HCM accounted for 7% of SCD in non athletes compared to only 2% in athletes, demonstrating a different incidence of HCM in different populations and potentially the effect of screening competitive athletes for HCM.
In the Italian registry, ARVC was found in approximately 11% of cases of SCD. The pathognomonic finding in ARVC is a diffuse or segmental loss of right ventricular myocytes replaced by fibro-fatty tissue and thinning of the right ventricular wall. These changes predispose to slow conduction, presence of diastolic potentials, and unidirectional block. Therefore, SCD, usually by VT that degenerates into VF, is frequent in ARVC (annual mortality approximately 2.3%).

Additionally, the development of right heart failure and left ventricular dysfunction increase the risk of SCD in ARVC.

2.3. Sudden cardiac death (SCD) in patients without structural heart disease

In about 5%–10% of cases of SCD, no underlying heart disease can be found at autopsy. Some of these (may be 50%) can be explained by genetic disorders that lead to ion channel dysfunction (“channelopathies”) or other abnormalities in the formation of the action potential.

Brugada syndrome accounts for approximately 20% of SCD in patients with structural normal hearts. It is characterized in the ECG by a coved-type ST-segment elevation in the right precordial leads. Brugada syndrome is caused by a genetic change of the sodium channel which causes loss of the action potential dome in the epicardium but not in the endocardium. This is seen in the ECG as a coved type ST-segment elevation in leads V1 and V2. It generates a transmural gradient that predisposes to local phase 2 reentry which in turn causes short-coupled ventricular premature beats, polymorphic VT and VF. The typical arrhythmia leading to SCD in Brugada syndrome is therefore VF. It can be triggered by sodium channel blockers, fever, vagotonic agents, beta blockers, antidepressants, hypokalemia and other conditions. SCD in Brugada syndrome occurs typically during sleep or at rest.

The long QT syndrome (LQTS) consists of a number of familial diseases with genetic variations of different potassium and sodium channels. All have in common a prolongation of the QT or QTc interval, respectively. This may, however, not be permanently visible from the ECG. Of the many types of LQTS, LQT1-3 are clinically the most important. LQT1 is the most frequent subtype and explains 30%–35% of cases. SCD in LQT1 usually occurs when sympathetic stimuli are present such as physical activity (particularly swimming and diving into cold water) or emotional stress. LQT2 is the second most frequent subtype and accounts for 25%–30% of LQTS cases. SCD in LQT2 frequently occurs in response to emotional stress and particularly sudden auditory stimuli such as ringing of an alarm clock or a telephone. Women in the postpartum period are specifically susceptible. In LQT2, up to 20% of patients have a non-diagnostic ECG. LQT3 is present in 5%–10% of LQTS patients who are at increased risk of SCD during bradycardia, specifically during sleep. Characteristically, ventricular arrhythmias in LQT3 are particularly lethal.

The SCD risk before 40 years of age is >50% when QTc is >500 ms in LQT1, LQT2, and in males with LQT3. In an international LQTS registry, the risk of SCD was associated with a QTc >530 ms, history of syncope in the past 10 years, and gender (10–12-year-old boys had a higher risk than girls, in the 13–20 age range, the risk was comparable). Symptomatic patients have a yearly mortality rate of 20% and 10-year mortality of 50% after a first event of ventricular arrhythmia if no treatment is installed.

The characteristic ventricular arrhythmia in LQTS is TdP, typically triggered by a short-long-short cycle (e.g. ventricular bigeminus with long postextrasystolic interval). To combine the information from the resting ECG, ventricular arrhythmia, clinical and familial history in order to establish an LQTs diagnosis, the Schwartz score has been developed.

A large number of drugs used in different medical indications can induce LQTS such as antibiotics, other anti-infectives, anti-parkinson drugs, anti-depressants, chemotherapy agents, neuroleptics, etc. Because SCD due to QT prolongation by non-antiarrhythmic drugs occurs in <1:10,000–1:100,000 exposed patients, the risk of drug-induced LQTS can remain undetected in clinical studies even if >5000 patients are enrolled. Therefore, some drugs have been removed from the market after many years of use, such as astemizole and cisapride. Antipsychotic drugs have a more than three fold increase in the risk of SCD. A permanently updated list of drugs with a risk of QT prolongation can be found e.g. at www.qtdrugs.org and www.crediblemeds.org.

In CPVT, ryanodine receptor mutations have been identified that lead to uncontrolled calcium release from the sarcoplasmic reticulum. Even though CPVT has a genetic etiology, most reported cases are sporadic, potentially due to the high lethality and to the fact that patients may not reach reproductive age unless correctly diagnosed and effectively
treated. If familial CPVT is found, there is often a family history of SCD at young age during adrenergic stress.

Recently, research has focused on the clinical meaning of early repolarization (ER). An ER pattern is characterized by J point elevation, distinct J waves with and without ST-segment elevation and slurring of the terminal part of the QRS in inferior limb and lateral precordial leads, and a combination of J wave, J point and ST-segment elevation, and a gigantic J wave.33,34 An ER pattern is commonly found in healthy young males and has been regarded as benign. However, experimental data showed that phase 2 reentry can easily be initiated in ER and trigger polymorphic VT or VF.37,38 With a prevalence of 1%–13% in the general population,39–42 ER is an insensitive ECG sign for an increased risk of SCD. Subgroups of ER patterns have been identified that have an increased risk of SCD: horizontal or descending ER patterns have been identified that have an increased risk of SCD.43 The observation of ER in the ECG has been associated with a higher NYHA functional class, a history of spontaneous or paroxysmal VT, etc. may add substantially to mortality in ICD patients.49 A death due to recurrent ventricular tachyarrhythmias, slow VT, etc. may add substantially to mortality in ICD patients.49 A death due to recurrent ventricular tachyarrhythmias, slow VT, etc. may add substantially to mortality in ICD patients.49 A death due to recurrent ventricular tachyarrhythmias, slow VT, etc. may add substantially to mortality in ICD patients.49

### 3. Electrophysiologic mechanisms of ventricular tachyarrhythmia

The basic electrophysiologic mechanisms leading to ventricular tachyarrhythmias (VT or VF) can be divided into three groups: 1. Abnormal automaticity, 2. Triggered activity, 3. Reentry.

#### 3.1. Abnormal automaticity

In abnormal ventricular automaticity, ventricular myocardial cells generate a spontaneous repetitive depolarization at a rate higher than that of normal automaticity. The underlying mechanism is usually a reduced resting membrane potential in the range between −70 and −30 mV. The more depolarized the resting potential, the faster the rate of abnormal automaticity. Abnormal depolarization of membrane potential is commonly a result of increased extracellular potassium, a reduced number or function of IK1 channels, or electrotonic influence of neighboring cells in the depolarized zone.35 Hypokalemia can lead to a major reduction in IK1, causing depolarization and the development of enhanced or abnormal automaticity, particularly in Purkinje fibers. Adrenergic activity can increase abnormal automaticity. Also a changed threshold for sodium influx can be responsible for a reduced resting membrane potential. The typical ECG correlated with abnormal automaticity is an accelerated idioventricular rhythm. Among others, abnormal automaticity plays a role as a mechanism of SCD in acute ischemia, myocarditis, and intoxication (e.g. cocaine). Abnormal automaticity primarily causes VT at any rate that can secondarily degenerate into VF.

#### 3.2. Triggered activity

Triggered activity follows the cardiac action potential and depends on preceding transmembrane activity. There are two subclasses of membrane potential oscillations, referred to as after depolarizations: early after depolarizations (EADs) and delayed after depolarizations (DADs). Early after depolarization (EAD) or DAD amplitudes that are sufficiently high to reach the membrane threshold result in a spontaneous action potential referred to as a triggered response. These triggered events give rise to extrasystoles, which can precipitate tachyarrhythmias.

EADs occur during phase 2 or 3 of the action potential, typically at slow heart rates. They develop when the balance of current during phase 2 and 3 of the action potential shifts in the inward direction.51 If the change results in a net inward current during the plateau of membrane potentials, it leads to...
an EAD. EADs develop particularly in the mid-myocardial M cells and Purkinje fibers, less in epicardial or endocardial cells. This difference is pronounced if the heart is exposed to drugs that prolong the action potential because IKs is weaker and late I Na stronger in M cells. The risk of development of catecholamine-induced EADs require a fast heart rate. Drugs can induce EADs at slow heart rates. In contrast, currents or increase inward currents. Class III antiarrhythmic currents and Purkinje fibers, less in epicardial or endocardial cells. They are also observed in cardiac tissue injury, electrolyte dysbalance, hypoxia, acidosis, ventricular hypertrophy and heart failure. EADs represent the typical mechanism of proarrhythmia by a number of drugs that inhibit potassium currents or increase inward currents. Class III antiarrhythmic drugs can induce EADs at slow heart rates. In contrast, catecholamine-induced EADs require a fast heart rate.

Delayed after depolarizations (DADs) occur in phase 4 after full repolarization, in contrast to EADs always at relatively high heart rates. DADs are observed in situations with increased intracellular calcium, e.g. digitalis- or catecholamine-induced. They occur in ventricular hypertrophy, heart failure, Purkinje fibers that survived myocardial infarction, and are the typical mechanism of ventricular outflow tract tachycardias. Particularly bidirectional ventricular tachycardia in CPVT is caused by DADs where the "leaky" ryanodine receptor leads to calcium overload during catecholamine stimulation. Also in digitalis-induced calcium overload, DADs can cause bidirectional ventricular tachycardia.

3.3. Reentry

In circus movement reentry, the activation wavefront propagates around an anatomic or functional obstacle and reexcites the site of origin. In this type of reentry, all cells recover from excitation and can be excited again when the next wavefront arrives. In contrast, in reflection and phase 2 reentry large differences of recovery from refractoriness exist between different sites. The site with delayed recovery excites its already recovered neighbor, resulting in a reentrant reexcitation.

Reentry can be classified as anatomic or functional, with an overlap in which both are important in creating reentry.

Circus movement reentry requires three conditions: 1. Unidirectional block, allowing the circulating wave to travel in one direction only. 2. Conduction block (fixed or functional), and 3. Areas of slow conduction where the tachycardia cycle length is longer than the longest refractory period of the circle to allow each site in the circuit to recover before the return of the circulating wave. Additionally, the excitable wave must progress along a distinct pathway, return to its point of origin and then follow the same path again. Interruption of the reentrant circuit at any point along its path should terminate the circus movement. Conduction velocity and refractoriness determine if reentry can be established. The length of the reentry circuit must be longer or equal to the wavelength. e.g. the product of conduction velocity and refractory period. Reduction of conduction velocity (e.g. by antiarrhythmic drugs) can therefore facilitate reentry.

Reentry in circus movements typically requires a specific substrate (e.g. scar or diseased myocardium) and occurs in ischemic and non-ischemic myocardial disease. However, reentry can also occur without anatomic obstacles as “functional reentry”. Premature impulses can propagate only in the direction of shorter refractory periods, create an arc of block around which the impulse circulates and reexcite its site of origin. In this “leading circle model”, tachycardia is not readily influenced by stimuli from areas outside the reentrant circuit and thus may be difficult to entrain. In the spiral wave concept, circulating waves are considered in the absence of an anatomic obstacle as mechanisms of functional reentry. The term spiral wave describes reentrant activity in 2 dimensions, e.g. from epicardium to endocardium. Spiral wave activity explains the ECG patterns of monomorphic and polymorphic VTs and VF. In monomorphic VT, the spiral wave is anchored and does not drift within the ventricular myocardium. In polymorphic VT and VF, the spiral wave drifts within the ventricular myocardium. The spiral wave concept explain the degeneration of VT into VF: When a single spiral wave responsible for VT breaks up, multiple spirals that drift can occur that are continuously extinguished and recreated.

In postmyocardial infarction tissue, figure 8 reentry can occur in the surviving epicardial layer that overlies an area of infarction. In the figure 8 model, a wavefront circulates in both directions around a line of conduction block rejoining on the distal side of the block. The wavefront then breaks through the arc of block to reexcite the tissue proximal to the block. The reentrant activation continues as 2 circulating wavefronts that travel in clockwise and counterclockwise directions around the two arcs.

Reentry can occur without circus movement by the mechanisms “reflection” and “phase 2 reentry”. In the concept of reflection, slow anterograde conduction of the impulse in Purkinje fibers is followed by a retrograde wavefront that produces a “return extrasystole”. Reflection results from the to f electrotonically mediated transmission of the impulse across the same in excitable segment and generates a closely coupled reflected reentry. Reflected reentry has been demonstrated in isolated atrial and ventricular myocardial tissues and in Purkinje fibers.

Also phase 2 reentry does not depend on circus movement and can appear to be of focal origin. Phase 2 reentry occurs when the dome of the action potential, most commonly epicardial, propagates from sites at which it is maintained to sites at which it is abolished, causing local reexcitation of the epicardium and the generation of closely coupled extrasystole. Severe spatial dispersion of repolarization is needed for phase 2 reentry. Phase 2 reentry has been proposed as the mechanism responsible for the closely coupled extrasystole that precipitates VT/VF in Brugada and early repolarization syndromes.

4. Conclusion

Our understanding of SCD has dramatically improved and multiple mechanisms have been identified on the levels of genes, cellular and clinical electrophysiology. Many of these findings have reinforced the importance of fundamental knowledge about the ECG to identify patients at risk and prevent SCD by drugs, ablation and ICD implantation.
Conflicts of interest

The author has none to declare.

REFERENCES


