Analysis of survival of 291 patients treated with implantable cardioverter – defibrillator

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Abstract

Introduction. The cardioverter – defibrillator (ICD) implantation is the method of treatment in patients with high risk of sudden cardiac death.
Aim. The aim of the study was to evaluate the survival of patients treated with ICD implantation and factors influencing the time of survival.
Material and methods. Retrospective analysis of documentation of 291 patients who underwent ICD implantation in Cardiology Department of Medical University in Lublin was performed.
Results. In the follow – up period 14.77% of patients died. The probability of 1000 days survival was higher in patients treated with β–blocker and lower in patients receiving furosemid, in patients with heart failure NYHA I was equal 96% and was by 4% higher than patients with NYHA II class and by 53% higher than in patients in NYHA III class (p 0.0001), while in patients with ejection fraction (EF) >35% was by 12% higher than in patients with EF <35% (p 0.05).

Key words:

implantable cardioverter defibrillator (ICD), survival, heart failure

Conclusions. Probability of 1000 days survival in patients with implanted ICD is equal approximately 90%. It is increased in patients with low NYHA class and treated with β – blocker and decreased in patients with low EF and receiving furosemid.

Introduction

Sudden cardiac death is regarded one of the major causes of mortality in developed countries. Since the first automatic cardioverter defibrillator implantation, this method of sudden cardiac death prevention has been widespread as an result of major therapeutic advances in treatment of ischaemic heart disease and heart failure and limited effectiveness of antiarrhythmic drugs. Implantation of cardioverter defibrillator is nowadays established method of therapy of patients who survived sudden cardiac death or in patients with high risk of live – threatenig cardiac arrhythmia. The effectiveness of this therapeutic method in secondary and primary prevention of sudden cardiac death was proven in several randomized interventional trials [1-3]. According to current guidelines, ICD implantation is an indicated method of management in patients who survived sudden cardiac death or hemodynamically unstable ventricular tachycardia (class I) and in patients at high risk of life – threatenig arrhythmias – as heart failure with low left ventricle ejection fraction, Brugada syndrome, long QT syndrome or hypertrophic cardiomiopathy (class IIa) [4].

As a result of clear indications for ICD implantation and the wide procedure availability, the number of patients with implanted device is systematically rising. The method decreases the risk of sudden cardiac death, but results in some adverse effects, among that the most frequent are inadequate therapies, impairing the quality of life, increasing the need of ICD replacement and even leading to ventricular arrhytmias [5]. Another everyday life problem in patients with implanted ICD is driving. Although in definite circumstances driving the private car is possible, professional drivers can not return to their previous occupation. Because of the potential risk of loss of conciousness, also working as a pilot, at high altitudes or in the close proximity of inducible furnaces or big electrical generators is forbidden. Despite of potential limitations for occupational work, ICD implantation in patients at producive age brings undoubtfull adventages resulting first of all from the increasing the time of life and the possibility of acivities previously infeasible for the patients because of underlining disorder [7].

The aim of the study was to evaluate the survival of patients treated with ICD implantation and determinate the factors influencing the time of survival.

Material and methods

We studied retrospectively documentation of 291 patients (74 women and 217 men) in age 60.7±14.6, with ICD implanted in Department of Cardiology Medical University in Lublin from 1998 to 2006 and then undergoing follow - up in outpatient clinic. Indications for ICD implantation are presented in the Table I. The following patient baseline data at the time of first ICD implantation were analyzed: age, gender, indications for ICD implantation, concomitant diseases, the degree of heart failure according to the New York Heart Association (NYHA) functional class, left ventricle ejection fraction (LVEF) evaluated echocardiografically, the presence of intraventricular conduction abnormalities including right bundle branch block (RBBB) or left bundle branch block (LBBB), previous electrophysiology study or ablation procedure, previous pacemaker implantation, previous coronary revascularisation or artificial valve implantation, pharmacotherapy and the type of implanted ICD including one chamber or two – chamber device and combined ICD with cardiac resynchronization therapy device.

The information about the fact of death was obtained from the patients' family members during phone call or from the data of Lubelskie Province Governor's Office.

Table I.
Indications for ICD implantation in investigated group of patients

Indication for implantation	Number of ICD implantations (% of patients)
SCD	159 (56)
CAD +VT	55 (19)
MADIT I	30 (10)
DCM + VT	24 (8)
MADIT II	8 (3)
Idiopathic VT	7 (2)
LQTS	4 (1,3)
HCM + VT	3 (1)
ARVC	1 (0,3)

ARVC – arrhythmogenic right ventricle cardiomiopathy; CAD – coronary artery disease; DCM – dilated cardiomiopathy; HCM – hypertrophic cardiomiopathy; ICD – implantable cardioverter defibrillator; LQTS – long QT syndrome; MADIT I and II – indications according to MADIT I and II trials [2,3]; SCD - sudden cardiac death; VT – ventricular tachycardia

Data were statistically analyzed using the Software STATISTICA 6.1 for Windows. The significance of differences between patients who died and patients who survived were analyzed using Mann – Whitney U test for continuous variables and two – sided exact Fisher test for categorical variables. Correlation was calculated using Spearman test. The Kaplan–Meier method and the log–rank test were used to compare survival between the compared groups of patients. Cox proportional hazard model was used to asses multivariate hazard ratio (HR) adjusted for potential risk factors. P values less than 0.05 were considered significant. The study was approved by the local bioethical comittee.

Results

In analyzed group (n=291) in the term of follow-up 43 patients died (14.77 %). The mean time from the implantation to death was equal 698 days (23.26 months). In 30 (69.8 %) patients the cause of death was considered as cardiac (1 patient died in the result of infective endocarditis, 3 in the result of myocardial infarction, 12 in the result of heart failure, in 14 cases the cardiac cause of death remains unprecized). In 6 cases the cause of death was not cardiac (4 deaths result from cancer and 4 from stroke). In 7 cases the information about the cause of death was not obtained.

Significant correlation between the death of patient and the age in the time of the first ICD implantation was observed (the mean age of patients who died was equal 68.4 years and patients who survived 59.3 years, p 0.0001). The correlation between the death of the patient and the type of implanted device was not confirmed, altrough the lowest (8,33%) mortality was observed in the group of patients with implanted cardioverter – defibrillator with cardiac resynchronization function (CRT – D) and the highest (16.98%) in patients with implanted two – chamber ICD, p= 0.63, R= 0.69.

In the investigated group summary 7 from 74 women (9.46%) and 36 from 217 men (16.59%) died. The difference was not significant (p= 0.13). In the Table II the number of deaths in dependence on indications for ICD implantation is presented.

The relationship between the number of survived resuscitations and the death was analysed, too, but any significant difference was not observed.

Significantly higher number of deaths was connected with the occurence of coronary artery disease with ventricular tachyarrytmias ($p < 0.001$), valvular disease (0.01), renal failure ($p < 0.01$), previous percutaneus coronary intervention ($p < 0.01$), previous ablation procedure ($p < 0.02$), sustained ventricular tachycardia ($p < 0.05$), treatment with furosemid ($p < 0.01$) and low ($\leq$35%) ejection fraction ($p < 0.02$). However, significantly lower number of deaths was

Table II.
Number of deaths in group of patients with ICD in dependence on indications for implantation

Indication for ICD implantation	Number of patients	Yes	%	No	%
SCD	159	22	13.84	137	86.16
CAD+VT	55	14	25.45	41	74.55
DCM+VT	24	2	8.33	22	91.67
MADIT I	30	3	10	27	90
MADIT II	8	1	12.50	7	87.50
Idiopatic VT	7	1	14.29	6	85.71
Summary	291	43	14.77	248	85.23

CAD – coronary artery disease; DCM – dilated cardiomiopathy; ICD – implantable cardioverter defibrillator; MADIT I and II – indications according to MADIT I and II trials [2,3]; SCD – sudden cardiac death; VT – ventricular tachycardia

observed in patients treated with β- bloker in comparison with patients, who did not receive these drugs and in patients with idiopathic ventricular fibrillation in comparison with other patients, Correlations of number of deaths and analysed clinical features are summarized in the Table III.

The correlation between the class of heart failure according to NYHA classification and survival of patients was also analyzed (NYHA class before first implantation was evaluated in 254 from 291 investigated patients) and statistical significancy was found (p= 0.001). Most frequently deaths occured in patients with heart failure in class NYHA III, most rarely in patients without clinical signs and symptoms of heart failure (NYHA I), what is presented in the Figure 1.

Also significantly higher ratio of deaths in dependence on the number of appropriate ICD therapies caused by VF occurence in the first year of follow up (p= 0.007) and the overall number of adequate interventions resulting from VF (p= 0.01) was observed in the investigated group. Similar differences in dependence on adequate therapies resulting from VT were not confirmed.

Kaplan-Meier analysis of selected factors influencing survival was performed. The probability of survival and the time of survival in dependence on patients' sex was determined. Probability of 1000 days survival in the group of women was equal 93% and was by 8% higher than for the man. (p 0.40).

Similar analysis was performed to evaluate the influence of β-blokers on the patients' survival. Among 63 patients who did not receive β-blockers, 15 patients died (23.81 %) and in the group of patients treated with β-blockers, died 28 from 248 patients (12.28%). In patients receiving β-blocker probability of 1000 days survival was equal 90% and was by 13% higher than in group of patients who did not receive β-blockers. Mentioned above differences tend to be significant (p 0.06).

The relationship of indications for ICD implantation (survived sudden cardiac death and coronary heart disease underlining ventricular tachyarrhythmia) and probability of survival was evaluated. In the group of patients who survived sudden cardiac death probability of 1000 days survival after ICD implantation was equal 90% and was by 15% higher than in group of patients with coronary heart disease and ventricular tachyarrhythmia (p 0.065). Similar analysis was performed taking into consideration the type of implanted device (two - chamber vs one – chamber ICD). Probability of 1000 days survival of patients with one chamber ICD (89%) was comparable to probability of survival of patients with two – chamber ICD altrough the difference was not significant (p= 0.74). Analysis of probability of survival in dependence on NYHA class at the moment of ICD implantation confirmed that probability of 1000 days survival in group of patients with NYHA I class was equal 96% and was by 4% higher than in group of patients with NYHA II class and by 53% higher than in group of patients in NYHA III class. Observed differences were significant (p 0.0001).

Table III.
Number of deaths in dependence on analysed clinical features

Feature	Death Mean number of deaths in patients without feature	Mean number of deaths in patients with feature	P value
DCM	14.47	15.87	0.78
Cardiac aneutysm	15.50	9.09	0.32
CAD	5.32	19.29	0.001
HCM	15.09	0.0	0.34
Hyperthyroidismus	13.89	20.51	0.27
Diabetes	14.46	16.67	0.70
Hypertension	14.49	15.03	0.89
ARVC	14.98	0.00	0.40
Valvular disease	10.73	21.05	0.01
Renal failure	12.94	27.78	0.01
COPD	14.23	20.83	0.38
LQTS	15.19	0.0	0.23
Idiopatic VT	16.67	2.56	0.02
Myocarditis	15.09	0.0	0.32
Syncope	17.56	12.50	0.22
sVT	9.52	17.74	0.05
VF	16.99	12.32	0.26
nsVT	13.92	15.79	0.65
CABG	14.17	18.92	0.44
PCI	11.87	23.61	0.01
Aneurysmectomia	14.63	25.00	0.56
Ablation	13.72	35.71	0.02
Pacemaker	14.80	14.63	0.97
Without AA drugs	14.98	0.0	0.40
Amiodaron	15.75	14.02	0.68
Sotalol	13.81	26.09	0.11
β-bloker	23.81	12.28	0.02
Mexiletine	14.39	23.08	0.38
Propafenon	14.80	14.29	0.95
Diltiazem	14.93	0.00	0.46
ACEI	11.43	16.63	0.22
Spironol	13.83	16.50	0.53
Furosemid	11.63	23.68	0.01
Statin	15.82	12.63	0.47
Chronic AF	13.79	23.33	0.16
Paroxysmal AF	12.75	19.54	0.13
Sinus tachykardia	14.12	19.44	0.39

Sinus bradykardia	13.55	18.18	0.32
Bradyarrhythmia	14.62	16.13	0.82
A–V block I°	14.29	17.59	0.54
A–V block II/III°	14.34	25.00	0.30
RBBB	15.16	7.14	0.40
LBBB	13.51	25.00	0.08
VT induced in EPS	14.29	21.43	0.36
VF induced in EPS	22.33	7.14	0.06
Electrical storm	7.2	4.87	0.11
EF < 35%	10.71	20.88	0.02

AA – antiarrhytmic; ACEI – angiotensin converting enzyme inhibitor; AF – atrial fibrillation; ARVC – arrhythmogenic right ventricle cardiomiopathy; A–V – atrio – ventricular; CABG – cardio – pulmonary bypass grafting; CAD – coronary artery disease; COPD – chronic obturative pulmonary disease; DCM – dilated cardiomiopathy; EF – ejection fraction; EPs – electrophysiology study; HCM – hypertrophic cardiomiopathy; LBBB – left branch bundle block; LQTS – long QT syndrome; PCI – percutaneus coronary intervention; RBBB – right branch bundle block; VF – ventricular fibrillation; VT – ventricular tachycardia

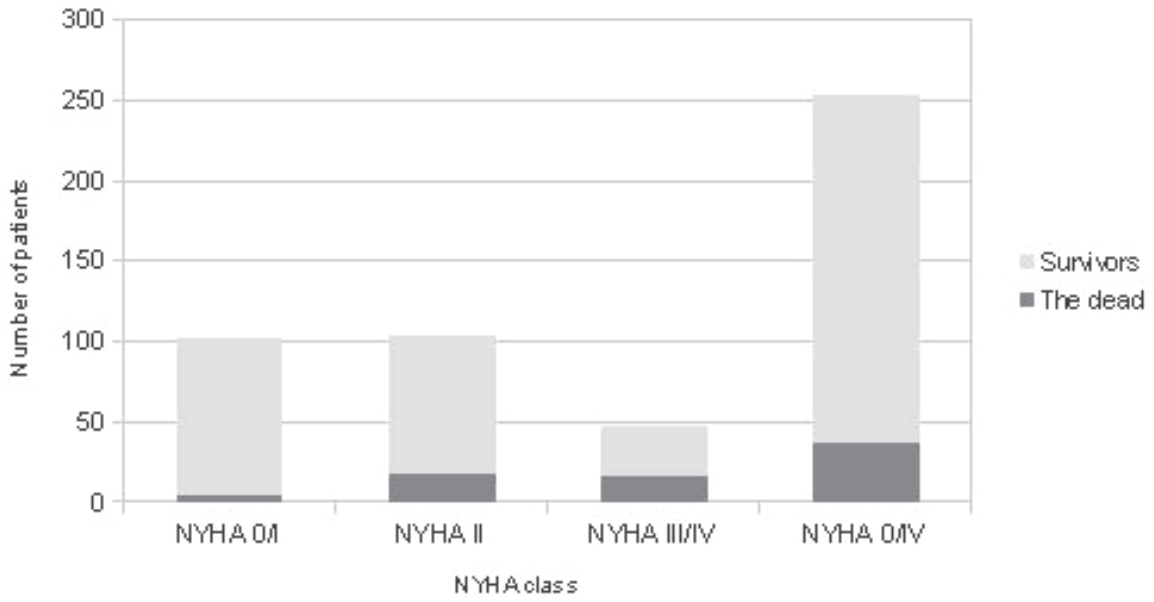

Fig. 1.
Number of deaths in patients in dependence on NYHA class before ICD implantation. NYHA = New York Heart Association; ICD = implantable cardioverter defibrillator

Analysis of the influence of EF at the moment of ICD implantation on patients' survival shown that the probability of 1000 days survival of patients with EF >35 % was equal 92% and was by 12% higher than in group of patients with EF ≤35 % (p 0.05). The significantly higher probability of 1000 days survival of patients, who were not treated with furosemid (91%) in comparison with patients receiving this drug (79%) was also observed (p 0.0004).

Multivariative proportional regression analysis was performed to evaluate the relationship between the risk of death in dependence on the age, ejection fraction, NYHA class at the moment of implantation an β-blocker and furosemid treatment. Significantly

higher risk of death was connected with older age (p= 0.0001), furosemid treatment (p= 0.01) and NYHA class before the first ICD implantation (p= 0.0001) and lower risk was observed in patients treated with β-blocker (p= 0.03).

Discussion

During follow up period in analysed group 43 patients died (14.7%). The most frequent were cardiovasuclar deaths, mainly caused by progression of heart failure. Probability of 1 year survival in the investigated group was equal 93%. Addictionaly, in analysed group of patients higher probability of 1000 days survival in patients with heart failure in NYHA class I (96%) in comparison to patients with NYHA class II (92%) and NYHA III (43%) was observed. Similarly, the probability of 1000 days survival of patients wit EF >35% before ICD implantation was significantly higher than in patients with EF ≤35% (92% vs 80%). Our results remains in concordance with the analysis of 3344 patients with ICD implanted in 1998 - 2000 years in 65 centers in Germany revealing that 93,5% of patients survived one year after implantation [8]. Authors of cited above study observed significantly higher mortality in patients with heart failure in NYHA II class and with EF <30% in comparison with patients in NYHA I class and with EF >30% (0.852 vs 0.975, p .0001).

In the publicated in 1997 study, Trappe and co – workers [9] evaluated potential benefits resulting from ICD treatment in group of patients with life threatening ventricular tachyarrthmias and impaired ventricular function. Authors described that during a mean follow up of 28 months 23% patients died. The cause of death of 2% of patients was sudden arrhythmia, in 1% of patients occured sudden death of probably not arrhytmhic cause, 14% died from cardiac causes (progression of heart failure, or myocardial reinfarction) and 5% from other non -cardiac reasons. Five – year survival in patients with NYHA I – II class was evaluated as 92-96%, and in group of patients with NYHA III class as 84%. Above mentioned authors evaluated the mean survival time after the first shock of ICD and did not found any significant differences between patients with mild moderate or severe left ventricle dysfunction. In the another study Portugeese investigators analysed group of 70 patients with ICD implanted in secondary prevention. After the mean four years follow – up period, overall mortality was equal 25%, 4,2% patients died as a result of sudden cardiac death and in 12.5% cases, the death was described as cardiac [10]. According to data from Latin American registry of implantable cardioverter defibrillator higher mortality of patients in class NYHA III-IV in comparison of patient in NYHA I-II class was observed. Overall mortality after 25 months of follow up was evaluated as 16.9%, and 64.6 % of deaths was considered as cardiac. One year mortality was equal 5.2 %. Chronic heart failure was the reason of 57% of deaths and 43% of deaths was described as sudden ones [11].

In our study significantly higher number of deaths resulted from older age, occurence of coronary heart disease underlining the ventricular tachycardia, valvular disease, renal failure, previous coronary angioplasty and low LVEF (≤35%) before the ICD implantation. There was no relationship between the mortality and sex of patients and indication for ICD implantation. Similarly, in above cited publication, an age >70 years, NYHA class III/IV and EF <30% was described as undependent risk factors of death in patients with implanted ICD [11]. As well, data obtained from large, multicenter studies, confirmed this observations [12-14]. Similar conclusion have presented authors of 2 – years analysis of patients with implanted ICD – CRT published in 2006 study [15]. In the investigated group of patients they reported 25% mortality, significantly higher in patients with coronary heart disease (14% vs 8%). Ischaemic etiology of heart failure and NYHA class >II were described as risk factors of death. In group of patients analysed in our study significantly higher risk of death was observed in patients treated with furosemid, that indirectly confirm the higher risk of death in patients with more severe heart failure. The risk of death in patients treated with β-blocker was significantly lower, that remains in concordance with results of other studies, indicating favourable

role of β-blocker treatment in patients with ICD [16]. It should be underlined that survival of patients depends not only on fact of ICD implantation, but on additional pharmacological treatment, too. On the other hand, it should be keep in mind that survival after ICD implantation is highly influenced by the severity of left ventricle damage. In recently published study evaluating the survival of patients with cardioverter – defibrillator implanted in secondary or primary prevention, authors did not report differences in 7 – years mortality in investigated groups. During the follow – up period 23% of patiets with ICD implanted in primary prevention and 30% of patient with device implanted in secondary prevention died. Overall mortality was equal 26.9% (4.2% per a year). Similarly as in our study, decreased LVEF (<35%) and chronic renal failure were regarded the independent risk factors of death, but the indications for ICD implantation (primary or secondary prevention) did not influence the mortality of patients [17]. Also another investigators did not observed differences in mortality of patients with ICD implanted in primary prevention in comparison with patients with the device implanted in secondary prevention [18,19]. The concordance of our data obtained in analysed group of 291 patients with the results from others, also multicentre studies confirm the agreement of management of patients treated in Cardiology Department of Medical University in Lublin with currently indicated strategies.

Conclusions

Probability of 1000 days survival in patients with implanted ICD was equal approximately 90%. It was increased in patients with low NYHA class and treated with β-blocker and decreased in patients with low EF and receiving furosemid.

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