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Sudden Cardiac Death

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ABSTRACT

Sudden cardiac death (SCD) continues to be a major health issue in many countries including Malaysia due to its large magnitude in all-cause mortality as well as the emotional and socioeconomic impact of the deceased leaving the love ones behind in an abrupt manner. Data in Malaysia shows that the majority of sudden natural deaths are due to sudden cardiac death and are in the productive age group of 41 to 50 years. A study in Germany pointed out that about 90% people who died of SCD actually had warning signs such as chest pain, breathlessness, nausea, vomiting, dizziness and fainting before they collapsed. The majority belonged to the high-risk group for SCD having had previous medical histories including coronary artery disease, cardiomyopathies, valvular heart disease, congenital heart disease, underlying electrophysiological abnormalities or are taking drugs which are capable of provoking ventricular tachyarrhythmias. The key step is to define a sequence of risk stratifiers that will identify patients who are at risk but in whom implantation of expensive devices will be cost-effective. Amongst the investigative tools proven to be helpful to achieve this are ECG screening for left ventricular hypertrophy, increased QRS width, T-wave alternans, heart rate variability, baroreceptor responsiveness, QT dispersion, and T-wave heterogeneity; Holter monitoring to demonstrate ventricular arrhythmias; and stress test in identifying ischaemia. Prompt action is crucial since restoring circulation as fast as possible improves the chances of survival. Family members and caregivers of people with heart disease and at increased risk should be trained to recognise symptoms and perform cardiopulmonary resuscitation (CPR) to reduce the likelihood of death from cardiac arrest. Training and prevention efforts should focus on how to recognise the emergency, CPR training, and automated external defibrillator (AED) use. An implantable cardioverter-defibrillator (ICD) is the preferred therapeutic modality in most survivors of SCD. The incidence of SCD can be reduced by improving the current situation through selection of high risk groups for initiation of therapies, education to the public on the awareness of early warning symptoms and early emergency management that should be readily available in the community.

Keywords: Sudden cardiac death, high risk groups, early warning symptoms therapies, emergency management

SUDDEN CARDIAC DEATH (SCD)

Sudden cardiac death (SCD) is defined as an instantaneous, unexpected death or death within 1 hour of symptom onset not related to circulatory failure in a person without any prior condition that would appear fatal.[1-2] In the United States, the prevalence SCD is

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estimated to be approximately 200,000 to 400,000 per year. It continues to be a major health issue in many countries including Malaysia due to its large magnitude in all-cause mortality as well as the emotional and socioeconomic impact of the deceased leaving the love ones behind in an abrupt manner.

A recent report from the data collected amongst 545 sudden natural autopsies gathered over a period of five years [3] from the University Malaya Medical Centre, Kuala Lumpur show that sudden cardiac deaths accounted for 65% of all sudden natural deaths. In the same report, they also concluded that 87% of these were males and the largest number of sudden natural deaths was in the age group of 41–50 years.[3] In Malaysia, the top two causes of mortality in government hospitals are from cardiovascular disease, with coronary artery disease being the major cause of death.[4] In addition, up to half of the patients who had the first heart attack died before reaching the hospital.[2] Therefore if SCD is not monitored it will continue to take a heavy toll in the productive age of the community in the country.

However, a recent study by Muller *et al.*[5] from Germany showed most people who died from sudden cardiac death may not have experienced sudden death after all. In 90% of the cases, they had symptoms earlier which lasted more than 5 minutes before they collapsed.[5] The median symptom duration was 20, 30 and 50 minutes for patients presenting with pulseless electrical activity, ventricular fibrillation and asystole respectively.[5] Moreover, up to two-thirds of these victims had a history of underlying heart disease which promotes the risk for cardiac arrest.[5]

Thus, by raising the awareness of the warning signs of cardiac arrest and providing emergency management to the high-risk patients, we may offer a window of opportunity to prevent sudden cardiac death. There are a few areas of interest that are recognised as having the potential to reduce the incidence of SCD which has long been regarded as an inevitable event.

RECOGNISING THE CLINICAL FEATURES OF CARDIAC ARREST

The study performed in Berlin also showed 72% of the cardiac arrests took place at home and 67% were witnessed by a bystander.[5] Researchers collected information on symptoms preceding cardiac arrest on 323 of the 406 cases[5] and the most common warning symptom was chest pain lasting from 20 minutes to 10 hours before the cardiac arrest, or a median of two hours.[5] Chest pain occurred in 25% of the cardiac arrests witnessed by others.[5] Breathlessness for 10 minutes was reported in 17% of witnessed cardiac arrests; nausea or vomiting for 90 minutes before the arrest in 7%.[5] Other common symptoms were dizziness or fainting.[5]

From the same report, a background history was available in 352 of the[5] patients. Researchers found that 106 of these cardiac arrest patients had a history of coronary artery disease that put them at increased risk for cardiac arrest, and 16 had experienced a previous cardiac arrest.[5]

Coronary Artery Disease

Up to 80% of patients who experience sudden cardiac death have coronary artery disease as the underlying anatomic substrate due to atherosclerotic changes of the coronary arteries.[6]

Even though less than half of the patients resuscitated from ventricular fibrillation showed evidence of myocardial infarction by elevated cardiac enzymes and less than a quarter had Q-wave myocardial infarction, several autopsy studies have reported that a recent occlusive coronary thrombus evidence by plaque fissuring, haemorrhage, and thrombosis was found in 15 to 64% of victims of sudden cardiac death.[7] In addition, significant cross-sectional coronary stenoses (in more than 75%) were found in ≈ 40% to 86% of patients who survived a cardiac arrest, depending on age and sex of the population studied.[6] Interestingly, chronic ischemia may exert a protective effect by causing the development of coronary collaterals that can help mitigate the extent of ischemia produced by sudden coronary occlusion.[6] This means an acute blockage of a minimally stenosed coronary artery can give rise to a more disastrous outcome than blockage of a severely stenosed coronary artery with the jeopardised myocardium protected by collaterals.[6]

Cardiomyopathy

Cardiomyopathies account for the second largest group of patients who experience sudden cardiac death. Hypertrophic cardiomyopathy has a prevalence of 2 in 1000 young adults and an incidence of sudden cardiac death of 2 to 4% per year in adults.[8] In patients with hypertrophic cardiomyopathy, a history of sudden cardiac death or sustained ventricular tachycardia, family history of sudden cardiac death, a diverse genotype, recurrent syncope, multiple episodes of non-sustained ventricular tachycardia, and massive left ventricular hypertrophy are the strongest risk factors for sudden cardiac death.[8-9]

The presence of mutations in the α-tropomyosin as well as in the β-myosin heavy chain gene has been associated with sudden cardiac death.[8-9] Idiopathic dilated cardiomyopathy is a substrate for 10% of sudden cardiac deaths in the adult population.[10] Mortality in patients with idiopathic dilated cardiomyopathy ranges from 10 to 50% annually, depending on the severity of the disease.[10] Syncope in patients with cardiomyopathy appears to be an important clinical variable that also identifies patients with a higher risk of sudden cardiac death.[10]

Arrhythmogenic right ventricular dysplasia (ARVD) is an important cardiomyopathy responsible for sudden death in young individuals and adults, with a gene defect recently localised to chromosomes 1 and 14 q23-q24.[11] It occurs as a familial disorder in about 30% of cases, with an autosomal dominant inheritance.[11] Exercise can precipitate ventricular tachycardia in these patients, with an annual incidence of sudden death estimated to be around 2%.[11] Classically, two pathological patterns, fatty and fibrofatty myocardial infiltration, have been identified on the histology of myocardium of such patients. In the fibrofatty variety, myocardial atrophy appears to be the consequence of acquired injury and myocyte death and repair by fibrofatty replacement, mediated by patchy myocarditis.[11] During sinus rhythm, intraventricular conduction may be sufficiently slow as to produce a terminal notch on the QRS complex that is called an epsilon wave.[11]

Valvular Disease

The risk of sudden death in asymptomatic patients with aortic valve disease appears to be low.[6] It was noted that even after aortic valve replacements, patients remain at some risk

for sudden cardiac death caused by arrhythmias, prosthetic valve dysfunction, or coexistent coronary artery disease.[6] Thus, sudden cardiac death is still the second most common mode of death after valve replacement surgery, with an incidence ranging from 2 to 4% over a follow-up of 7 years, accounting for approximately 20% of the post-operative deaths.[1]

Congenital Heart Disease

An increased risk of sudden cardiac death due to arrhythmias has been found predominantly in four congenital conditions, including tetralogy of Fallot, transposition of the great arteries, aortic stenosis, and pulmonary vascular obstruction.[6] Sudden cardiac death has also been described as a late complication after surgical repair of complex congenital cardiac lesions, such as tetralogy of Fallot and transposition of the great arteries, and in patients with primary or secondary pulmonary hypertension.[1]

Primary Electrophysiological Abnormalities

Patients with primary electrophysiological abnormalities represent a group in whom mechanical function of the myocardium is normal and an electro-physiological derangement represents the primary cardiac problem. This includes patients with the congenital long-QT syndrome, Wolff-Parkinson-White syndrome, several types of distinctive ventricular tachycardias, idiopathic ventricular fibrillation[12] (including a newly described entity characterised by right bundle-branch block and ST-segment elevation, namely, Brugada's syndrome) [13], congenital complete AV block, and a variety of acquired abnormalities such as the acquired long-QT syndrome and acquired diseases of the sinus node, AV node, and His-Purkinje system, such as Lenegre's disease or Lev's disease.[2]

In 1992 the Brugada brothers described a syndrome characterised by an electrocardiographic pattern resembling a right bundle branch block with a peculiar coved-type of ST segment elevation in leads V1 to V3, polymorphic ventricular arrhythmias causing episodes of syncope or sudden cardiac death in structurally normal hearts. A fascinating recent discovery is that the gene responsible for the Brugada syndrome, the cardiac sodium channel gene SCN5A on chromosome 3[13] is the same gene, with different defects, that causes LQT3 syndrome.[6]

The idiopathic (congenital) long-QT syndrome is caused by prolongation of repolarisation due to abnormal movement of sodium ions into or potassium ions out of the cardiac myocyte, creating prolonged periods of intracellular positivity.[14] Such prolongation of repolarisation (or long QT intervals on electrocardiogram) can lead to the development of early after-depolarisations which can then lead to Torsade de pointes and SCD in such patients.[14] Analysing the genetic abnormalities can also stratify the risk of SCD among patients with congenital long QT syndrome. At least 7 sub-types of congenital long QT syndrome have been described according the underlying genetic defects.[14]

Patients with the Wolff-Parkinson-White syndrome have a risk of sudden cardiac death estimated to be 1 per 1000 patient-years of follow-up.[15] Almost all survivors of sudden cardiac death with Wolff-Parkinson-White syndrome have had symptomatic arrhythmias before the event, but up to 10% experience sudden cardiac death as their first manifestation

of the disease.[15] The responsible mechanism, most probably, is the development of atrial fibrillation, with rapid conduction to the ventricles over the accessory pathway that produces ventricular rates so rapid that the rhythm degenerates to ventricular fibrillation.[15]

Sudden unexplained nocturnal death can occur in young, apparently healthy males of Southeast Asian origin and has several names, such as *lai-tai* (sleep death, Laos), *pokkuri* (sudden and unexpected death, Japan), and *bangungut* (to rise and moan in sleep, Philippines).[6] The cause(s) is unknown.

Drugs

Apart from underlying cardiac diseases, class I and III anti-arrhythmic drugs have long been known to be capable of provoking ventricular tachyarrhythmias and sudden cardiac death by prolonging the ventricular repolarisation and causing torsades de pointes. Certain non-anti-arrhythmic drugs such as non-sedating antihistamines, antipsychotics and antibiotics (macriolides, atimalarials, antifungals, etc) can also prolong ventricular repolarisation and lead to sudden cardiac death. Drug interactions between those that can prolong QT interval during poly-pharmacy can be fatal, even with apparently innocuous medications.[16] Even widely prescribed medications such as non-sedating anti-histamine are capable of prolonging QT interval and such medications should not be prescribed to those at risk of developing torsades de pointes such as those with congenital long QT syndrome, cardiac disease, liver disease, electrolyte disturbance or on concurrent medications which promote prolonged QT interval.[17]

Therefore it is important that those who have underlying conditions as described above to be informed of their risk of SCD. They should be educated in prompt emergency care should they have any of the warning signs of SCD since survival of sudden cardiac arrest depends on prompt emergency care.

SEARCH FOR SCD PREDICTORS IN A GENERAL COMMUNITY

Apart from targeting those already known to have underlying heart disease, people in the general population are also at risk of SCD. In fact, Myerburg & Castellanos predict that the majority of people who die of SCD do not seem to be at high risk.[2]

However, applying therapies to a group of patients in whom the absolute incidence of sudden death is somewhere between 0.1 and 0.2% means applying costly therapy, with potential side effects, to many patients, the vast majority of whom will see no benefit.[2] Thus, we need to identify high-risk patients among those who seem to be at low risk.

The key step is to define a sequence of risk stratifiers that will identify patients who are at risk but in whom implantation of expensive devices will be cost-effective. The simple ECG could be a useful tool. Left ventricular hypertrophy seems to be independently predictive of SCD, whereas increasing QRS width predicts total mortality.[18] T-wave alternans, heart rate variability, baroreceptor responsiveness, QT dispersion, and T-wave heterogeneity are other non-invasive tests that may be used singly, or more likely in combination with others, to select patients at risk.[19-22] Holter monitoring to demonstrate ventricular arrhythmias is a proven risk stratifier, wheareas electrophysiological studies have a limited predictability and are too expensive and invasive to be used as a screening tool.[16]

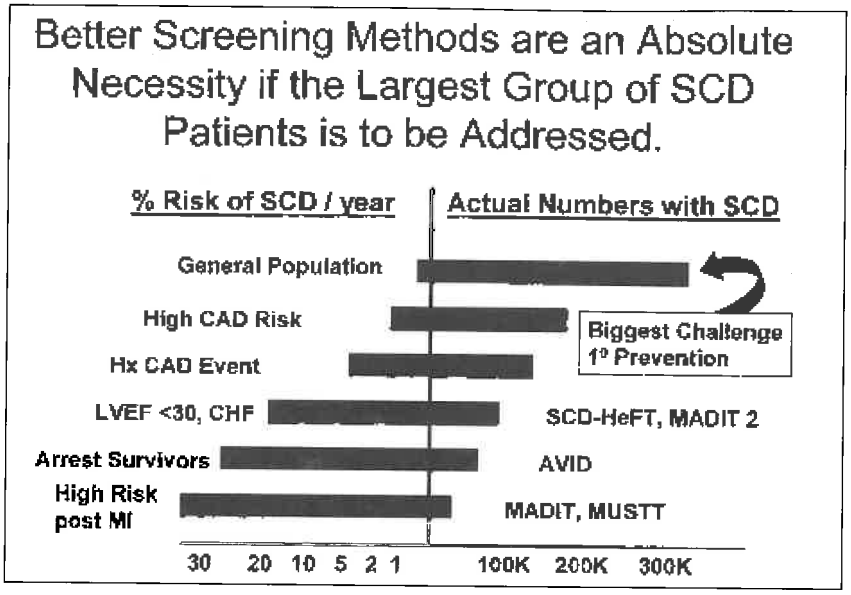

Figure 1. Need for better screening methods to identify the largest group at risk. Adapted from Myerburg and Castellanos.[2]

In addition, identifying the amount of myocardium at jeopardy by ischemia is important. Therefore, identifying multi-vessel coronary disease non-invasively would be useful. Stress test is a useful screening test but high-resolution computed tomography and PET scan are modalities with potential but never been proven as a screening tool due to the high radiation exposure. LVEF and a clinical evaluation of heart failure are easily obtainable. The signal-averaged ECG independently predicted total mortality but suffered from low positive predictive value.[8] Thus, it is likely that physicians will use a tiered approach to risk stratification to maximise selection of patients who are at high-enough risk so that devices could be implanted in a cost-effective manner.[22] Obviously, a reduction in the cost of such devices will make their application more cost-effective in a broader number of patients. Nevertheless, it is important to note that even if all high-risk patients were identified and appropriately treated, most patients dying suddenly would be unprotected.

ACTIONS TO REDUCE SCD DEATHS

The general population should be taught about sudden cardiac death and its warning signs as well as on cardio-pulmonary resuscitation (CPR). It is best if these are taught as part of school and higher learning curriculum. Patients at higher risk should be identified and educated on the action plans should they have any of the warning signs. Prompt response and the availability of emergency facilities are essential since an increase in the time to response means a lesser chance of survival.

QUICK TREATMENT IS CRUCIAL

This generally involves administration of cardio-pulmonary resuscitation (CPR), shock treatment to the chest to reset the heart's rhythm (defibrillation) and advanced life support. Restoring circulation as fast as possible improves chances of survival.

The study by Muller *et al.* showed bystanders performed CPR on 57 patients, and 13 of those patients (23%) survived to hospital discharge.[6] Only 4% of cardiac arrest patients who did not receive bystander CPR survived.[6] Researchers found CPR attempts occurred more often in public locations (26%) than at home (11%).[6]

Thus, the results suggest family members and caregivers of people with heart disease and at increased risk should be trained to recognise symptoms and perform CPR to reduce the likelihood of death from cardiac arrest. Training and prevention efforts should be focused on how to recognise the emergency, CPR training, and automated external defibrillator (AED) use. In the United States of America, only about 3% of all victims of sudden cardiac arrest victims eventually survived to leave the hospital without any neurological sequele.[2] Given the facts that AEDs are likely to have a significant impact on survival of out-patient sudden cardiac arrest, these findings would suggest that AEDs should be stratergically placed in the neighbourhood and communities.

IMPLANTATION OF ICD (Implantable Cardiac Defibrilator)

An implantable cardioverter-defibrillator (ICD) is the preferred therapeutic modality in most survivors of SCD. This change in practice is based upon improvements in device technology, clinical trials demonstrating improved outcomes with an ICD compared to pharmacology therapy, and concerns about the toxicity associated with antiarrhythmic drugs.[23-25] Although the ICD does not prevent malignant ventricular arrhythmias, these arrhythmias are generally terminated promptly when they occur.

It has been thought that patients with a life-threatening ventricular tachyarrhythmia due to a transient or reversible cause (most often an ischemic event) have a low risk for recurrent SCD after correction of the underlying problem. However, most such patients remain at high risk for SCD.[26-27] As an example, an acute ischemic event implies the presence of underlying coronary artery disease and areas of both scar and viable myocardium can provide a continued substrate for arrhythmia, even if coronary revascularisation is performed.

In conclusion, sudden cardiac death has a huge impact on overall mortality and is a burden to the affected families and nation. Therefore, we should try to reduce the incidence of SCD by improving the current situation through selection of high risk groups for initiation of therapies, education to public on the awareness of early warning symptoms and early emergency management that should be readily available in the community. The future looks brighter but more research should be conducted and cost-effective therapies should be available to most high-risk individuals with the potential for sudden cardiac death.

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