ORIGINAL ARTICLE

Long-term survival of patients with implantable cardioverter - defibrillators implanted on the basis of a secondary prevention indication

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ABSTRACT

Background. The efficacy of therapy with implantable cardioverter-defibrillators is usually evaluated according to the total mortality of ICD patients. The aim of this study is to analyze the total mortality of long-term followed ICD patients, to evaluate mortality according to the main diagnosis, and to analyze the effect of myocardial revascularization in patients with coronary artery disease.
Patients and Methods. We observed 138 consecutive patients, mean age 62.0±12.2 years (108 M, 30 F), with mean LVEF 0.38±0.14, who, in the period from October 1995 to December 2002, for secondary preventive reasons, had ICDs implanted because of malignant ventricular arrhythmias. The mean follow-up was 47.35 months. 99 patients had CAD (coronary artery disease), 16 CMP (dilated cardiomyopathy), 5 ARVC (right ventricle dysplasia) , 4 LQT syndrome, 1 valvular defect, and 13 patients were without structural heart disease.
Results. The total mortality in the group of patients was 22% (31 patients). The main cause of death, in 84% of our patients, was fatal heart failure. There was no sudden death in our group of patients. The highest mortality (27%) was in patients with CAD, while nobody died in the group of patients without structural heart disease. The higher mortality was in patients where revascularization could not be performed before ICD implantation (38% versus 20%). One-year survival of the whole group of patients was 90% , two-year survival 87%.
Conclusions. The survival of ICD patients is shorter if CAD is present and there is no possibility to revascularize patients before ICD implantation.
Key words: ICD, total mortality, secondary prevention.

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INTRODUCTION

More than 155 years (1) have passed since the first description of ventricular fibrillation in an animal experiment on a dog's heart (M. Hoffa 1849), and its therapy – defibrillation (2) - has been known since 1947; nonetheless ventricular fibrillation remains the main cause of sudden coronary death. In Europe 2,500 people have a heart arrest every day, and 90% of these events are caused by ventricular fibrillation (3). The individualization of sudden coronary death risk introduced a new method into clinical practice in 1981 – the implantation of cardioverter-defibrillators (ICD) (4). Their effectiveness in reducing total mortality was first documented in the field of secondary prevention – in patients who had suffered cardiac arrest (AVID trial) (5) and, subsequently, in the field of primary prevention – in patients with risk markers (left ventricular dysfunction, symptomatic non-sustained ventricular tachycardia …) without, however, sustained malignant arrhythmia in their histories (MADIT I, MADIT II) (6-8). Modern ICD systems are very sensitive in detecting malignant arrhythmia, they are highly specific in discriminating between supraventricular and ventricular arrhythmias, they apply graded therapy (antibradycardial, antitachycardial, cardioversion, defibrillation). More than 150,000 are implanted every year in the world; in the Czech Republic the ratio is approx. 55 ICDs per 1 million inhabitants.

The aim is to determine, on the basis of long-term prospective monitoring of a group of ICD patients indicated for this therapy for secondary prevention, reasons for total mortality; to divide this into deaths due to cardiac and extra-cardiac causes; to compare the mortality according to nosological units; to evaluate the effect of revascularization performed in patients with coronary artery disease (CAD); and to compare the acquired values of total mortality with published historical data from the time when patients were treated with medication only.

PATIENTS AND METHODS

The group of patients included 138 consecutive patients, average age 62.0±12.27 years (range 19 to 83 years); 108 men and 30 women. On the basis of valid indication criteria, ICDs were implanted in all patients during the period from October 1995 to December 2002. The mean period of follow-up was 47.35 months (Tab. 1).

The evaluation of total mortality included all consecutive patients indicated for ICD implantation for secondary prevention of sudden coronary death, i. e.:

- patients after cardiac arrest during malignant arrhythmia,
- patients with sustained forms of ventricular arrhythmias resistant to antiarrhythmic therapy,
- patients with a history of syncope and inducible hemodynamically compromising arrhythmia during programmed ventricular stimulation.

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Tab. 1. Group of patients

Category	Number N
Number of patients	138
Mean follow-up (in months)	47.35
Age	
Average (SD)	62.0 (12.27 %)
Mean	66.0
Min/max.	19/83
Sex	
Men108	(78.3 %)
Women 30	(21.7 %)

Tab. 2. Scope of the disease in CAD patients

Number of affected vessels	n	%
1VD	10	10.1
2VD	9	9.1
3VD	22	22.2
IM	2	2.0
IM+1VD	8	8.1
IM+2 (3)VD	44	44.4
Not known	4	4.0
Total	99	100.0

Tab. 3. Revascularization performed in CAD patients

Type of revascularization	N	%
No revascularization	56	56
Total revascularization	23	23
Partial revascularization	20	20
Total	99	100

Patients were divided into 5 groups to allow comparison according to nosological units:

- CAD (coronary artery disease),
- DCMP (dilated cardiomyopathy),
- LQTsy (long QT interval syndrome),
- ARVC (arrhythmogenic right ventricular dysplasia/cardiomyopathy),
- no structural heart disease.

Following ICD implantation, all patients were checked before release from hospital, one month after release and then every 3 to 6 months (depending on the number of ventricular tachydysrhythmia relapses).

In the group of CAD patients total mortality was monitored and deaths classified as cardiac or non-cardiac. In the case of coronary deaths we investigated to find out whether the death was sudden or due to progression of the primary cardiac disease.

The average LVEF in our group was 38±14%. 57% of the patients had a significantly reduced LVEF (below 30%).

As expected, the main etiology of malignant arrhythmias was CAD, present in 99 patients (71.7%) in our group. Table 2 shows the scope of the disease in individual CAD patients. More than 75% of the CAD patients had multivessel coronary disease. Table 3 shows that 43% of the CAD patients had at least a partial revascularization of the coronary bed performed before implantation. Revascularization was not possible in 56% of the patients.

Tab. 4. Etiology of malignant arrhythmias

Nosological unit	n	%
CAD	99	71.7
CMP	16	11.6
ARVC	5	3.6
LQT	4	2.9
Ventricular disease	1	0.7
Unknown	13	9.5
Total	138	100.0

Tab. 5. Causes of death

Cause of death	n	%
Fatal heart failure	26	84
Malignancy	1	3.2
Pulmonary embolism	1	3.2
Acute myocardial infarction	1	3.2
Stroke	1	3.2
Unknown cause	1	3.2
Total	31	100

Other etiological factors are summarized in Table 4. Altogether 16 patients suffered from dilated cardiomyopathy, 5 patients were diagnosed with arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVC). Besides clinical and, in some cases, echocardiographic evidence, the diagnosis was confirmed by nuclear magnetic resonance imaging of the heart. LQT syndrome was diagnosed in 4 patients. This diagnosis was confirmed by gene mutation evidence. One patient had an ICD implanted because of ventricular tachycardias following an earlier replacement of the aortic ventricle because of significant stenosis of the aorta. No structural heart disease was proven in 13 patients, and in their case the etiology of malignant arrhythmias remains unknown.

The standard Kaplan-Meier method was used to analyze survival. Patient survival was evaluated from the date of the implantation to the date of death or to the date of the last known data on the patient's survival. Patients who did not die during the follow-up period were evaluated as to the date of the last acquired data on survival.

The log-rank test was used to compare survival of two groups of patients. Due to the length of the follow-up of patients it was not possible to determine the mean survival of the whole group and the possibility of multidimensional modeling of patient survival was limited.

RESULTS

During the follow-up, 31 ICD patients (22% of the group) died. Total one-year survival of the monitored group was 90%, two-year survival 87% (Fig. 1).

The most common cause of death, in 84% of the cases, was fatal heart failure. One patient died of acute MI with acute heart failure, one of acute pulmonary embolism. In the case of two patients the causes of death were stroke and malignant tumor in the orofacial area. In the case of one patient there are no data available on the manner and cause of death. Table 5 summarizes the causes of death of the ICD patients.

It can be stated, after having divided mortality according to nosological units, that the lowest mortality was recorded in patients with

no structural disease of the heart and with the LQT syndrome (no patient died). On the other hand, the statistically significant highest mortality during the whole follow-up period was recorded in CAD patients (27%). The mortality of patients with DCMP was 20%. The 19% mortality of ARVC patients was undoubtedly distorted by the small number of 5 patients (Fig. 2).

The evaluation of survival in dependence on performed revascularization proved a tendency of higher mortality in patients in whom revascularization had not been performed. Due to the small number of patients, it has not been possible so far to determine a statistical significance in the difference between the partially and totally revascularized groups (Fig. 3).

DISCUSSION

Published data from the 1970s and 1980s for patients with sustained ventricular tachydysrhythmias treated with antiarrhythmics give the incidence of sudden coronary death during a two-year follow-up period of 45% and total two-year mortality of up to 60% (9-11). As early as 1989, Winkle and his colleagues (12) published the results of one of the large clinical follow-up trials of CAD patients. The authors reported an 8% reduction in the incidence of sudden coronary death during their four-year follow-up of a group of CAD patients compared to a group of patients treated pharmacologically with amiodarone or d, l sotalol. The ICD effect on total mortality, however, remained unclear. Many other studies were designed to compare actual mortality with "projected" mortality, i. e. the anticipated mortality in the same group of patients. The anticipated mortality was based on the hypothetical estimate of the mortality of the same group of patients in a situation without ICDs. The study of Bocker et al. (13) in 1993 deserves mention. The authors included into their mortality estimate only patients with very rapid primary ventricular tachydysrhythmia, frequencies over 240/min. The analysis showed that the estimated mortality of this group would have been 30%. But not a single patient from within the actual group died during the 18-month follow-up period. Such data document the fact that the ICD reduces not only mortality caused by sudden coronary death but also the overall mortality of their carriers. One limitation in the presentation of these results is the absence of a group of patients with a similar profile, but without ICDs. The authors also did not take into account the effect of cardio-pulmonary resuscitation.

Other studies, therefore, compared CAD patient survival with a group of patients with a similar disease profile, but without ICDs. Powell et al. (14) compared the total mortality of CAD patients with a control group treated with antiarrhythmics. The study included 331 patients after cardiac arrest during malignant ventricular tachydysrhythmia, divided the patients into two groups; serial testing of antiarrhythmics was performed by programmed ventricular stimulation. During the five-year follow-up period, the total mortality in the pharmacologically treated group was 28%, in the ICD group 17.4 %. Similar results were described by Newman et al. (15). They compared the mortality of 60 CAD patients with a group of 120 control patients included in the same nosological unit, receiving the same pharmacotherapy, having the same ejection fraction and clinical arrhythmia. The mortality of the ICD group was 10%, the mortality of the control group 30%. Large multi-centric trials like CAST, CAMIAT, EMIAT, AVID (16-19) presented a similar outcome.

The total mortality in our group of ICD patients, during a 47.35-month follow-up period, was 22%. Similar mortality, 17%, has been observed by Pitschner (20) during a 5 year follow-up of a group of 203 ICD patients. Most of the deaths in his group were classified as non-sudden cardiac deaths. In our group, too, 26

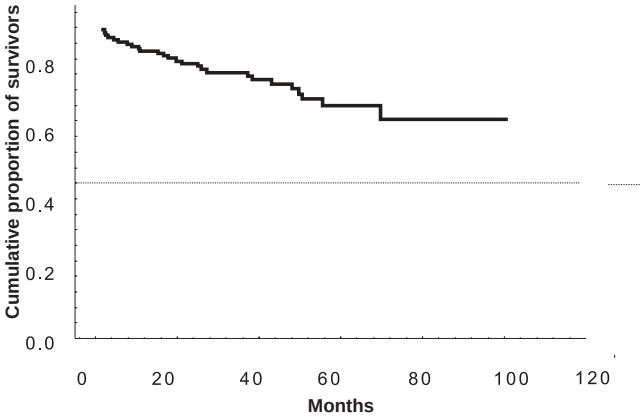

Fig. 1. Total survival of ICD patients group

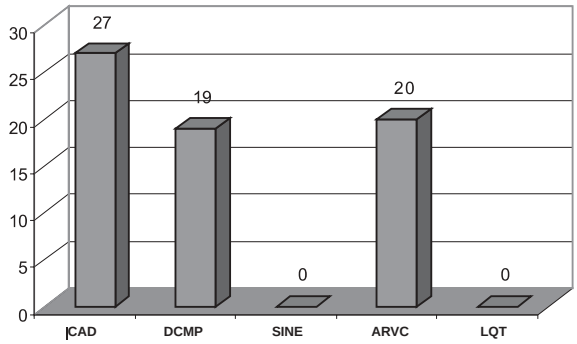

Fig. 2. Mortality according to nosological units
CAD – coronary heart disease, DCMP – dilated cardiomyopathy, SINE – without structural heart disease, ARVC – arrhythmogenic right ventricular dysplasia/cardiomyopathy, LQT – long QT interval syndrome

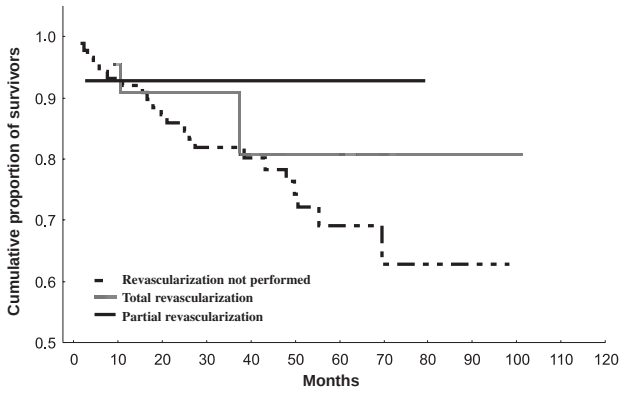

Fig. 3. Survival of patients without revascularization

patients (84%) died of non-sudden cardiac event. Three patients (9.6%) died of sudden cardiac death (acute myocardial infarction with acute heart failure, acute pulmonary embolism, unknown cause of death). Two patients (6.4%) died of non-cardiac disease. Besides the one patient where we do not know the cause of death none of the deaths has been classified as sudden arrhythmic death.

Our outcomes correspond with the findings of other authors. E. g. Pires et al. (21) give the incidence of sudden cardiac death in a group of ICD patients of 1.5%. It is known from published data that the presence of multi-vessel disease in CAD patients and circumstances in which it is not possible to revascularize limit the survival of CAD patients (22-24). In our group of CAD patients with ICDs, we observed an unequivocal trend towards longer survival of patients who had partial or total revascularization performed before ICD implantation. The highest mortality in the CAD group can be explained by concurrent left ventricular dysfunction and coronary artery disease. In the case of the other groups (DCMP, ARVC, LQT, without structural heart disease) one or both of these risk indicators are absent.

CONCLUSION

Implantable cardioverter-defibrillators are very effective in minimizing the risk of sudden coronary death. Our findings show that they also reduce the total mortality of patients implanted for secondary prevention reasons. Before the implantation of an ICD it is necessary to assess in every CAD patient the possibility of performing revascularization, which is a significant factor in long-term survival.

Abbreviations

ARVC	- arrhythmogenic right ventricular dysplasia/cardiomyopathy
AVID	- antiarrhythmics versus implantable defibrillator
CAD	- coronary artery disease
CAMIAT	- Canadian Amiodarone Myocardial Infarction Arrhythmia Trial
CAST	- Cardiac Arrhythmia Suppresion Trial
DCMP	- dilated cardiomyopathy
EMIAT	- European Myocardial Infarction Amiodarone Trial
ICD	- implantable cardioverter-defibrillator
LQTsy	- long QT interval syndrome
LVEF	- left ventricle ejection fraction
MADIT	- Multicenter Automated Defibrillator International Trial
MADIT II	- Multicenter Automated Defibrillator International Trial II

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