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EXPERIENCE OF USING THE OF SUBCUTANEOUS CARDIOVERTER-DEFIBRILLATORS IN THE WORLD PRACTICE: REVIEW

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The article provides a review of international clinical studies on the use of a subcutaneous implantable cardioverter-defibrillator (ICD) in comparison with classical intravenous defibrillation systems. Subcutaneous ICDs have shown themselves to be a worthy alternative to intravenous defibrillating systems for the primary prevention of sudden cardiac death, when the patient is not indicated for anti-tachy stimulation and anti-brady stimulation. World experience on the use of subcutaneous ICDs proves the safety and effectiveness of the functioning of the subcutaneous ICD system, excluding from the patient's life the formidable risks associated with the implantation procedure and further functioning of the classical intravenous ICD system.

Key words: cardioverter-defibrillator; subcutaneous cardioverter-defibrillator; sudden cardiac death; ventricular tachycardia; ventricular fibrillation; fatal arrhythmias

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Sudden cardiac death (SCD) continues to be the leading cause of death among those of working-age and creatively active people (the age range is from 35 to 55 years). According to various sources, between 326,000 and 350,000 people per year die from SCD in the United States [1, 2], and between 200,000 and 250,000 people per year in the Russian Federation [3].

The main cause of SCD is fatal arrhythmias (up to 90% of cases), such as suddenly developed ventricular fibrillation (VF) or ventricular tachycardia (VT) [4, 5]. Several international clinical trials have demonstrated the high efficacy of implantable cardioverter-defibrillators (ICDs) in preventing cardiac arrest (6). It is thought that the ICD should be regarded as the primary and secondary prevention of SCD, and as a means of relieving VTs refractory to medication and catheter-based therapies [3].

Today, more than 1,000 devices per 1 million people (including pacemakers and ICDs) are implanted in developed European countries and the USA. In Russia, this figure exceeded 250 per 1 million population. Based on this fact, there are now hundreds of thousands of patients in Russia with devices already implanted, and this number is increasing rapidly every year (about 37,000 implantations per year) [7]. In Russia, the number of ICD implantations has been increasing since the early 1990s, but the number of implantation does not cover the entire list of people in need. The need for an ICD per 1 million inhabitants is between 50 and 400 operations per year (according to various studies). For example, 1.3 ICDs per 1 million population were implanted in Russia in 2006, 9 ICDs per 1 million population in 2011, just over 13 ICDs per 1 million population in 2013, and 18 ICDs per 1 million population in 2018 [8].

However, like any treatment method, intravenous ICD systems have a number of peculiarities related to the implantation procedure and the further functioning of the system, e.g. mechanical damage to the electrodes due to the patient's active movements, the need to limit the motor activity of the patient's upper shoulder girdle, bacterial infections and bedsores of the ICD and electrodes, infective endocarditis, occlusion of the superior vena cava and subclavian vein, mechanical damage to the tricuspid valve, the complexity of the procedure for implanting intravenous electrodes not only in non-standard anatomy but also on a previously operated heart (tricuspid valve replacement, Mustard, Fontan, etc.), difficulties in implanting epicardially located electrodes, epicardial shock coil, especially taking into account the anatomical peculiarities in children [9], high risks of complications during implantation of the system, such as pneumothorax, hemothorax, hemopericardium, perforation of the heart wall, damage to the tendon apparatus and papillary muscles. All this has led leading ICD developers to consider developing a defibrillation system that would reduce the above risks, if not conclusively, then at least to a minimum. The first subcutaneous ICD (S-ICD) Emblem from Boston Scientific (Marlborough, Massachusetts, USA) was introduced.

The history of the development and introduction of the subcutaneous ICD into clinical practice begins in 2002, with the first generation being released in 2009. The first trials showed high efficacy in controlling induced VF with a subcutaneous ICD from the first shock, but because of its

design and location relative to the heart, significantly higher defibrillation thresholds (DFT) were observed compared to those of transvenous ICDs [10]. In addition to the above, the subcutaneous ICD has a number of important features that need to be considered when choosing an ICD for each patient individually: no prolonged stimulation beyond the first 30 seconds after shock, no possibility of anti-tachy pacing, extracardiac detection of cardiac signals, increased casing size and weight compared to transvenous ICDs. Infection and bedsores of the ICD bed and electrodes continue to occur. In the case of a subcutaneous ICD, however, the dreaded risks associated with the implantation procedure and the continued operation of intravenous ICD systems are avoided.

To date, 75,000 subcutaneous ICDs have been implanted worldwide. The largest multicenter studies dedicated to proving the effectiveness of the subcutaneous ICD are: completed IDE and EFFORTLESS (subsequently, the registry), PRAETORIAN, UNTOUCHED, and uncompleted PRAETORIAN-DFT, MADIT-SICD.

The IDE study is a prospective, multicenter study conducted in the United States that included 321 patients. In this study, 99% of patients had no device-related complications after 180 days of follow-up, and all spontaneous VTs were successfully managed. S-ICD treated a total of 112 VT/VF episodes, of which 38 were polymorphic during the electrical storm. All but 1 episode was effectively controlled by S-ICD, and 1 episode was controlled spontaneously [11].

The PRAETORIAN study is a multicenter, single randomized, controlled, prospective study consisting of two comparison groups of subcutaneous ICDs and transvenous ICDs (S-ICD and TV-ICD, respectively), with blinded endpoint assessment. The study began in 2011, all participating centers had sufficient experience in implantation of subcutaneous and intravenous ICDs. The main objective of this study was to demonstrate that S-ICD is not inferior to TV-ICD in patients with a class I or IIa indication for ICD therapy who have no indication for cardiac stimulation. The primary end point was a set of inappropriate shocks and complications associated with the ICD. Complications included: implant-associated infection, implant-associated bleeding, thrombotic event, pneumothorax, hemothorax, cardiac wall perforation, cardiac tamponade, electrode dislocation and reimplantation of the system to the contralateral side. Secondary endpoints included number of effective motivated shocks, number of inappropriate shocks, complications of the implant procedure, reimplantation to the contralateral side, all-cause mortality, serious adverse cardiac events, cardiac syncope, time to successful ICD therapy, effectiveness of first shock, implant procedure time, fluoroscopy time, post implantation hospitalization rate. Additional subgroup analysis was planned according to age (<50, 50-75, >75 years), patient gender, body mass index, presence of ischemic cardiomyopathy, diabetes mellitus, PR interval >200 ms, QRS width ≥120 ms, and left ventricular ejection (left ventricular (LV) ejection fraction <35%) [12].

A total of 849 patients were included in the study; the follow-up period was 48 months; patients were observed in 39 medical institutions from 6 European countries and the United States (patients from the United States accounted for only 7%). The S-ICD and TV-ICD subgroups were divided 1:1 by the number of patients. The mean age of the patients was 63-64 years (54 to 70 years), and the number of included patients with ischemic cardiomyopathy predominated over those with nonischemic cardiomyopathy and was 67.8% for S-ICD and 70.4% for TV-ICD versus 23.2% and 23.1%, respectively. The mean LV ejection fraction was 30% for both subgroups (25% to 35%). According to the distribution of functional class (FC) of heart failure according to NYHA, FC II prevailed among patients (48.5% in the S-ICD group and 53.0% in the TV-ICD group), FC I was 34.0% and 31.8%, respectively, and FC III-IV were 17.5% and 15.2%, respectively. In the S-ICD and TV-ICD patient groups, mortality from noncardiac causes was comparable (P=0.200). The mortality rate from SCD was also comparable (18 cases in each group). The percentage of implant-related complications was 5.9% for the S-ICD group and 9.8% for the TV-ICD group (P=0.110). The percentage of complications related specifically to the electrode for the S-ICD group was 1.4% and 6.6% for the TV-ICD group (P=0.001). The system had to be explanted due to infection in 8 patients in the TV-ICD group and 4 patients in the S-ICD group. A 4-year follow-up analysis showed a ratio of inappropriate shocks: 9.7% in the S-ICD group and 7.3% in the TV-ICD group. Given the value of the results obtained, it was decided to extend the study under the name PRAETORIAN XL [12].

Currently, the world community is waiting with great interest for the results of the PRAETORIAN-DFT study [13]. The purpose of the study is to move away from the DFT for S-ICD implantation, because we are all aware of the risks of complications when provoking VF, even in the conditions of very well equipped modern operating rooms.

The EFFORTLESS registry was maintained at 42 clinics. In 2017, complete data were published with an average observation period of 3.1 years. Physician observation data, including quality of life, were systematically collected for 60 months after implantation. The study population of patients with implanted S-ICDs was 472, including 241 (51%) included prospectively, with a mean follow-up period of 558 days (range 13-1342 days, median 498 days). The proportion of men was 72%, the mean age was 49±18 years (range, 9-88 years), the mean LV ejection fraction was 43±18%, and 58% had an LV ejection fraction <35%. The primary endpoints were complication rates at 30 and 360 days and inappropriate shocks applied to atrial fibrillation and other supraventricular tachycardias. The incidence of complications was 4.1% at 30 days and 8.4% at 1 year. In the first year of follow-up, 8.1% of patients had inappropriate shocks, of which 1.5% had supraventricular tachycardia. After 3.1 years of follow-up, these figures were 11.7% and 2.3%, respectively. The same incidence of inappropriate shocks was found in the START study, in which the S-ICD showed excellent discrimination of NVT. During the period of observation, 317 spontaneous episodes of rhythm disturbances were registered in 85 patients. Of these, 169 (53%) episodes required ICD therapy; 93 episodes were ventricular tachycardia and ventricular fibrillation [14].

The following data were obtained in the group with a mean follow-up period of 6.1 years, in which 58% of patients underwent planned ICD replacement. The S-ICD battery had an average charge life of 5.6 years. The incidence of complications was 3%. The annual incidence of inappropriate shocks was 3%, of which the annual incidence of inappropriate shocks was 4%. One patient died of an electrical storm and marked bradycardia. Regarding individual episodes of VT/VF, the rate of rhythm recovery after the first discharge was 88.5%, and the overall successful clinical conversion after a maximum of five discharges was 97.4%. The frequency of inappropriate shock discharges over 360 days was 7%, most of which were due to hypersensitivity (62 of 73 episodes), mostly due to extracardiac signals (94% of hypersensitivity episodes). Device explantation was required in 24 patients due to development of S-ICD bed infection (2.4%), 4 patients due to ineffective cardioversion (0.4%), and 1 patient due to development of need for cardiac pacing (0.1%) [14]. Thus, early results from the EFFORTLESS registry suggest comparable incidence of complications and inappropriate shock discharges in patients with a fully subcutaneous ICD and patients with intravenous ICD systems.

The prospective, non-randomized UNTOUCHED trial included a total of 1,116 patients with latest generation S-ICD requiring primary prevention of SCD, with a LV ejection fraction <35%. This study was conducted specifically to assess the most common indications for subcutaneous ICD implantation in a real population. Also, this study presented the perioperative and 30-day safety results of the S-ICD implantation procedure. Patients were predominantly male, mean age was 56±12 years, mean LV ejection fraction was 26±6%, and the proportion of patients with ischemic cardiomyopathy was 54%. This study included patients with a wider range of comorbidities compared with previous S-ICD studies, such as hypertension and diabetes, similar to the patients included in the MADIT-RIT study; in addition, the included patients were older and in a higher NYHA heart failure class. S-ICDs were successfully implanted in 1112 (99.6%) patients. The DFT was performed in 82.1% of patients; 99.2% of the episodes of induced VF were stopped effectively from the first cardioversion, in 0.8% either shock electrode repositioning or repeated cardioversion was required. Thirty-day follow-up showed no complications in 95.8% of patients. There were 7 cases of infection associated with the device, in 0.8% of cases the electrode or device body had to be repositioned. These data confirm the positive results obtained in earlier S-ICD registries, despite the lower LV ejection fraction and an extended spectrum of comorbidities in the studied patients [15].

The post-marketing S-ICD study is a prospective registry conducted in the United States, including 1,637 patients [16]. In this registry, the mean age of the patients was 53±15 years and the mean LV ejection fraction was 32.0±14.6%. There were comorbidities in the study group: 74% of patients had heart failure, 62% had hypertension, 34% had diabetes mellitus, and 13% of patients had chronic renal failure on chronic hemodialysis. Induced VF was successfully terminated in 98.7% of cases, 91.2% at 65 J. Among the thirty-day complications identified in 3.7% of patients, complications were related to the ICD (S-ISD bed infection in 0.5% of cases, in 0.3% of cases there was ineffective cardioversion).

The IDE and EFFORTLESS studies were later combined [17]. Due to the existing risk of misdiagnosing various supraventricular tachycardias as events requiring cardioversion, the SMART Pass algorithm was developed. The recruited group of patients, consisting of 1,984 patients, was observed for 1 year, of whom 33% of the observed patients had the SMART Pass filter programmed. This discrimination algorithm showed a significant decrease in incorrectly applied shocks over the observation period (9.9% vs. 3.7%, P<0.001). Another very effective algorithm for discriminating true ventricular tachycardia from supraventricular or atrial fibrillation tachycardia is called Insight, its effectiveness is reviewed in the Start study. For diagnostic purposes, S-ICD has an atrial fibrillation monitor algorithm in its software, thanks to which up to 25 episodes of atrial fibrillation episodes are stored in the device memory [18].

Electrodes for implantation retroperitoneally to reduce the voltages of effective shock discharges and enable extracardiac cardiac pacing are in the process of research. Another promising development is the study of the correct functioning of the S-ICD system and the electrodeless pacemaker to provide pacing and antitachycardia function. The plan is to adapt electrode-free pacemaker to work with S-ICD so that VT detection is performed by S-ICD, and antitachycardia and antibradycardia pacing are performed by electrode-free pacemaker system. This interaction of the two state-of-the-art systems is a promising development for patients who simultaneously need both antibradycardia pacing and antitachycardia therapy.

CONCLUSION

Thus, a subcutaneous ICD can be a worthwhile alternative to intravenous systems for the primary prevention of SCD when the patient is not indicated for antitachycardia and antibradycardia stimulation. Global experience with subcutaneous ICDs proves their safety and effectiveness. It is particularly important to avoid the risk of infectious complications in high-risk patients, in patients with a mechanical tricuspid valve prosthesis, and in patients after surgery to correct congenital heart disease. We believe that the subcutaneous ICD, while having several advantages and disadvantages, can rightfully line up with modern single-chamber ICD systems, provided a detailed approach to the selection of an ICD model for each patient is strictly individualized.

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