ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN – POLONIA
VOL. LXI, N 2, 119 SECTIO D 2006

Interfaculty Chair and Department of Public Health, Cardiology Department
Medical University of Lublin

MARCIN DZIDUSZKO, TERESA WIDOMSKA-CZEKAJSKA

Sudden cardiac death – most frequent causes, risk factors, individual and population-based prevention

Sudden cardiac death (SCD) is a sudden and unexpected death due to heart-related reasons occurring within an hour after the initial severe symptoms preceded by the loss of consciousness. It may occur in people with the diagnosed heart disease as well as in seemingly healthy individuals.

The number of sudden cardiac deaths in the USA is estimated at 300–450,000 per year. There is no reliable database concerning the percentage of such events in Poland. Given the recognized incidence rate of sudden cardiac death determined at 1/1000/year, the number of SCDs in Poland can be estimated at 38,000 deaths per year. The statistical data obtained in the Framingham Heart Study showed that only 5–10% of sudden cardiac deaths occur in individuals who have not been diagnosed for ischemic heart disease or heart failure. The risk factors that influence the incidence of sudden cardiac death include: age, sex, medical history of heart disease. It was found that the incidence of SCD in the male population aged from 60 to 69 is eight times as high as the average for the whole population. The Maastricht study proved that SCD occurred in 21% of male deaths and 14.5% of female deaths. 80% of these accidents took place at home, while approximately 15% out-of-home, including 40% unwitnessed cases of SCD. In addition, it was also found that 75% of the whole number of SCD cases occurred in men over 50, and the vast majority of these accidents took place between 8 a.m. and 6 p.m. The Framingham Heart Study indicated an increased risk of SCD between 7 and 9 a.m., while the Beta Blocker Heart Attack Trial – between 8 and 11.

According to Braunwald the most frequent causes of sudden cardiac death include: ischemic heart disease with infarction (80% SCD), nonischemic structural heart diseases (10% SCD), including hypertrophic cardiomyopathy, congestive cardiomyopathy, arrhythmogenic left ventricular cardiomyopathy. They are followed by non-ischemic and non-structural diseases accounting for 5% of reported SCDs – long QT syndrome, Brugada syndrome as well as severe mechanical conditions (5% SCD), such as cardiac or aorta rupture and heart contusion.

Ischemic heart disease, the most frequent death cause in developed countries, accounts for approximately 80% of sudden cardiac death cases (10). In 20% of patients sudden death is the first and only symptom of the disease. The factors increasing the risk of SCD include all manner of factors that influence the development of ischemic heart disease, such as: overweight, tobacco smoking, being male, hypertension, diabetes, lipid disorders (primarily including inappropriate LDL level) as well as stress. The essential cause of SCD is coronary atheromatosis. The post-mortem examinations of patients with diagnosed sudden cardiac death performed in 1974 by Lieberthson showed that the most frequent changes in coronary vessels included: critical vascular stenosis (94%), 3-vessel disease (60%), atheromatous rupture (56%). In 1984, on the basis of the analysis of vascular changes autopsy

in 100 individuals subjected to autopsy, Davies and co-workers recognized atheromatous injuries in 95%, and intravascular thrombus in 74% of cases (4). On the basis of the 24-hour ECG reports made by Holter test, it was found that the patients whose sudden cardiac death occurred during the test died due to ventricular tachycardia deteriorating to ventricular fibrillation or due to primary ventricular fibrillation, i.e. not preceded by ventricular tachycardia. It was found that the most frequent mechanism to release arrhythmia is re-entry mechanism. During electrophysiology tests performed in patients who have survived sudden cardiac arrest ventricular tachycardia is frequently provoked, which confirms the presence of the substrate that triggers arrhythmia. The mere presence of the substrate is not sufficient for the occurrence of life-threatening heart rate disorders. The factors that modify the substrate include mainly: ischemia (ischemia-related biochemical disorders), impaired left ventricular contractility (the presence of the healed infarct, particularly cardiac aneurysm, but also functional disorders occurring in recent ischemia) as well as electric instability of the heart (among others, stimulated by an increased catecholamine excretion). The risk group especially threatened with SCD is constituted by patients with recent myocardial infarction. The negative risk factors in this patient group include: reduced ejection fraction (EF<35%), diagnosed cases of non-sustained ventricular tachycardia (nsVT) as well as reduced sinus rhythm variability. SCD prevention in ischemic patients is based on the application of non-electrophysiological drugs such as: (β-blockers, ACE inhibitors, aldosterone antagonists, cholesterol-reducing drugs, antiplatelet drugs). Out of antiarrhythmic drugs, amiodarone should be put first especially for the patients with prior myocardial infarction and sustained ventricular tachycardia. The patients with a history of myocardial infarction, with EF < 40%, diagnosed nsVT and ventricular tachycardia induced in an electrophysiology test are recommended to undergo the prophylactic implantation of cardioverter defibrillator (ICD) as part of primary prevention. The ICD implantation as secondary prevention is also recommended in people who have survived SCD.

Sudden cardiac death represents a basic clinical problem in hypertrophic cardiomyopathy (HCM) – a disease which is most frequently characterised by cardiac hypertrophy (mainly left ventricular hypertrophy) without the increase of the heart chambers. The research available shows that annual mortality rate for this disease reaches 1–6% (8). Sudden cardiac death is the initial symptom of the disease in 20% and more frequently affects people at the age of 10–35 (4–6% per year) than people over 40 years old (1–2%). The deaths in the age range from 10 to 35 account for 80% of the total of sudden deaths in HCM. SCD in this group affects patients with no previously observed symptoms and no prior diagnosis of the disease. The majority of these accidents (60%) occur as a consequence of minor or moderate physical effort, while in 40% the triggering factor is hard physical effort.

It seems that hypertrophic cardiomyopathy is the most frequent cause of sudden deaths in young people practising sports. The risk factors of sudden death include: family history, mutation in the genes that encode the beta myosin heavy chain or T troponin, increased mass or thickness of the left ventricular walls, obstruction of the left ventricular outflow tract and diagnosed nsVT in a Holter test. The factor that is prognostically poor is arrhythmia during physical effort. The other factors of that kind include ventricular rhythm disorders, syncope cases and cardiac arrest (33% of patients with these factors die within the following year) as well as inadequate height or an RR reduction during physical effort. The SCD prevention includes pharmacological treatment e.g. amiodarone, β-blockers, calcium blockers, septal ablation, electrostimulation and surgical treatment as well as ICD implantation. The indication for ICD implantation in secondary prevention is medical history of SCD, while in primary prevention – the presence of at least two risk factors (family history of SCD, syncopes, nsVT, interventricular septum thickness > 3 cm, effort-related hypotension).

Dilated cardiomyopathy (DCM) is a disease characterised by enlargement of the heart chambers with a general impairment of contractility and reduced heart muscle mass. It accounts for 5–10% of the total number of cases of the sudden cardiac death, at the same time sudden cardiac death accounting for 30% of the total deaths in patients diagnosed with DCM (1). SCD rarely occurs as an initial symptom of the disease (approx. 3%). The major cause of sudden cardiac death are malignant ventricular arrhythmias that account for 60–80% of deaths (ventricular fibrillation, sustained ventricular tachycardia deteriorating to ventricular fibrillation). The remaining 20–40% of sudden deaths develop as a mechanism of electromechanical dissociation or acquired complete atrioventricular block. Ventricular tachycardia (VT) deteriorating to ventricular fibrillation (VF) was observed in 62% of DCM deaths, while in 13% the sudden death was preceded by polymorphous ventricular tachycardia (TdP) or primary ventricular fibrillation and in 17% SCD resulted from bradyarrhythmia. Bradyarrhythmia and electromechanical dissemination account for 50% of cases of sudden cardiac death in the group of patients with an advanced level of heart failure. The major risk factors of sudden cardiac death include: reduced ejection fraction, increased end-diastolic left ventricular dimension, presence of nsVT, syncopes, ventricular arrhythmia (polymorphous premature ventricular complex, pairs). The incidence of nsVT is considered the best single indicator of risk, while the left ventricular ejection fraction is believed to be the best indicator of predicting total mortality. Patients with dilated cardiomyopathy are administered pharmacological treatment in primary prevention (among others, β-blockers, amiodarone) and ICD implantations in high risk patients (low EF, nsVT, syncopes). In primary prevention ICD implantation is optional (with possible dual-chamber stimulation in case of asynchrony of ventricular contraction).

Arrhythmogenic right ventricular dysplasia, a primary heart disease characterised by the replacement of the myocytes of the cardiac muscular tissue with fat or connective tissues, accounts for 12.5–25% of cases of sudden cardiac death, especially in people under the age of 40 (3). SCD occurs as the initial symptom of the disease in 7–12% of patients. Three mechanisms of rhythm disorder development were described which may result in sudden death in this disease. The first one is based on the replacement of proper muscular tissue cells with connective or fat tissue, which leads to the creation of heart areas that are electrically unstable. The second mechanism is connected with the phenomenon of oversensitivity to catecholamines (frequent occurrence of rhythm disorders caused by stress or effort), while the third one is concerned with an inappropriate activity of ion channels which results in ventricular repolarization disorders. The risk factors of SCD among patients have not been determined precisely, but left ventricular obstruction, reported sVT history, reduced EF <40% and left ventricular dilation are mentioned among others. The treatment involves ICD implantation both in case of multiple risk factors and in secondary prevention. Sotalol, amiodarone and β-blockers are applied in primary prevention.

Long QT syndrome (LQTs) is characterised by excessive QT intervals (QTc > 460 ms) in the standard electrocardiogram with the tendency to ventricular tachycardia which may lead to syncopes, loss of consciousness or sudden cardiac death. Inborn and acquired forms of the disease are known. The occurrence of polymorphous ventricular tachycardia (TdP) deteriorating to ventricular fibrillation represents a major SCD mechanism in LQTs patients. Bradycardia and compensatory interval following an additional stimulation consititute the TdP triggering factors. The mortality rate in LQTs is approximately 1–2% per year. The patients with subclass III and the length QTc >500 ms are the most threatened with SCD. A higher incidence of TdP was observed during morning hours, in adult women and male minors. Further risk factors include: history of loss of consciousness, inefficient β-blocker treatment, history of sudden cardiac arrest, family history of sudden deaths, bradycardia tendency. The treatment involves, among others, large doses of β-blockers, left sympathetic cardio

denervation (LSCD), heart pacermaker implantation (in patients treated with maximum doses of β-blockers and significant tendency to bradycardia) as well as ICD implantation (secondary prevention following the SCD and primary prevention in patients resistant to the administered treatment or with threatening family history).

The acquired QT syndrome may result from pharmacotherapy (certain antiarrhythmic, antihistamine drugs, antibiotics, Ca-blockers, psychotropic drugs), electrolyte disorders, hypothermia, injuries of the central nervous system, *anorexia nervosa*.

Another cause of SCD is the Brugada syndrome (BrS) – a disease characterised by occurring sudden cardiac deaths (considerably more frequent in male population) and fainting in the mechanism of polymorphous ventricular tachycardia or ventricular fibrillation with a co-existing ECG image involving right bundle branch block and elevation of ST section in V1-V3 leads. According to the type of changes in ECG there are three kinds of the disease. The Brugada syndrome is described as an electric heart disease as in most cases no organic changes in cardiac structures are found in post-mortem autopsy (11). The Brugada syndrome is considered the second most frequent cause of death of young men with no organic heart disease following road accidents. According to the available studies it is estimated that the Brugada syndrome is the cause of 4–12% of sudden deaths and 20–50% of sudden deaths in patients with no organic heart disease (12). In the group of patients with idiopathic ventricular fibrillation the connection with the Brugada syndrome was recognised in 3–24%. Sudden death occurs usually at rest and at night. Brugada showed that patients with history of cardiac arrest are threatened with the 69% risk of SCD recurrence, while the risk of people with diagnosed syncopes and ECG changes class 1 is estimated at 19% (2). The patients with the Brugada syndrome can be classified as symptomatic (diagnosed ST changes, history of TPV or VF, syncopes) and asymptomatic (mere ECG changes). We can also distinguish a group of patients with the latent Brugada syndrome whose electrocardiographic changes are only revealed having been provoked by calcium blockers (ajmaline, prokainamide, flecainide).

The group of patients with high risk of sudden cardiac death involves patients with class 1 ECG changes, male population (SCD risk 5.5 times higher than in female population), patients with induction of ventricular arrhythmia at an electrophysiology test (SCD risk 8 times as high), history of syncopes, cases of ventricular fibrillation and ventricular tachycardia.

The average incidence of sudden cardiac death in total population was calculated on the basis of the available studies according to the pattern 1/1000/year. Population prevention would be connected with the necessity of its application in 999 people in order to prevent one such case. With regard to this fact, out of the total population the high risk group was distinguished including, among others, ischemic patients, patients with hypertrophic and dilated cardiomyopathy. The prophylaxis in patients is based on pharmacotherapy, while in a small group of significantly high risk (e.g. patients with prior cardiac arrest) ICD implantation is applied as an option. In case of ischemic heart disease, which is the most frequent cause of SCD, the broadly understood prevention involves all manner of actions that reduce the chance of the disease occurrence, such as promotion of physical activity, anti-smoking campaign and cholesterol level control.

The most efficient drug in SCD prevention among antiarrhythmic medicines is amiodarone, which belongs to class III of the Vaughan Williams classification. The BASIS study showed a considerable reduction in mortality rate of patients with prior myocardial infarction with complex ventricular rhythm disorders as compared with the placebo-controlled group (5% vs 13%). In the GESICA study amiodarone contributed to the 28% mortality reduction in patients with congestive heart failure, while in the CASCADE study a considerable mortality reduction was observed in patients with a history of cardiac arrest taking amiodarone as compared with the group treated with

class I antiarrhythmic drugs. The other important studies that indicate the efficiency of amiodarone therapy in patients with myocardial infarction include: CAMIAT (18% reduction of total mortality, 38% reduction of VF incidence), EMIAT (32% reduction of arrhythmic death incidence).

The factor of great significance in the prevention of sudden cardiac death is β-blockers, especially in the population of patients with ischemic heart disease. The analysis of the available studies evaluating β-blocker application in patients after myocardial infarction showed the reduction of total mortality rate by 20%, and the incidence of sudden cardiac death reduced by 30% as compared with the placebo-controlled group (Conolly, 1999).

Another analysis of the influence of β-blocker intake on the reduction in SCD incidence involving 31 studies showed that in 13 of them the reduction was estimated at 51% vs 43% in a β-blocker-free group (Bhargava, 2004). The CAPRICORN study indicated the reduction in SCD incidence in patients with prior myocardial infarction, left ventricular failure taking carvedilol as compared with the placebo-controlled group (12% vs 15%). The reduction in mortality rate was also shown (PAMI, stent-PAMI, CADILLAC studies) in the group taking β-blockers before the coronary angioplastic surgery. The COPERNICUS study carried out among 2289 patients with chronic heart failure, EF < 25% indicated 35% reduction in the risk of sudden death in the group of patients treated with carvedilol as compared with the placebo-controlled group.

In patients with congestive heart failure, 45% reduction in SCD incidence was shown in the group controlled by standard treatment (ACE inhibitor, digitalization, diuretic drugs), CR metoprolol (MERIT-HF study) (5). The CIBIS II study indicated 42% reduction in sudden cardiac death incidence in patients with ischemic cardiomyopathy taking bisoprolol (7).

Other drugs that reduce the risk of sudden cardiac death include: Angiotensin-converting Enzyme inhibitors (ACE-I). Their administration in the group of patients with a moderate or advanced heart failure results in 30–54% reduction in SCD incidence (Bhargava, 2004). Patients after myocardial infarction also benefit from ACE-I use. In the EUROPA study it was proved that perindopril had a positive influence on the incidence of sudden deaths as compared with the placebo-controlled patients after infarction.

The RALES study indicated a positive influence of aldosterone blockers (spironolactone) on the reduction of mortality in the group of patients with chronic heart failure taking diuretic drugs, ACE-I and digoxin (9). The following studies: 4S, CARE and LIPID indicated a positive impact of statin on the reduction in mortality rate of patients after myocardial infarction.

Pharmacological treatment can significantly reduce the risk of the occurrence of sudden cardiac death. However, at the moment of cardiac arrest (most frequently in the mechanism, of VF) the only efficient way to rescue an individual is to terminate ventricular arrhythmia. In the group of patients with a history of sudden cardiac arrest or belonging to the group of high risk of SCD, the most efficient way to secure patients' chances of survival is ICD implantation (especially given that 40% of cases of cardiac arrest occur unwitnessed). The results of the studies published indicate the purposefulness of such a procedure. For example, the CIDS study (ICD vs amiodarone) showed that the survival rate in the ICD group is increased by 19.6%, in the MADIT study – by 46%, and in the MADIT II study – by 31%.

The immediate initiation of rescue actions is a highly significant factor that conditions the chances of survival of people with sudden cardiac arrest. Taking such actions by accident witnesses considerably increases the chance of survival. Basic Life Support procedures involve resuscitation actions according to an ABC scheme: clearing the airways, breathing check for approximately 10 seconds and giving two rescue breaths in case of respiratory arrest, checking the pulse in arteries or assessment of circulation signs such as: movement, cough or respiration. In case of cardiac arrest,

an external heart massage is commenced (100 pushes per min) and artificial respiration with the proportion of 15 bridge pressures to 2 breaths (in children under 7, the proportion should be 5:1). If there is an opportunity to use an automated external defibrillator (AED), it should be a priority (6).

The American experience proves the high efiiciency of the use of automated external defibrillators by witnesses of sudden cardiac arrest. AED is a device that enables to recognise automatically and differentiate between dangerous arrhythmias. The role of AED operator is merely limited to starting the device and acting according to the guidelines offered by the device. The study using automated external defibrillators at Chicago airports confirmed their high efficiency even among people who had not been previously trained in their operation. Another study carried out in the USA – Public Access Defibrillation Trial (PAD), showed that the efficiency of AED rises in the group of rescuers who have done additional trainings in the operation of automated external defibrillators in addition to the the Cardio-Pulmonary Resuscitation (CPR) trainings which are common in the United States.

The most frequent mechanism of sudden cardiac arrest is ventricular fibrillation (75–80%), whose occurrence requires immediate defibrillation (in case of an inefficient initial shock of 200 J, the subsequent 300 and 600 J or a respective biphasic shock of 150 J is applied). Given that defibrillation is performed within the initial three minutes following cardiac arrest, the chance of survival equals 74%. If defibrillation is impossible to perform or the first three shocks are inefficient, external heart massage and supplementary ventilation are supposed to be administered along with pharmacotherapy (adrenaline, amiodarone, liodcaine, buffer solutions). The attempt to commence defibrillation should be restored every 30–60 seconds.

In case of the diagnosed electromechanical dissemination, the procedure should involve external massage, ventilation and pharmacotherapy (atropine, adrenaline, buffer solutions, in case of recognized cardiac standstill as a primary mechanism of cardiac arrest, the application of external stimulation (Zoll's electrodes) or heart temporary pacing should be considered. Despite proper rescue actions the chance of surviving cardiac arrest in the mechanism of cardiac standstill and electromechanical dissemination does not exceed 5%.

Aside from pharmacotherapy and implantable devices such as ICD, an essential factor to increase the chances of survival of sudden cardiac arrest is broad social education on basic life support and the operation of automated external defibrillators which can more and more frequently be found in public places such as shopping centres or airports. Such actions are particularly important as the vast majority of SCD occur out of hospital, and the time of the arrival of professional emergency services exceeds the period of five minutes, after which irreversible changes are made due to cerebral anoxia. The appropriate resuscitation actions taken by witnesses can determine the survival of people with sudden cardiac arrest.

REFERENCES

1. Antezano E. S.: Sudden cardiac death. J. Intensive Care Med., 18, 313, 2003.
2. Brugada J. et al.: Long term follow-up of individuals with electrocardiographic pattern of right bundle-branch block and ST segment elevation in precordial leads V1-3. Circulation, 105, 73, 2002.
3. Czarnowska E. et al.: Arytmogenna kardiomiopatia (dysplazja) prawej komory. Kard. Pol., 58, 58, 2003.
4. Davies M. J., Tomas A.: Thrombosis and acute coronary artery lesions in sudden cardiac ischemic death. N. Engl. J. Med., 310, 1137, 1984.

5. Domański M. et al.: A comparative analysis of the results from 4 trials of β-blocker therapy for heart failure: BEST, CIBIS-II, MERIT-HF and Copernicus. J. Cardiac. Faliure, 9, 354, 2003.
6. Field J.: Nowe zasady resuscytacji w nagłym zatrzymaniu krążenia: międzynarodowe zalecenia dotyczące resuscytacji i leczenia kardiologicznych stanów nagłych z 2000 r. Curr. Opinion in Kardiol., wyd. polskie, 1, 20, 2003.
7. Leizorovicz A.: Bisoprolol for the treatment of chronic heart failure: a meta-analysis on individual data of two placebo-controlled studies-CIBIS and CIBIS II. Cardiac Insufficiency Bisoprolol Study. Am. Heart J., 2, 143, 2002.
8. Maron B., Fannapazir L.: Sudden cardiac death in hypertrophic cardiomyopathy. Circulation 85, 57, 1992.
9. Pitt B. et al.: The effect of spironolactone on morbidity and mortality in patients with severe heart failure. N. Eng. J. Med., 341, 709, 2003.
10. Priori S. G. et al.: Task force on sudden cardiac death, European Society of Cardiology. Eur. Heart J., 22, 1374, 2001.
11. Remme C. A. et al.: Diagnosis and long term follow-up of the Brugada syndrome in patients with idiopathic ventricular fibrillation. Eur. Heart J., 22, 400, 2001.
12. Zespół Brugadów. Raport z II konferencji uzgodnieniowej przyjęty przez Heart Rhythm Society i European Rhythm Association. Med. Praktyczna, 7–8, 42, 2005.

SUMMARY

The most frequent causes of sudden cardiac death include: ischemic heart disease with infarction, nonischemic structural heart diseases, including hypertrophic cardiomyopathy, congestive cardiomyopathy, arrhythmogenic left ventricular cardiomyopathy. They are followed by non-ischemic and non-structural diseases and severe mechanical conditions. The average incidence of sudden cardiac death in total population was calculated on the basis of the available studies according to the pattern 1/1000/year. Aside from pharmacotherapy and implantable devices such as ICD, an essential factor to increase the chances of survival of sudden cardiac arrest is broad social education on basic life support and the operation of automated external defibrillators which can more and more frequently be found in public places such as shopping centres or airports.

Nagła śmierć sercowa – najczęstsze przyczyny, czynniki ryzyka, zapobieganie populacyjne i indywidualne

Do najczęstszych przyczyn występowania nagłej śmierci sercowej zaliczyć należy: chorobę niedokrwienną serca z zawałem, strukturalne choroby serca bez podłoża niedokrwiennego, w tym kardiomiopatię przerostową, kardiomiopatię zastoinową, arytmogenną kardiomiopatię prawej komory, choroby serca bez podłoża niedokrwiennego i bez zmian strukturalnych oraz ostre przyczyny mechaniczne. Średnią częstość występowania nagłej śmierci sercowej w populacji ogólnej określono na 1/1000/ rok. Oprócz stosowania farmakoterapii i wszczepialnych urządzeń, takich jak ICD, ważnym czynnikiem zwiększenia szansy przeżycia nagłego zatrzymania krążenia jest możliwie najszersza edukacja społeczeństwa w zakresie udzielania podstawowych zabiegów ratujących życie oraz obsługi automatycznych defibrylatorów, które coraz częściej znajdują się w dużych skupiskach ludzkich, jak centra handlowe czy lotniska.