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CONTEMPORARY APPROACHES IN PREVENTION OF SUDDEN CARDIAC DEATH

Tomislav Kostić[1,2], Marina Deljanin-Ilić[2,3], Dragana Stanojević[1], Dragan Milić[4,5], Goran Koraćević[1,2], Svetlana Apostolović[1,2], Zoran Perišić[1,2], Sonja Šalinger-Martinović[1,2], Miodrag Djordjević[5,7], Mladjan Golubović[4,5], Milan Lazarević[4,6]

Sudden cardiac arrest and sudden cardiac death (SCD) are terms that are often used in medicine as synonyms. Sudden cardiac death is defined as "natural, unexpected cardiac death that occurs within one hour of the onset of acute symptoms and is accompanied by a sudden loss of consciousness." The presence of heart disease may be known from before, but the timing and manner of death are unexpected. Coronary artery disease (CAD) is responsible for 75-80% of all SCD. While atherosclerosis is a primary disease in middle-aged and elderly people, in children and young adults (< 35 years), malignant arrhythmias that occur in the cardiac ventricles - monomorphic or polymorphic ventricular tachycardia, and ventricular fibrillation are the most common cause of SCD. The etiology of heart rhythm disorders may be associated with underlying heart disease, but it is most commonly idiopathic in young people. A number of studies have confirmed that malignant arrhythmias are the immediate cause of death. The etiology of cardiac arrhythmias may be related to underlying heart disease, but it may also be idiopathic. Secondary prevention of sudden cardiac death involves the treatment of those who have been fortunate to survive sudden cardiac arrest or have documented hemodynamically unstable ventricular arrhythmias, and the primary prevention is the treatment of those who are at increased risk of sudden cardiac death but without documented prior cardiac arrest or malignant ventricular arrhythmias. Given that the most common arrhythmia preceding cardiac arrest is ventricular tachycardia (VT) that degenerates into ventricular fibrillation (VF), prevention of sudden cardiac death involves effective interruption of ventricular tachycardia (VT). Based on the results of studies and clinical data, it can be concluded that implantation of ICD significantly reduces mortality in both primary and secondary prevention compared to patients who received medication alone. Also, patients who have a pacemaker system in addition to defibrillator therapy and resynchronization therapy have significantly better quality of life, increased left ventricle ejection fraction, and better echocardiographic parameters. Also, the administration of drug therapy in patients with implanted pacemakers reduces the frequency of DC shock delivery, thereby preserving myocardial function and reducing the damage that occurs when current passes through the heart muscle. Implantable cardioverter defibrillators have brought a new chapter in the treatment of the very high risk cardiovascular patients.

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[1]Clinic of Cardiovascular Diseases, Clinical Center Niš, Niš, Serbia
[2]University of Niš, Faculty of Medicine, Department of Internal Medicine, Niš, Serbia
[3]Institute for Rehabilitation and Prevention of Cardiovascular Diseases "Niška Banja", Serbia
[4]Clinic of Cardiothoracic Surgery, Clinical Center Niš, Serbia
[5]University of Niš, Faculty of Medicine, Department of Surgery, Anesthesiology and Reanimatology
[6]University of Niš, Faculty of Medicine, Department of Microbiology and Immunology, Niš, Serbia
[7]Clinic of General Surgery, Clinical Center Niš, Niš, Serbia

Contact: Tomislav Kostić
48 Dr. Zoran Djindjić Blvd., 18000 Niš, Serbia
E-mail: tomislav.kostic1977@gmail.com

Introduction

Sudden cardiac arrest and sudden cardiac death are terms that are very often used in medicine as synonyms. However, the definitions of these two terms are fundamentally different.

Sudden cardiac arrest is defined as "a sudden cessation of cardiac activity due to which the patient becomes unresponsive to external stimuli, normal respiratory function ceases and signs of circulation such as pulse activity are absent." If resuscitation measures are not taken quickly, this condition progresses to sudden cardiac death.

Sudden cardiac death is defined as "natural, unexpected death due to cardiac causes that occurs within one hour of the onset of acute symptoms and is accompanied by sudden loss of consciousness." The presence of heart disease may be known from before, but the time and manner of death are unexpected.

Unexplained sudden cardiac death that occurs in individuals aged > 1 year is known as "unexplained sudden cardiac death syndrome", while in individuals aged < 1 year this phenomenon is referred to as "sudden, unexplained death in childhood" (1).

Sudden cardiac death accompanied by negative pathological and toxicological findings is referred to as "sudden cardiac death syndrome due to arrhythmia".

The etiology of sudden cardiac death (SCD) can be:

- ischemic,
- nonischemic and
- non-cardiac.

Coronary heart disease (CHD) is responsible for 75–80% of all SCD cases. While atherosclerosis is the primary disorder in middle-aged and elderly people, children and young people (< 35 years), the cause of SCD is most often malignant arrhythmias that occur in the heart chambers - monomorphic or polymorphic ventricular tachycardia and ventricular fibrillation. The etiology of heart rhythm disorders may be related to the underlying heart disease, but in young people it is most often idiopathic. Also, in addition to malignant arrhythmias, the cause of SCD in young people can be anomalies of the coronary arteries, especially the anomalous origin of the left coronary artery from the pulmonary artery or from the right coronary sinus. In addition to the above causes, it is interesting to note the fact that recent studies have proven a link between air pollution (fine particles with an aerodynamic diameter < 2.5 μm and ozone) and outpatient cardiac arrest (1, 2).

Possible causes of SCD

◇ Myocardial infarction (including myocardial infarction without ST elevation)

◇ Coronary artery abnormalities

◇ Coronary spasm (especially in male smokers without previous KB or with minimal KB)

◇ Prolonged QT syndrome - can be inherited (usually caused by congenital ion channel defects) or acquired (caused by drugs that block the sodium channel known as hERG)

◇ Shortened QT interval syndrome

◇ Brugada syndrome

◇ Early repolarization syndrome

◇ Catecholamine polymorphic ventricular tachycardia

◇ Cardiomyopathies, heart failure, valvular disease, congenital heart defects

◇ Risk factors for SCD largely coincide with risk factors for coronary heart disease, which especially refers to:

- age,
- male gender,
- positive family history of coronary heart disease,
- elevated LDL cholesterol levels,
- hypertension,
- smoking and
- diabetes.

There are also studies that indicate specific risk factors such as:

- Increased heart rate - an independent risk factor for SCD regardless of whether there is heart disease or not. The basis of this connection is not completely clear, but a decreased parasympathetic activity is possible.• excessive alcohol consumption
- electrocardiographic changes in the ST segment and T wave (depression and inversion of the T wave) - may be a risk factor for SCD in patients in whom angina pectoris has not been verified. The corrected QT time > 420 msec in the longer period can be a predictor of SCD, while in the shorter period the predictors of SCD occurrence can manifest as a dispersion of the QT interval, as well as higher amplitudes in the change of T waves amplitudes.
- genetic and hereditary diseases (Brugada syndrome, QT anomaly, adrenergic polymorphic VT) - indicate the importance of family history and genetic testing in the prevention of SCD.
- condition after myocardial infarction - in high-risk patients after myocardial infarction according to various studies (EMIAT, CAMIAT, TRACE, SWORD, DIAMOND-MI) the cumulative incidence of arrhythmic mortality reaches 5% after one year and 9% at the end of the second year, while the incidence of nonarrhythmic cardiac deaths were 4% and 7%, respectively, in the same follow-up period. It is interesting that with the introduction of thrombolytic therapy, the relationship between arrhythmic and non-arrhythmic death did not change significantly.
- Left ventricle ejection fraction (LVEF) - is the most important prognostic parameter in the implementation of primary and secondary prevention of SCD. The value of LVEF ≤ 40% is the most important predictor of SCD. In cases where the LVEF is 10-15%, sudden death is not the most common and is then associated with bardiarrhythmias or electromechanical dissociation rather than ventricular tachyarrhythmias.
- clinically registered VT as well as patients who have already been successfully resuscitated (3, 4).

The joined mechanism of SCD developement, which may be caused by various etiological factors, includes marked activation of the sympathetic nervous system and massive release of catecholamines during the stress response. One of the effects of prolonged catecholamine increase involves the activation of α- and β-adrenoceptors. Activation of β-adrenoreceptors is thought to play a crucial role in the development of SCD. Activation of the stimulatory regulatory G protein (Gs protein - one of the five main components involved in the cyclic AMP (cAMP) signaling pathway) associated with β-adrenoreceptors leads to the activation of adenylyl

cyclase which catalyzes the formation of cAMP from ATP. The formation of cAMP leads to the activation of protein kinase A, which subsequently induces the phosphorylation of voltage-gated L-type calcium channels. Phosphorylation of these channels leads to a significant increase in the influx of Ca_2^+ into cardiomyocytes during cardiac action potential, which further triggers the release of Ca_2^+ from the sarcoplasmic reticulum via the rianodin receptor. This calcium alteration is known to induce ventricular arrhythmias that are often associated with SCD. In addition to the harmful cascade that affects β-adrenoreceptors, it is thought that α-adrenoreceptors may play a significant role in vascular remodeling, proliferation, and hypertrophy during stress responses. Stimulation of α-adrenoreceptors with increased concentration of catecholamines also causes negative effects on coronary arteries.

Prolonged exposure to high levels of circulating catecholamines results in coronary spasm causing myocardial ischemia, which may contribute to the occurrence of etiological factors leading to SCD. Ischemia associated with coronary spasm can also cause aortic pressure reduction and dilatation of arterio-venous shunts leading to multidimensional hypoxia. The detrimental effects of elevated catecholamine levels and their role in the pathogenesis of SCD are further potentiated when these molecules are susceptible to autooxidation. Catecholamine oxidation products lead to the generation of aminochromes that have been shown to have a detrimental effect on cardiomyocytes. The formation of these end products of catecholamine oxidation directly correlates with the increase of superoxide anions and subsequently formed hydrogen peroxide, which is known to cause DNA degradation, protein denaturation and lipid damage, thus increasing the risk of SCD at the molecular level. During the mentioned response to stress, an increased incidence of platelet aggregation and atherosclerotic plaque formation was also noted, which further increases the risk for SCD. Elevated levels of circulating catecholamines have been shown to increase platelet aggregation, resulting in an increased risk of developing coronary artery occlusion leading to myocardial infarction. These conclusions led to the formation of a unique theory for stress-induced SCD that brings together several different etiologies into a single molecular phenomenon (1, 4, 6).

It should also be noted that increased oxidative stress is often associated with vascular endothelial damage. It is known that the endothelium is intimately associated with the regulation of vascular tone, platelet activity, leukocyte adhesion and thrombosis. Damage to this inner lining of the vascular bed can cause serious consequences of various etiologies. In particular, a prolonged response to stress may result in excessive release of endothelin-1 from the endothelium, which may lead to an increased risk for SCD. Endothelin-1 is normally responsible for vasoconstriction and is thought to be in complex equilibrium with vasodilators such as nitrogen monoxide (NO). When this balance is disturbed by excess endothelin-1, patients often suffer from vasospasm, which leads to tissue ischemia and possible necrosis. This imbalance is further complicated by the detrimental effects of oxidative stress leading to endothelial damage and impaired NO release. This disorder may be directly related to the increased risk of SCD through the development of coronary artery disease (3-5).

Diagnosis and screening of patients at risk of SCD

Regarding the diagnosis or screening patients at increased risk for SCD, an ECG, as one of the basic, non-invasive diagnostic procedures, can be helpful. Since many diseases have, as an accompanying manifestation, the disturbance of the electrical conductivity of the heart, this diagnostic method can enable a quick insight into the existing abnormalities and its' progression. It has been noted that 95% of patients who have a high risk of SCD exhibit abnormalities on the ECG. However, ECG findings are very often not specific for SCD and require further diagnosis in order to confirm the existence of a risk factor.

ECG testing can provide insight into the etiology that potentially classifies a patient into a group of people at risk for developing SCD. Arrhythmogenic dyspalsa of the right ventricle is classically manifested by inverted T waves in the middle precordial leads, dilated or fragmented QRS complexes, as well as abnormal complexes on the S wave in the right leads. Patients with evidence of arrhythmogenic right ventricular dysplasia are further examined to assess the possible presence of comorbidities and the potential risk for SCD. In contrast to right ventricular arrhythmogenic dysplasia, congenital coronary artery disease does not normally present with any specific changes on the ECG. In addition, any arrhythmias that occur as a secondary manifestation of the underlying disease may provide information of the potential risk for SCD, but require further investigation to be of clinical significance.

Another important non-invasive imaging technique for detecting the risk of developing SCD in patients is echocardiography. The use of echocardiography may be particularly useful in the detection of valvular abnormalities, aortic root dilatation, left ventricular dysfunction, and left ventricular EF assessment. This diagnostic method is ideal for use in patients with hypertrophic and dilated cardiomyopathy, but cannot be used for the purpose of diagnosing conditions such as congenital coronary anomalies. In certain cases, echocardiography may be used to establish the suspicion of an abnormal origin of the coronary arteries, but it is usually often necessary to conduct further screening to obtain an accurate diagnosis. The parameters obtained on echocardiographic examination have low sensitivity in predicting the risk of developing SCD. The presence of scarring and heterogeneity of myocardial tissue have been shown to be directly related to the developement of cardiac arrhythmias, which is a direct cause of SCD.

Cardiac magnetic resonance imaging is also one of the non-invasive imaging techniques that quantifies scarring and is considered to have predictive significance in patients at risk for SCD. This diagnostic method enables the visualization of the myocardial scar using gadolinium amplification, which has been proven to have an extremely strong correlation with the histopathological finding. Magnetic resonance imaging is also characterized by high spatial resolution, which enables the differentiation of different scar patterns and the detection of interstitial fibrosis and edema. In addition, the topographic distribution of late gadolinium enhancement allows the differentiation of different types of cardiomyopathies, which is of great benefit in stratifying the risk of SCD in patients.

The application of invasive diagnostic procedures, such as cardiac catheterization, is of great importance for determining the etiological factor that caused the changes in the coronary blood vessels. The main benefits of cardiac catheterization include evaluating the presence of coronary artery disease, valvular disease, and/or aortic disease. This invasive procedure can also detect the presence of congenital anomalies of the coronary arteries, which can place the patient in a group at risk for developing of SCD. Cardiac catheterization is most often used when there is a clinical suspicion of coronary heart disease after non-invasive diagnostic procedures (1, 5).

Primary and secondary prevention of sudden cardiac death

Sudden cardiac death is one of the greatest health problems of modern man, and its prevention is one of the greatest challenges of modern cardiology. Sudden cardiac death is an extremely big problem in middle and highly developed countries, because its expression is often the first and last at the same time. Four methods are available for primary and secondary prevention of sudden cardiac death:

1. Drug therapy (antiarrhythmics)
2. Surgical methods to reduce left ventricular arrhythmic focus
3. Catheter ablation of arrhythmic focus
4. Implantation of an implantable cardioverter defibrillator (ICD)

Cardioverter defibrillator (ICD) implantation provides the best prevention of sudden cardiac death, both secondary and primary, and there is no alternative in any of the drugs known today, in selected high-risk patients. It is significant that a recent indication for its implantation is a primary prevention of sudden cardiac death. Of special significance nowadays is the development and use of resynchronization therapy and implantable cardioverter defibrillator in the treatment of heart failure (7).

A number of studies have confirmed that malignant arrhythmias are the immediate cause of death. The etiology of heart rhythm disorders may be related to the underlying heart disease, but it can also be idiopathic. Secondary prevention of sudden cardiac death involves treating those who are lucky enough to survive sudden cardiac arrest or have documented hemodynamically unstable ventricular arrhythmias, and primary prevention involves treating those who are at increased risk for sudden cardiac death but without documented previous cardiac arrest or malignant ventricular arrhythmias. Since the most common arrhythmia that precedes cardiac arrest is ventricular tachycardia (VT), which degenerates into ventricular fibrillation (VF), prevention of sudden cardiac death involves effective cessation of ventricular tachycardia (VT). Large multicenter studies in the 1990s demonstrated the ineffectiveness of antiarrhythmics, including amiodarone in the prevention of sudden cardiac death in those patients in whom VT/VF could not be prevented by treatment of underlying heart disease, and showed significantly better survival in patients treated with implantable CD cardioverter defibrillators (8, 9).

Ventricular fibrillation (VF) and ventricular tachycardia (VT) are the most common causes of sudden cardiac death in the first hours after AIM. They usually occur during the first hour or the first 24 hours. In the last 40 years, with the organization of coronary units, hospital mortality has decreased from 30% to 10-15%, primarily due to the prevention and treatment of arrhythmias and conduction disorders. Ventricular tachycardia may present as nonsustained (lasting 30s) or sustained VT (lasting > 30s). They can often be accompanied by syncope, which depends primarily on the hemodynamic situation in the AIM. Ventricular fibrillation (VF) is most common in the first hour after the infarction, and then the frequency decreases during the first 24-48 hours. Up to 80% of all VF in AIM occur in the first 4 hours. Epidemiological data show that the frequency of primary fibrillation is significantly reduced, most likely due to the correction of electrolyte disorders, due to therapeutic measures that reduce the size of the infarction, as well as due to the early use of B blockers. Unlike VF caused by myocardial ischemia, which is most common in the first hours, VF caused by major necrosis, severe heart failure, left ventricular aneurysm, and other severe AIM complications occurs later, after 48 h (secondary fibrillation) and has a poor prognosis (5).

Implantable cardioverter defibrillators (ICDs) are devices that are designed primarily to conduct therapy for treatment of heart rhythm disorders. In 1980, in cooperation with engineers, Mirowski began the realization of the project of creating an implantable device whose task was to recognize and stop heart rhythm disorders leading to sudden cardiac death. In the period from 1980 to 1985, the device was called the Automatic Implantable Defibrillator, and in 1985 its use was approved by the FDA. In Serbia, the first such device was implanted by Prof. Dr. Milan Bane Djordjevic in 1986 at the Clinical Center of Serbia. Today, modern ICD devices are similar in appearance and function to standard bradycardia pacemakers. They use a lithium-vanadium battery due to the reliability of the energy source

and the need to transfer a larger amount of energy in a short period of time (10, 11).

Earlier defibrillators had epicardial patch electrodes, which made necessary to perform the operation with a thoracotomy approach, until today when the placement of the electrode is performed endovenously, practically the same as with standard antibradycardial pacemakers. Detection of heart rhythm disorders is a specific and basic function of the ICD. This detection is based on heart rate, frequency, but requires individual programming, practically for each patient. Detection criteria in ICD have evolved at least as much as therapeutic ones. Initially, the only detection criterion was the number of detected R-R intervals, and to date, detection algorithms have been perfected to prevent maldetection of VT, VF, false detection of VT/VF instead of atrial arrhythmias or sinus tachycardia. Different manufacturers offer different discriminatory criteria, but all have retained the R-R interval stability criterion. Another discriminatory criterion used by all companies is the analysis of the beginning of fast R-R intervals (onset) which avoids false detection of VT in the case of sinus tachycardia. Additional criteria have been introduced with the aim of even better discrimination of VT/VF, such as the criterion of QRS complex width, intrinsic QRS pattern (template) and automatic analysis of P-QRS ratio (PR logic). The greatest advancement in the technological sense was the introduction of gradual tiered therapy, which means that the detected VT is treated with the least aggressive therapy, antitachycardia burst stimulation of different duration of V-V stimulus. After a series of more aggressive ATP options, synchronous cardioversion with a lower current is applied, and finally defibrillation with a maximum current (30-40J). In the case of VF, the maximum strength of the DC shock is applied immediately, with the possibility of changing the polarity (15, 16).

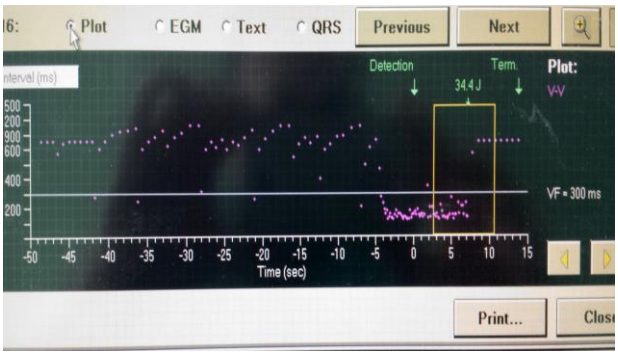

Figure 1. Intracardiac ECG of the ICD, with HF detection and successful therapy

Indications for implantation and therapy with implantable cardioverter defibrillator

Class I

- In patients who have survived cardiac arrest due to VF or haemodynamically threatening VT, and that it is possible to exclude causes resulting from reversible conditions (A)
- In patients with structural heart disease and spontaneous VT (B)
- In patients with obscure syncope with electrophysiologically induced VT or VF (B)
- In patients with EF < 35%, which is a consequence of AIM and from which at least 40 days have passed, and the patient is in functional NYHA class II or III (A)
- In patients with non-ischemic dilated cardiomyopathy and EF ≤ 35%, NYHA class II or III (B)
- In patients with non-repetitive VT after AIM, EF < 40%, and with the possibility of causing VF or VT in electrophysiological examination (B).

ICD installation can be applied:

Class IIa (C)

- In patients with repetitive VT with normal or approximately normal ventricular function
- In patients with hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia, sarcoidosis of the heart, Chagas' disease, in the syndrome of prolonged QT interval who had syncope or VT
- In patients with Brugada syndrome who had syncope or VT (11, 12).

Primary prevention in patients with structural heart disease and damaged left ventricle and/or symptoms of heart failure is currently one of the greatest challenges in cardiology. Primary prevention of sudden cardiac death refers to patients with structural myocardial disease and damaged left ventricle with decreased EF. Several studies have shown the benefit of an implanted ICD over drug therapy. Namely, with a decrease in EF below 35%, the frequency of malignant arrhythmias is not linear

but exponential, so that the occurrence of these life-threatening arrhythmias is significantly higher below this EF limit. The MADIT study showed a 54% reduction in overall mortality in patients with EF < 35% and implanted ICD due to ischemic heart disease. MUSTT study in patients with reduced EF < 35% showed that in the group of patients with ICD the reduction in mortality due to arrhythmias was 75% and the reduction in overall mortality by 60%. These two studies were the first for primary prevention in high-risk patients. The SCD-HEFT study was designed to show if amiodarone or ICD reduce overall mortality in patients with coronary heart disease or nonischemic cardiomyopathy classified as NYHA class II or III and an EF of less than 35%. Patients were randomized into 3 cohorts:

- 847 with placebo,
- 845 with amiodarone, and
- 829 with ICD.

The main conclusion of the study was that patients with congestive heart failure in class II and III, EF less than 35%, with good optimal drug therapy had mortality in the controlled placebo group of 7.2% per year for 5 years. A simple ICD, programmed only for a detection zone of 188/min, and therapeutically only for maximum DC shock reduces mortality by 23%. Amiodarone when taken for primary prevention does not increase survival and has the same effect on primary prevention as placebo. The MADIT II study examined the prophylactic benefit of ICD in patients with coronary heart disease, EF < 30%, who had at least one myocardial infarction. The study showed an absolute reduction in mortality in the group of patients with ICD compared to the group with conventional therapy.

Patients with ICD had a 31% reduction in mortality compared to the group of patients with conventional therapy. Both groups of patients had equivalent and necessary doses of B blockers, ACE inhibitors, diuretics, digitalis and aspirin. The findings of the MADIT II study showed that in patients with myocardial infarction and left ventricular dysfunction, prophylactic administration of ICD significantly increased survival. The inducibility of VT by NEPS, performed during ICD implantation, was associated with more frequent use of VT therapy and reduced use of VF therapy. In one of the recent studies, Moss et al. have shown that the cumulative probability of appropriate VT/VF ICD therapy was40% in the period of 4 years after implantation, which confirms the benefit of ICD in a longer follow-up period (11, 12).

Special groups of patients prone to developing malignant arrhythmias that particularly benefit from ICD implantation are those with: congenital heart disease, hypertrophic cardiomyopathy, Brugada syndrome, idiopathic VT/VF, left ventricular noncompaction, long and short QT interval syndromes, right ventricular arrhythmogenic dysplasia, infiltrative cardiomyopathies (13, 14).

Secondary prevention is indicated in patients who have survived cardiac arrest or sustained VT. Numerous randomized studies have shown that the use of ICD is associated with a reduction in mortality compared with patients treated with any type of drug therapy.

Since the middle of the last decade of the last century, many studies of secondary prevention of sudden cardiac death have been launched to compare the effects of antiarrhythmics, most commonly amiodarone, with ICD in patients with documented, haemodynamically unstable, recurrent ventricular arrhythmias in survivors. Secondary prevention of sudden cardiac death refers to the prevention in those groups of patients who had life-threatening arrhythmias (VT or VF). The most notable of these are the AVID, CIDS, and CASH studies. In each of the studies, ICDs showed a significant and undoubted improvement in survival compared with antiarrhythmics, from 20% in the CIDS study, more than 38% and 39% in the CASH and AVID study to as much as 73% in the Dutch DUTCH CES study. The AVID study was one of the most significant studies of secondary prevention of sudden cardiac death. The study included 1,016 patients and the results showed that the reduction in mortality in the group of patients with ICD compared to drug therapy was 38% in the first year after implantation compared with the group treated with amiodarone or sotalol. In the second year of follow-up, a reduction in mortality of 26% was found, and in the third 30% in relation to patients treated with antiarrhythmics. After this study, for the first time, it was accepted that ICD significantly increased survival in patients with malignant ventricular arrhythmias, and the attitude about ICD implantation, only if antiarrhythmics proved ineffective, was changed. The CIDS and CASH studies also showed a significant reduction in mortality compared to drug therapy (7, 9, 11).

Conclusion

Based on the results of studies and data from clinical practice, it can be concluded that ICD implantation significantly reduces mortality in both primary and secondary prevention compared to patients who received only drug therapy. Namely, patients with implanted resynchronization therapy pacemaker system, in addition to a defibrillator, have significantly better quality of life, increased LVEF, as well as echocardiographic parameters. Also, the use of drug therapy in patients with implanted pacemakers reduces the frequency of DC shock delivery, which preserves myocardial function and reduces the damage that occurs when current passes through the heart muscle. Implantable cardioverter defibrillators have opened a new chapter in the treatment of the cardiovascular patients at the highest risk.

References

1. Earley A, Persson R, Garlitski AC, Balk EM, Uhlig K. Effectiveness of implantable cardioverter defibrillators for primary prevention of sudden cardiac death in subgroups a systematic review. Ann Intern Med 2014; 160(2):111-21. [CrossRef] [PubMed]
2. Rahmawati A, Chishaki A, Ohkusa T, Sawatari H, Tsuchihashi-Makaya M, Ohtsuka Y, et al. Influence of primary and secondary prevention indications on anxiety about the implantable cardioverter-defibrillator. Journal of Arrhythmia 2016;32(2):102-7. [CrossRef] [PubMed]
3. Schaer B, Kühne M, Reichlin T, Osswald S, Sticherling C. Incidence of and predictors for appropriate implantable cardioverter-defibrillator therapy in patients with a secondary preventive implantable cardioverter-defibrillator indication. Europace 2016;18(2):227-31. [CrossRef] [PubMed]
4. Lee DS, Hardy J, Yee R, Healey JS, Birnie D, Simpson CS, et al. Clinical Risk Stratification for Primary Prevention Implantable Cardioverter Defibrillators. Circulation Heart Failure 2015;8(5):927-37. [CrossRef] [PubMed]
5. Milašinovic G. Implantabilni kardioverter defibrilatori. In: Ostojić M, Kanjuh V, Beleslin B, editors. Kardiologija. Beograd: Zavod za Udzbenike; 2011.
6. Kostić T, Deljanin Ilić M, Perišić Z, Milić D, Đorđević M, Golubović M, et al. Design and development of novel therapeutics for coronary heart disease treatment based on cholesteryl ester transfer protein inhibition - *in silico* approach. J Biomol Struct Dyn 2019;19:1-10.
7. Kostić T, Stanojević D, Gudelj O, Milic D, Putnik S, Perisic Z, et al. Implantable cardioverter defibrillator-powerful weapon in primary and secondary prevention of sudden cardiac death. Vojnosanit Pregl 2019;76 (10):1007-13. [CrossRef]
8. Kostić T, Momčilović S, Perišić ZD, Apostolović SR, Cvetković J, Jovanović A, et al. Manifestations of Lyme carditis. Int J Cardiol 2017;232:24-32. [CrossRef] [PubMed]
9. Kostić T, Perišić Z, Koraćević G, Stanojević D, Milić D, Vladimir Mitov V, et al. Resynchronization therapy in patients with heart failure. Acta medica medianae 2013;52(2):10-4. [CrossRef]
10. Watkins L JR, Guarnieri T, Griffith LS. Implantation of the automatic implantable cardioverter defibrillator. J Card Surg 1998;3:1-7. [CrossRef] [PubMed]
11. Moss AJ. MADIT II and its implications. Eur Heart J 2003;24:16-18. [CrossRef]
12. Mond HG, Proclemer A. The 11th world survey of cardiac pacing and implantable cardioverter-defibrillators: calendar year 2009-a World Society of Arrhythmia's project. Pacing Clin Electrophysiol 2011;34: 1013-27. [CrossRef] [PubMed]
13. Kostić T, Perišić Z, Ilić S, Stanojevic D, Koracevic G, Djindjic B, et al, Implantation of an ICD and DFT testing in patient with persistens left superior vena cava. Russ J Cardiol 2015;4(120):38-40. [CrossRef]
14. Kostić T, Perišić Z, Stojković A, Stanojevic D, Djindjic B, Koracevic G, et al. Oversensing as a cause of inappropriate implantable cardioverter defibrillator therapy-case report. Acta medica medianae 2013; 52(4):44-7. [CrossRef]
15. Kostić T, Perišić Z, Djidjić B, Koracevic G, Zivkovic M, Stojkovic A, et al. Clinical opinion: Brugada syndrome and sick sinus syndrome-case which we meet in our practice. Russ J Cardiol 2014;1(105):49-51. [CrossRef]
16. Kostić T, Perišić Z, Stanojević D, Djindjic B, Koracevic G, Mitov V, et al. Brugada syndrome. Acta Medica Medianae 2015;54(2):37-40. [CrossRef]

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SAVREMENA PREVENCIJA NAPRASNE SRČANE SMRTI

Tomislav Kostić[1,2], Marina Deljanin-Ilić[2,3], Dragana Stanojević[1], Dragan Milić[4,5], Goran Koraćević[1,2], Svetlana Apostolović[1,2], Zoran Perišić[1,2], Sonja Šalinger-Martinović[1,2], Miodrag Đorđević[5,7], Mlađan Golubović[4,5], Milan Lazarević[4,6]

[1]Klinika za kardiovaskularne bolesti, Klinički centar Niš, Niš, Srbija
[2]Univerzitet u Nišu, Medicinski fakultet, Katedra za internu medicinu, Niš, Srbija
[3]Institut za rehabilitaciju i prevenciju kardiovaskularnih bolesti „Niška Banja", Niška Banja, Srbija
[4]Klinika za kardiohirurgiju, Klinički centar Niš, Niš, Srbija
[5]Univerzitet u Nišu, Medicinski fakultet, Katedra Hirurgija sa anesteziologijom i reanimatologijom, Niš, Srbija
[6]Univerzitet u Nišu, Medicinski fakultet, Katedra Mikrobiologija sa imunologijom, Niš, Srbija
[7]Klinika za hirurgiju, Klinički centar Niš, Niš, Srbija

Kontakt: Tomislav Kostić
Bulevar dr Zorana Đinđića 48, 18000 Niš, Srbija
E-mail: tomislav.kostic1977@gmail.com

Naprasni srčani zastoj i naprasna srčana smrt su termini, koji se u medicini vrlo često koriste kao sinonimi. Naprasna srčana smrt (NSS) definiše se kao "prirodna, neočekivana smrt usled srčanih uzroka, koja nastaje unutar jednog sata od početka akutnih simptoma i praćena je naglim gubitkom svesti". Prisustvo srčanog oboljenja može biti poznato od ranije, ali su vreme i način smrti neočekivani. Koronarna bolest (KB) odgovorna je za 75% – 80% svih slučajeva NSS. Dok je ateroskleroza primarni poremećaj kod ljudi srednje i starije životne dobi, kod dece i mladih osoba (< 35 godina) uzrok NSS najčešće predstavljaju maligne aritmije, koje se javljaju u srčanim komorama – monomorfna ili polimorfna komorska tahikardija i ventrikularna fibrilacija. Etiologija poremećaja srčanog ritma može biti povezana sa osnovnim srčanim oboljenjem, ali je kod mladih osoba najčešće idiopatska. Veći broj studija potvrdio je to da su maligne aritmije neposredni uzrok smrti. Etiologija poremećaja srčanog ritma može biti vezana za osnovno srčano oboljenje, ali može biti i idiopatska. Sekundarna prevencija naprasne srčane smrti podrazumeva lečenje onih koji su imali sreće da prežive iznenadni srčani zastoj ili imaju dokumentovane hemodinamski nestabilne komorske aritmije, a primarna prevencija podrazumeva lečenje onih koji imaju povišen rizik od nastanka naprasne srčane smrti, ali bez dokumentovanog prethodnog srčanog zastoja ili malignih komorskih aritmija. S obzirom na to da je najčešća aritmija, koja prethodi srčanom zastoju, komorska tahikardija (VT), koja degeneriše u komorsku fibrilaciju (VF), prevencija naprasne srčane smrti podrazumeva efikasno prekidanje komorske tahikardije (VT). Na osnovu rezultata studija i podataka iz kliničke prakse, može se zaključiti da implantacija implantabilnog kardioverter defibrilatora (ICD) značajno smanjuje smrtnost i u primarnoj i u sekundarnoj prevenciji, u odnosu na bolesnike koji su primenjivali samo medikamentnu terapiju. Sem toga, bolesnici kod kojih je ugradnjom pejsmejker sistema, pored defibrilatorske ostvarena i resinhronizaciona terapija, imaju značajno bolji kvalitet života, povećanje EF, kao i ehokardiografske parametre. Takođe, primena medikamentozne terapije kod bolesnika sa ugrađenim pejsmejkerom smanjuje učestalost isporučivanja DC šoka čime se postiže očuvanje miokardne funkcije i smanjuju se oštećenja koja nastaju prilikom prolaska struje kroz srčani mišić. Implantabilni kardioverter defibrilatori doneli su novo poglavlje u lečenju najrizičnijih kardiovaskularnih bolesnika.

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Ključne reči: *naprasna srčana smrt, primarna i sekundarna prevencija, implantabilni kardioverter defibrilator*