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Original Article

Effect of implantable cardioverter defibrillator on primary prevention of sudden cardiac death in high-risk patients

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Abstract: Objective: To investigate the effect of implantable cardioverter defibrillator (ICD) on primary prevention of sudden cardiac death (SCD) in patients with high risk. Methods: This retrospective analysis included 70 patients who received primary prevention of SCD by ICD implantation in Huzhou Central Hospital from March 2016 to May 2019. Based on survival, 15 patients who died during follow-up were placed into the death group and the 55 patients who survived were set as the survival group. The two groups were compared in terms of sex, age, non-sustained ventricular tachycardia (VT), diastolic pressure, systolic pressure, left ventricular ejection fraction (LVEF), urea nitrogen, serum creatinine, history of diabetes, history of atrial fibrillation, history of myocardial ischemia, history of dilated cardiomyopathy, history of hypertrophic cardiomyopathy, type I Brugada wave and cardiac function classification. Further, we analyzed the proportion of discharge, the survival of patients (Kaplan Meier method), and the risk factors of patient death (Logistic regression). Results: The analysis of baseline data showed that patients in the death group had older age and higher level of serum creatinine than the survival group (P<0.05), and the number of patients with non-sustained VT≥5 times/24 h in the survival group was higher than that in the death group (P<0.05). There was no obvious difference in other baseline indexes between the two groups (P>0.05). In addition, there was no difference in the proportion of patients receiving appropriate/inappropriate discharge (P>0.05) between the two groups. Follow-up data showed that 15 cases (21.43%) of spontaneous VT/ventricular fibrillation events were correctly diagnosed by pacemakers and properly treated by ICD (discharge or antitachycardia pacing (ATP)), while 55 cases (78.57%) received inappropriate ICD treatment. There were 15 patients (21.43%) who died during follow up, including 6 cases of cardiac insufficiency, 1 case of SCD, 2 cases of acute myocardial infarction, 1 case of respiratory failure, and 5 cases of unknown etiology; the survival time was (20.27±7.06) months. Logistic regression analysis showed that age and serum creatinine were the risk factors of patient death. Conclusion: Primary prevention with ICD implantation benefits SCD patients. Non persistent VT≥5 times/24 h is a predictive value for ICD implantation in patients receiving primary prevention of SCD. Age and serum creatinine are risk factors for death.

Keywords: Implantable cardioverter defibrillator, primary prevention, sudden cardiac death

Introduction

Heart failure is caused by a variety of diseases [1]. Ischemic heart disease and dilated cardiomyopathy caused by myocardial infarction are common causes in clinical practice [2]. Studies have shown that patients whose left ventricular ejection fraction (LVEF) is ≤0.35 present with a higher all-cause mortality due to heart failure than patients whose LVEF is 0.36-0.45, but the prevention of sudden cardiac death (SCD) mainly depends on the use of an implantable cardioverter defibrillator (ICD) [3, 4]. Early studies have confirmed that ICD implantation can significantly reduce the risk of death in patients with heart failure who have had unstable hemodynamics or ventricular tachycardia (VT) [5].

In 1980, the ICD was first designed by Mirowski, and this opened up a new therapeutic field for malignant arrhythmia [6]. The internal defibrillator can deliver shock defibrillation within 10-20 seconds, and the success rate of the defibrillation is almost 100%. The first ICD in China was implanted in 1992 [7]. Indications for ICD implantation include: (1) ventricular fibrillation (VF) or cardiac arrest caused by VT due to non-transient or reversible causes; (2) spontaneous sustained VT; (3) for patients with syncope from unknown cause, sustained VT or VF with bleeding flow disorder that can be induced by cardiac electrophysiological examination, and drug treatment that is ineffective or intolerable; (4) non-sustained VT caused by old myocardial infarction with left heart failure, and sustained VT or VF can be induced by cardiac electrophysiological examination and cannot be inhibited by antiarrhythmic drugs; and (5) family hereditary diseases caused by malignant arrhythmia that cannot be effectively controlled by drugs [8]. ICD mainly includes two parts, a pulse generator and an electrode wire system, which identifies arrhythmias and releases energy. With the continuous development of technology, the pulse generator becomes smaller in size and lighter in weight. At present, ICDs used in clinic are the third and fourth generation products, which have multiple functions such as electric shock defibrillation, anti-tachycardia pacing (i.e., for VT) and anti-bradycardia pacing (i.e., for bradycardia, similar to universal pacemakers) [9].

In 2018, the *American College of Cardiology (ACC) and the American Heart Association (AHA) Heart Failure Guidelines* first recommended ICDs [10]. However, there are relatively few patients who received ICD implantation in China, and the proportion with primary prevention is low. For example, multi-center studies reported that in Israel and Canada, about 30% patients received ICD for secondary prevention [11, 12], while a recent study by Fuwai Hospital in China showed that among the 428 patients with ICD implantation, 89% were secondary prevention, and only 11% (less than 50 cases) were primary prevention [13].

Sudden death is a serious challenge in the clinic, especially SCD, which accounts for 75% of sudden death and 15%-20% of total death [14]. Clinical trials have proven that implanting ICDs, such as SCD-HeFT, AMIOVIRT, MADIT and MADIT-II, for the primary prevention of SCD can effectively reduce the total mortality or the arrhythmia-related mortality. However, Danish registration research showed that only 7.8% of patients with primary prevention of SCD received correct discharge treatment after implanting ICD [15]. Tanno et al. pointed out that the standard of MADIT-II was not suitable for Japanese patients [16]. This study collected follow-up data and analyzed the prevention effect of ICD implantation on SCD. The innovation of this study was that we collected real follow-up data and conducted systematic statistical analysis, so as to reflect the real preventive effect of ICDs on SCD, and the significance of this study is to provide data reference for clinical practice.

Materials and methods

Clinical data

This study was approved by the Ethics Committee of Huzhou Central Hospital. Retrospectively, we analyzed the data of 70 patients who received ICD implantation for primary prevention of SCD in Huzhou Central Hospital from March 2016 to May 2019. Based on survival, 15 patients who died during follow-up were placed into the death group and 55 patients who survived were in the survival group.

Inclusion criteria: (1) patients who were implanted with ICD to prevent SCD; (2) patients who were continuously followed up until death or the deadline; (3) patients with complete data; (4) patients who were 18 years old or older.

Exclusion criteria: (1) patients with other organic diseases, cancer or psychiatric diseases; (2) patients who failed to be followed up.

Follow up after discharge

The follow up was conducted in all patients, every 6 months after ICD implantation. The pacemaker data were retrieved through the pacemaker programmable controller. Then, the patients were assigned into a survival group and a death group according to follow-up data. The survival time of patients who died was recorded. Survival time was calculated from ICD implantation to the date of death or the deadline of the last follow-up, which was May 2022.

Observation indexes

(1) The clinical data in the two groups were collected and analyzed, including age, systolic pressure, diastolic pressure, LVEF, left ventricu-

Table 1. Comparison of the measurement data

Index	Survival group (n = 55)	Death group (n = 15)	t	P
Age (years old)	61.09±3.82	67.07±3.81	-5.378	<0.001
Systolic pressure (mmHg)	123.29±6.09	122.20±10.46	0.520	0.605
Diastolic pressure (mmHg)	76.35±4.08	78.87±7.93	-1.693	0.095
LVEF (%)	34.05±4.88	31.67±7.14	1.512	0.135
Left ventricular end diastolic diameter (mm)	69.85±3.91	68.20±4.28	1.423	0.159
Urea nitrogen (mmol/L)	3.45±0.21	3.51±0.19	0.993	0.324
Serum creatinine (umol/L)	126.02±23.01	111.93±14.79	2.241	0.028
Survival time (months)	28.71±4.49	20.27±7.06	5.655	<0.001

Note: Left Ventricular Ejection Fraction (LVEF).

lar end-diastolic diameter, urea nitrogen, serum creatinine, survival time, sex, non-sustained VT≥5 times/24 h, history of diabetes, atrial fibrillation, myocardial ischemia, dilated cardiomyopathy, hypertrophic cardiomyopathy, type I Brugada wave, complete right bundle branch conduction, complete left bundle branch conduction, cardiac function classification.

(2) The discharge therapy events were collected and compared between the two groups. Appropriate discharge therapy was defined as a discharge therapy induced by sustained VT or VF. Three associate professors of cardiology with research orientation in electrophysiology were responsible for evaluating the appropriate discharge therapy according to the intracavity electrocardiogram. The key points for differentiation included the shape and width of QRS wave in the intracavitary electrocardiogram, the sudden occurrence of arrhythmia, the stability of cardiac cycle, interference or T-wave oversensing. In addition, dual chamber ICD can also be identified according to ratio of atrium and ventricle, origin point of atrioventricular and atrioventricular conduction relationship. Otherwise, it is an inappropriate discharge.

(3) According to the follow-up, death events were recorded, and the risk factors of patient death were analyzed.

Statistical analysis

All data were processed by SPSS 22.0 software. The measurement data were expressed by (x ± s), and were compared between the two groups by independent sample t-test. The counting data were expressed in [n (%)], and were compared between the two groups by χ^2 test. Logistic regression was employed to analyze the risk factors of patient death. The survival curve was estimated by Kaplan-Meier method. The difference was significant when P<0.05.

Results

The clinical baseline data in the two groups

The clinical data analysis showed that the death group had older age and higher level of serum creatinine than the survival group (P<0.05), and the number of patients with non-sustained VT≥5 times/24 h in the survival group was higher than that in the death group (P<0.05). There was no difference between the two groups in sex, diastolic pressure, systolic pressure, LVEF, left ventricular end diastolic diameter, urea nitrogen, history of diabetes, history of atrial fibrillation, history of myocardial ischemia, history of dilated cardiomyopathy, history of hypertrophic cardiomyopathy, type I Brugada wave, complete right and left bundle branch conduction and cardiac function classification (P>0.05). Detail information is shown in **Tables 1** and **2**.

Analysis of patient discharge therapy events

As shown in **Table 3**, during the follow-up, there were 15 patients with appropriate discharge treatment and 10 patients with inappropriate discharge treatment, and the differences in the proportions of patients with appropriate discharge treatment or inappropriate discharge treatment were not significant between the survival and death groups (P>0.05).

Description of patient follow-up

The 70 patients were followed up until May 2022, and the pacemakers functioned normal-

Table 2. Comparison of the counting data

Index	Survival group (n = 55)	Death group (n = 15)	χ^2	P
Sex (male, %)	40 (72.73%)	11 (73.33%)	0.002	0.963
Non-sustained VT≥5 times/24 h	25 (45.45%)	2 (13.33%)	5.132	0.023
Diabetes	12 (21.82%)	2 (13.33%)	0.530	0.466
Atrial fibrillation	9 (16.26%)	2 (13.33%)	0.082	0.775
Ischemic myocardium	17 (30.90%)	7 (46.67%)	1.299	0.254
Dilated myocardium	25 (45.45%)	6 (40%)	1.090	1.296
Hypertrophic obstructive myocardium	1 (1.82%)	0 (0%)	0.277	0.599
Type I Brugada wave	0 (0%)	1 (6.67%)	3.720	0.054
Complete right bundle branch conduction	0 (0%)	1 (6.67%)	3.720	0.054
Complete left bundle branch conduction	7 (12.73%)	1 (6.67%)	0.428	0.513
Cardiac function classification ≥III	7 (12.73%)	8 (53.33%)	1.729	0.189

Note: Ventricular Tachycardia (VT).

Table 3. Analysis of patient discharge therapy events

	Number of patients	Appropriate discharge	Inappropriate discharge
All patients	70	15 (21.43%)	10 (14.29%)
Survival group	55 (78.57%)	11 (20%)	8 (14.55%)
Death group	15 (21.43%)	4 (26.67%)	2 (13.33%)
χ^2		0.311	0.014
P		0.577	0.905

ly. According to the data collected from the pacemakers during follow-up, it was observed that 15 cases (21.43%) of spontaneous VT/VF events were correctly diagnosed by pacemakers and properly treated by ICD (discharge or ATP), including 126 discharges in one case and 19 ATP treatments. Of the remaining 55 cases (78.57%), 10 cases (14.29%) received inappropriate ICD treatment (discharge or ATP) due to wrong diagnosis of the pacemaker. Among them, 6 cases (60%) were with single chamber ICDs. Moreover, 44 patients were diagnosed with 271 occurrences of VF (204 correct times, accounting for 75.3%), 433 occurrences of VT (217 correct times, accounting for 50.1%), 492 occasions of discharge therapy (270 correct times, accounting for 54.9%), 765 occasions of ATP therapy (342 correct times, accounting for 44.7%), including 158 occasions of effective termination of ventricular arrhythmia (accounting for 46.2%). The causes of 10 cases of inappropriate ICD treatment are as follows. There were 5 cases of atrial fibrillation/atrial flutter with fast ventricular response (including 1 case of 98 instances of inappropriate discharge and 208 occurrences of ATP treatment), 3 cases of supraventricular arrhythmia with or without non-specific ventricular conduction, 1 case of false perception and 1 case of T wave oversensing. Circumferential pulmonary-vein ablation was performed in 2 patients with inappropriate discharge due to frequent atrial fibrillation and rapid ventricular response, and no error was recorded after the operation. One patient went to the hospital for radiofrequency ablation due to continuous VT discharge or ATP treatment.

Analysis of postoperative survival results

During follow-up, 15 patients (21.43%) died, including 6 cases of cardiac insufficiency, 1 case of SCD, 2 cases of acute myocardial infarction, 1 case of respiratory failure and 5 cases of unknown etiology; the mean survival time was (20.27±7.06) months. The Kaplan-Meier survival curve of the 70 patients after operation is shown in **Figure 1**.

Risk factors of patient death

As shown in **Table 4**, the Logistic regression analysis showed that the age (B = 2.496, S.E. = 0.818, Wald = 9.315, P<0.05, OR = 1.130) and serum creatinine (B = 0.237, S.E. = 0.202, Wald = 5.670, P<0.05, OR = 0.968) were the risk factors of patient death.

Discussion

The most common direct cause (about 83%) of SCD is malignant ventricular arrhythmia, which

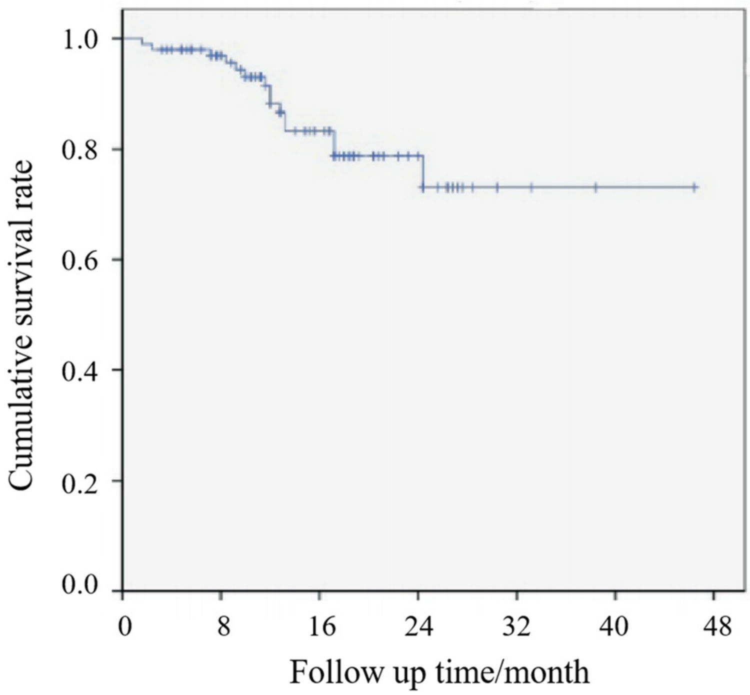

Figure 1. Postoperative cumulative survival curve of the 70 patients.

Table 4. Risk factors of patient death

Index	B	S.E.	Wald	P	OR	EXP (B) of 95% C.I.	
						lower limit	higher limit
Age	2.496	0.818	9.315	0.002	1.130	0.946	1.007
Serum creatinine	0.237	0.202	5.670	0.025	0.968	0.960	0.979
Constant	-12.292	3.929	8.786	0.002	0.000		

Note: 95% C.I.: 95% Confidence Interval.

is manifested as VT and VF [17]. SCD is characterized by sudden, rapid and high mortality. The key to reduce the mortality of these patients is to implement effective electric shock within a few minutes, but only 2%-15% can be treated in time. Epidemic data shows that the incidence of SCD is higher in men than in women, and it has a predilection for people aged 50 to 60 years old. The survival rate was reported to be less than 1% [18].

In this study, there were 15 among the 70 cases had correct discharge or ATP treatment, accounting for 21.43%, indicating that ICD implantation can benefit the primary prevention against SCD. However, according to the programmed data of the pacemakers, the proportion of primary discharge and ATP effective treatment was not high, which was possibly related to the setting of the parameters, and should be gradually improved in clinical practice in the future. There were 10 cases who were treated inappropriately, including 6 cases with single lumen ICD and 4 cases with double lumen or triple lumen, and there was no difference between the two groups (P>0.05). Among these 10 cases, 5 cases had atrial fibrillation with fast ventricular response, which is similar to existing research reports. For such patients, in addition to the current drug treatment, it is also considered that circumferential pulmonary-vein isolation would benefit. In this study, 2 patients underwent circumferential pulmonary-vein isolation, and their situation is still good.

At present, the most important indicator in primary prevention of SCD is LVEF≤35%, but patients with relatively high LVEF can also have SCD. Lucas et al. [19] pointed out that in the primary prevention of SCD, the protective effect of ICD was not related to the LVEF of patients. Their study also showed that 1/3 of patients with scar related VT after myocardial infarction had LVEF≥40%. In this study, there were 13 cases (18.57%) with LVEF>40% detected by echocardiography, including 10 cases in the survival group (accounting for 18.18% in the group) and 3 cases in the death group (20.0%), and 11 cases (15.71%) had 35%<LVEF≤40%, including 9 cases in the survival group (16.36%) and 2 cases in the death group (13.33%). In this study, LVEF was re-evaluated by gated myocardial perfusion tomography (resting) in 9 of the 70 patients. LVEF was >35% in 6 patients. This motivates us to find a better and more accurate LVEF value as a diagnostic standard, and to prevent LVEF>40% in a timely manner, for instance, whether it is possible to jointly predict LVEF value by adding evaluation indicators, such as the left ventricular end diastolic diameter with statistical differences in this study. Non-sustained VT can be reliably recorded by dynamic electrocardiogram. However, the natural variation rate of non-sustained VT can be as high as 70%. It was reported that the sensitivity of non-sustained VT to predict SCD or total death was 31%-71% [20], and the positive predictive value was 20%-71%, but the negative predictive value was as high as 72%-93%. We found that the non-sustained VT≥5 times/24 h recorded by dynamic electrocardiogram was significant (P<0.05) in the primary prevention of SCD by implanting ICD. Therefore, the non-sustained VT≥5 times/24 h was a predictive index worthy of reference.

Kaliská et al. found some death related factors, including age and renal function impairment, which is consistent with this study. Studies also found some other risk factors including sex, LVEF, ischemic heart disease, etc. [20, 21]. In terms of sex and LVEF, researchers conducted a 4-year follow-up in patients implanted with ICD for primary prevention, and found that age ≥75 years, chronic kidney disease, and LVEF≤0.20 were risk factors for death [22, 23]. However, Zhang et al. [24] showed that sex and LVEF differences did not cause significant changes in the risk of death. The reason for the different results from the studies may be the different population and follow-up time.

In the United States, there are about 3 million cases of SCD every year, with a survival rate of 5% [25]. According to a survey in Hong Kong in 1997, the incidence of SCD was 1.8/100,000. According to the data from the key research projects in the 10th Five Year Plan of China led by Fuwai Hospital, the incidence of SCD in China was 4184/100,000. It was calculated in 2009 that with a population of 1.3 billion in China, the number of people who will die from SCD each year could reach 544,000 [26]. Primary prevention of SCD is our focus, because it has been reported that nearly 95% of patients with ICD should receive primary prevention of SCD [27]. However, currently in China, only 9.33% to 33.33% of the population with primary prevention of SCD is implanted with ICD, which is significantly lower than 55.7% in western countries [26]. This shows that the primary prevention of SCD is particularly important.

The shortcomings of this study are that there were a small number of cases, not long enough follow-up time, and no data about the time of the first event after ICD/CRT-D implantation, which will be improved in future studies.

Disclosure of conflict of interest

None.

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