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ORIGINAL PAPER

Analysis of causes of death in patients with implanted defibrillators

Herbert Nägele[1] · **Eike Gröene**[1] · **Daniel Stierle**[1] · **Matthias P. Nägele**[2]

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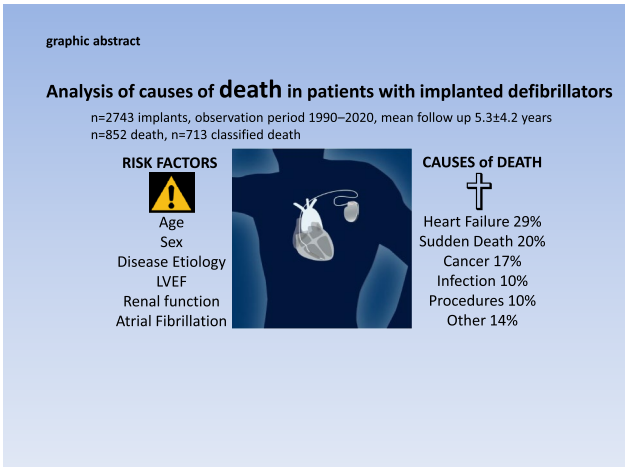
Abstract

Aims Implantable cardioverter defibrillators (ICDs) are used for primary or secondary prevention of sudden cardiac death. We sought to clarify prognosis and causes of death after ICD implantation.

Methods and results A total of 2743 patients with ICDs implanted during 1990–2020 were analyzed. Median age was 68.5 (59.6–74.6) years; 21% women, median left ventricular ejection fraction (LVEF) was 30 (23–35), 52% had an ischemic etiology and 77% had a primary preventive indication. Mortality rate after 10 years was 22, 44, 55, and 72% in the 1st, 2nd, 3rd, and 4th age quartile, respectively. The calculated median sex and age adjusted loss of life years compared to the average German population was 9.7 (6.1–14.0) years. Prognosis was independently related to sex, age, LVEF, and glomerular filtration rate. 713 out of 852 deaths could be classified to a specific cause. Congestive heart failure (CHF) accounted for death in 214 (30%) and sudden death (SD) for 144 patients (20%). Postmortem interrogation of devices in 74 patients revealed VT/VF in 39 and no episodes in 35 patients. Cancer was identified as the cause of death in 121 patients (17% of cases), of which 36 were bronchial carcinomas. 73 (10%) of patients died due to infection. 67 patients (9%) died within 24 h of procedures. Compared to other causes, significantly more life years were lost associated with procedures and SD: 9.3 (5.7–12.9) versus 12.1 (7.4–15.2) and 11.9 (7.6–17.8) years.

Conclusion Life expectancy of ICD patients is lower than for the general population. Mortality is predominantly due to CHF, but there is still a considerable rate of SD. The occurrence of cancers, most importantly bronchial carcinomas, and infections, warrants protective measures. Some deaths during procedures are possibly preventable. Patients with ICDs comprise a vulnerable cohort, and treatment has to be optimized in many directions to improve prognosis.

Graphic abstract



Keywords Implantable cardioverter defibrillator · Heart failure · Prognosis · Sudden death · Infection · Cancer · Procedures

Extended author information available on the last page of the article

Introduction

Implantable cardioverter defibrillators (ICDs) are used in ischemic and non-ischemic heart disease for primary and secondary prevention of sudden cardiac death (SCD). Their efficacy in heart failure with reduced ejection fraction was questioned in recent studies which reported a declining rate of SCD independent of ICDs in recent years, suggesting a lower impact on survival than anticipated [1, 2]. Yet, all-cause mortality in these patients remains high despite modern pharmacological therapies [3]. Data on long-term mortality and non-cardiac causes of death in patients with ICDs are still scarce. The goal of our study was to analyze the various causes of death in patients with ACIDs after long-term follow-up.

Methods

The study was a retrospective analysis of patients who received an ICD implantation for primary and secondary preventive indications between 1990 and 2020 and were clinically followed in the cardiology outpatient unit by the first author in three hospitals in Hamburg, Germany. Data on these implantations were collected and patients were observed for mortality using hospital and cardiology practice charts and information from families.

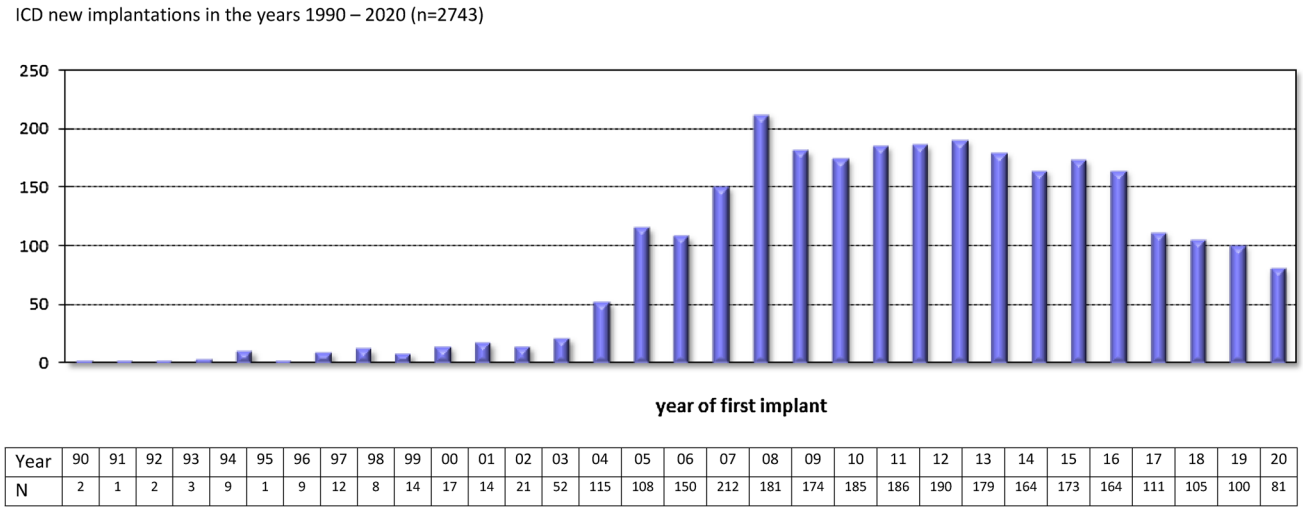
Mode of death was defined as sudden death (SD), e.g., unwitnessed death or within 1 h of first symptom or non-sudden death [4]. Procedural death was defined as occurring within 24 h of an invasive procedure without a non-procedural explanatory cause of death. Estimated glomerular filtration rate (eGFR) was calculated according to the MDRD formula ($175 \times \text{serum creatinine}^{-1.154} \times \text{age}^{-0.203} \times 1.212$ (if patient is black) $\times 0.742$ (if female). Years lost were calculated as survival with ICD subtracted from sex and age adjusted life expectancy from publicly available German life tables [5]. SPSS 27 (IBM, Armonk, U.S.A.) was used for statistical analysis. A p value of < 0.05 was deemed significant. Chi-squared and Kruskal Wallis tests were used to determine the differences between groups, depending on the kinds of data. Non-normal variables were reported as median (interquartile range [IQR]). Cox regression analysis was performed to clarify the influence of several variables on mortality. Kaplan–Meier 1-survival analysis was used, and differences between the groups were tested for significance with the log-rank test. Competitive risk analysis was performed with SPSS 27, R Plugin 36.0. This procedure uses the R cmprsk package created by Bob Gray [6].

The study was approved by the ethics committee of Hamburg, Germany (registration number PV5597).

Results

Baseline characteristics

2743 ICD patients with a median age of 68.5 (59.6–74.6) years) were observed for a median period of 4.4 (1.9–7.7) years. In the early years, implantation rates were low but increased after 2003 (Fig. 1). Diagnoses are shown in Table 1. Most patients had ischemic ($n = 1371$, 50%) or dilated cardiomyopathy ($n = 1056$, 38.5%). 114 (4.1%) patients had valvular heart disease; followed by several mixed and rare rhythm diagnoses. A total of 301 patients (10.97%) were lost during follow-up and were censored at the time of last contact. Of 38 patients that underwent heart



Year	90	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20
N	2	1	2	3	9	1	9	12	8	14	17	14	21	52	115	108	150	212	181	174	185	186	190	179	164	173	164	111	105	100	81

Fig. 1 ICD new implantations in the years 1990–2020 ($n = 2743$)

Table 1 Patients diagnoses ($n=2743$) in alphabetical order

	N	%
Alcoholic cardiomyopathy	8	0.29
Amyloidosis	5	0.18
ARVD	7	0.26
Brugada syndrome	5	0.18
Chemotherapy induced cardiomyopathy	14	0.51
DCM	1056	38.5
DCM and VCM	6	0.22
Ebsteins anomaly	1	0.04
Endomyokardial fibrosis	1	0.04
HCM	8	0.29
HOCM	23	0.94
ICM	1371	49.98
ICM and VCM	52	1.9
Long QT Syndrome	4	0.15
Lupus erythematodes	1	0.04
Myokarditis	3	0.11
Non-compaction cardiomyopathy	1	0.04
Peripartum cardiomyopathy	1	0.04
Idiopathic ventricular fibrillation	19	0.69
RVOT VT	1	0.04
Sarcoidosis	12	0.44
Takotsubo cardiomyopathy	1	0.04
Transposition of great arteries	1	0.04
TVP post HTx	8	0.29
Unclassified	17	0.62
VCM	113	4.12
Ventricular septal defect	1	0.04
WPW syndrome	1	0.04

ARVD arrhythmic right ventricular dysplasia, *ChemoCM* chemotherapy induced cardiomyopathy, *DCM* dilated cardiomyopathy, *HCM* hypertrophic cardiomyopathy, *HOCM* hypertrophic obstructive cardiomyopathy, *HTx* heart transplantation, *ICM* ischemic cardiomyopathy, *TVP* transplant vasculopathy, *VCM* valvular cardiomyopathy, *WPW* Wolff Parkinson White syndrome

transplantation (HTx), 34 survived for more than 1 day and were censored at the day of transplantation. Four fatalities were within 24 h of HTx and were classified as procedural deaths. In 24 patients, ICDs were explanted and not replaced or deactivated due to the lack of an indication ($n=12$) or infection ($n=12$); they were censored at the time of explantation. 18 patients received a left ventricular assist device (LVAD). Three patients died during LVAD implantation they were classified as procedural deaths (Table 2).

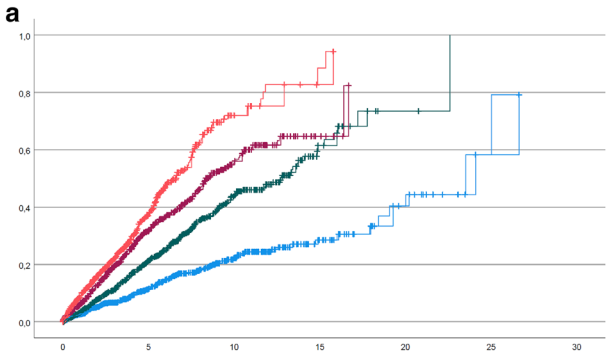
All-cause mortality stratified by patient characteristics

Mortality after 10 years was 22, 44, 55, and 72% in the 1st, 2nd, 3rd, and 4th age quartile, respectively (1st quartile

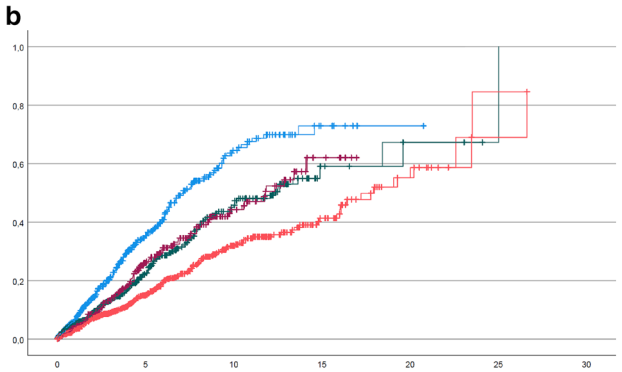
Table 2 Multiple Cox regression analysis of the influence of baseline variables (female sex, age, LVEF, eGFR, heart rate (HR), atrial fibrillation (AF), and coronary artery disease (CAD)) on survival in 2743 ICD patients

Variables	B	SE	Wald	df	*P* Value	Exp(B)
Female sex	− 0.358	0.140	6.502	1	**< 0.011**	0.699
Age	0.021	0.006	13.102	1	**< 0.0001**	1.021
LVEF	− 0.028	0.006	25.255	1	**< 0.0001**	0.972
eGFR	− 0.024	0.003	86.347	1	**< 0.0001**	0.976
HR	− 0.004	0.003	2.402	1	0.121	0.996
AF	0.184	0.121	2.315	1	0.128	1.202
CAD	0.128	0.104	1.512	1	0.219	1.137

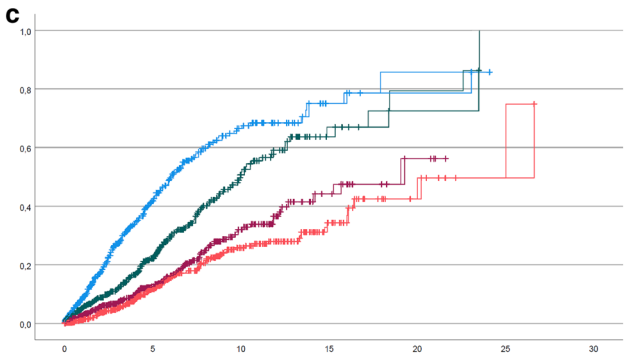
p values < 0.05 are in bold



1-survival curves: age quartiles; blue=1st (n=684), green=2nd (n=687), purple=3rd (n=686), red=4th (n=686), log-rank p<0.001

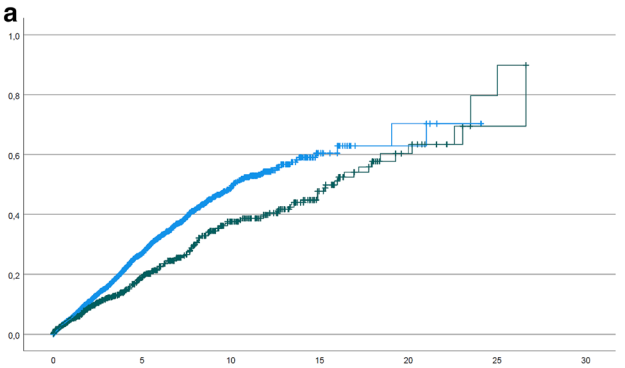


1-survival curves: LVEF quartiles; 1st=blue (n=529), 2nd=green (n=517), 3rd purple (n=414), 4th=red (n=704), log-rank p<0.001

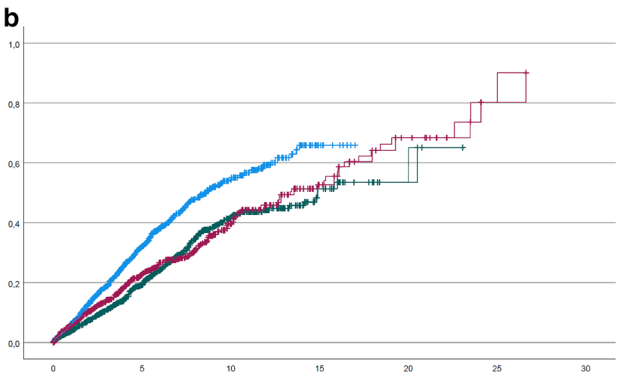


1-survival curves: eGFR quartiles; red=1st (n=525), purple=2nd (n=498), green=3rd (n=512), blue=4th (n=512), log-rank p<0.001

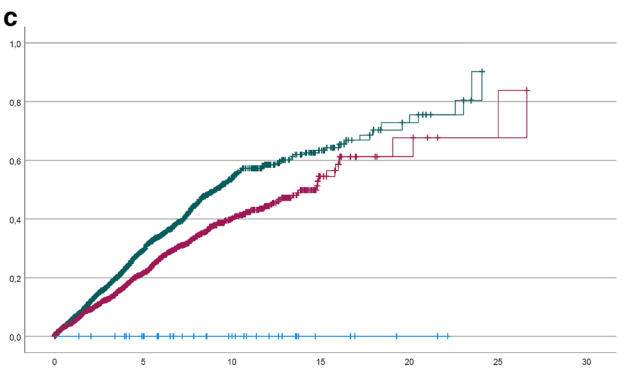
Fig. 2 **a–c** Kaplan–Meier 1-survival functions of patients after ICD implantation: **a** age quartiles: 1st quartile 15.4–59,6 years, 2nd quartile > = 59.6 years < 68.5 years, 3rd quartile > = 68.5 years < 74.58 years, and 4th quartile > = 74.58–89.2 years; **b** LVEF quartiles: 1st quartile < 23%, 2nd quartile > = 23% < 30%, 3rd quartile > = 30% < 35%, and 4th quartile > = 35%; **c** eGFR quartiles: 1st quartile < 49, 2nd quartile > = 49 < 65, 3rd quartile > = 65 < 81, and 4th quartile > = 81; remaining cases tables are shown in supplementary Table IV



1-survival curves: indication; blue=primary (n=2114), green=secondary (n=629), log-rank p=0.002



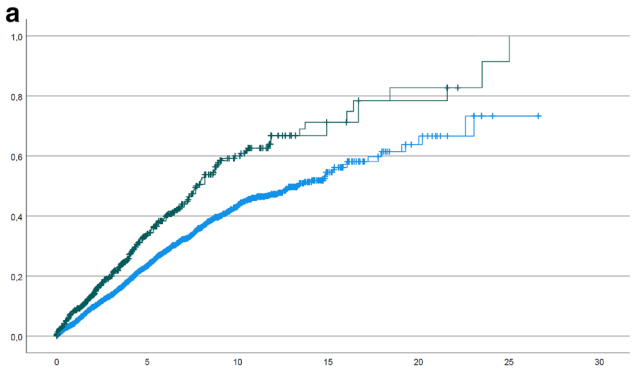
1-survival curves: device types; blue=CRT (n=1113), green=DDD (n=965), purple=VVI (n=664), log-rank p<0.001



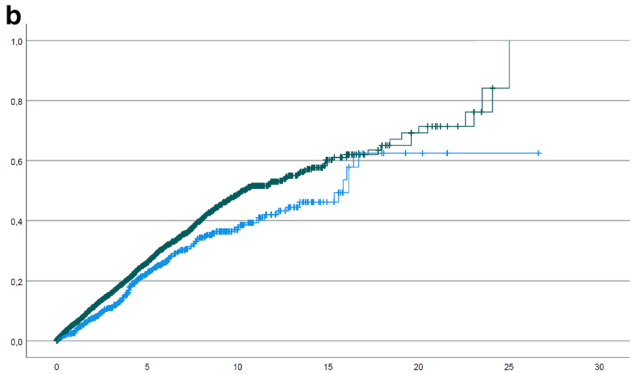
1-survival curves: etiology; blue=pure electrical (n=37), green=ischemic (1423), purple=non-ischemic (n=1266), log-rank p<0.001

Fig. 3 **a–c** Kaplan–Meier 1-survival functions of patients after ICD implantation: **a** primary vs secondary indication, **b** device types, and **c** etiology; remaining cases tables are shown in supplementary Table IV

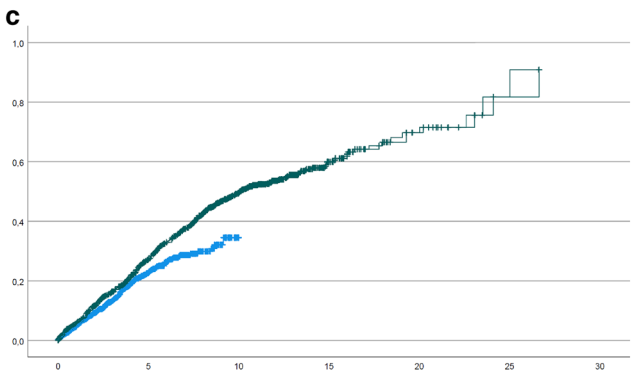
15.4–59,6 years, 2nd quartile > = 59.6 years < 68.5 years, 3rd quartile > = 68.5 years < 74.58 years, 4th quartile > = 74.58–89.2 years). Survival times are significantly different between age quartiles ($p < 0.001$, Fig. 2a). The median left ventricular ejection fraction (LVEF) was 30 (23–35) % (analyzed in 2164 patients, as values are missing in 579 cases). An analysis in regard to quartiles of baseline LVEF was performed. Mortality rate after 10 years was 22%, 44%, 55%, and 72% in the 1st, 2nd, 3rd, and 4th age quartile,



1-survival curves: atrial fibrillation; green=yes (n=2079), blue=no (n=536), log-rank p<0.001



1-survival curves: gender; green=male (n=2166), blue=female (n=578), log-rank p=0.002



1-survival curves: period of 1st implantation; green=1990-2009 (n=1290), blue=2010-2020 (n=1453), log-rank p<0.001

Fig. 4 **a–c** Kaplan–Meier 1-survival functions of patients after ICD implantation: **a** atrial fibrillation; **b** gender, and **c** period of first implantation; remaining cases tables are shown in supplementary Table V

respectively (1st quartile < 23%, 2nd quartile > = 23% < 30%, 3rd quartile > = 30% < 35%, 4th quartile > = 35%). Survival times are significantly different between high and low LVEF quartiles ($p < 0.001$, Fig. 2b). Quartiles 2 and 3 are overlapping. Median baseline creatinine level was 1.08 (0.88–1.38) mg/dl corresponding to a median eGFR of 65 (49–81) ml/

Table 3 Patient's characteristics according to the classification of death (continuous descriptive data as median and quartiles)

Classification	*N*	Women (%)	CAD (%)	AF (%)	LVEF (%)	eGFR (ml/min/1.73m^2)	Age at implant (years)	Age at death (years)	ICD survival (years)	Years lost (years)
Cancer	121	22	50	22	30 (20–35)	63 (47–83)	71 (65–75)	75 (70–78)	3.8 (2.1–6.0)	10.1 (6.3–13.2)
CHF	214	19	60	27	25 (20–30)$^{+}$	55 (39–70)	71 (66–76)	76 (70–81)	4.2 (1.9–7.3)	9.3 (5.7–13.8)
Infection	73	5.8*	56	26	30 (21–35)	55 (43–70)	71 (63–76)	76 (69–80)	3.8 (1.5–5.9)	9.6 (5.5–12.9)
Other	94	19	60	28	30 (22–35)	54 (38–67)	71 (65–75)	76 (71–80)	4.2 (1.8–7.0)	9.0 (6.2–13.0)
Procedures	67	10	70	27	25 (20–35)$^{+}$	55 (40–75)	69 (63–74)$^{\&}$	73 (68–77)$^{\&}$	2.7 (0.9–5.2)$^{\&}$	12.1 (7.4–15.2)$^{\&}$
SD	144	17	64	20	25 (20–35)$^{+}$	52 (38–72)$^{\$}$	68 (60–74)$^{\&}$	72 (65–78)$^{\&}$	3.4 (1.4–5.5)$^{\&}$	11.9 (7.6–17.8)$^{\&}$
Unclear	139	22	58	23	30 (25–35)	59 (44–76)	73 (67–79)	78 (72–83)	3.5 (1.6–6.7)	8.5 (4.9–11.8)
Total	852	18	59	23	26 (20–35)	56 (41–73)	71 (65–76)	75 (69–80)	3.7 (1.6–6.3)	9.7 (6.1–14.0)

*$p < 0.03$ Infection vs other others
$^{+}p < 0.05$ CHF, procedures and SD vs others
$^{\$}p < 0.05$ SD vs others
$^{\&}p = 0.02$ Procedures and SD vs others

min/1.73 m^2 (analyzed in 2056 patients with available measurements). Analysis in regard to quartiles of baseline eGFR was performed. Mortality rate after 10 years was 67, 51%, 32, and 26% in the 1st, 2nd, 3rd, and 4th eGFR quartile, respectively (1st quartile < 49, 2nd quartile > = 49 < 65, 3rd quartile > = 65 < 81, 4th quartile > = 81). Survival times are significantly different between eGFR quartiles ($p < 0.001$, Fig. 2c). As to the indication, a primary prophylactic indication was made in 2114 (77%) of cases, 629 (23%) had a secondary indication (sustained/hemodynamic intolerable VT or resuscitation due to VT/VF). Kaplan–Meier analysis comparing primary and secondary prevention indications in 2743 patients was performed. Patients with primary versus secondary indication were significantly older (66.9 ± 10.9 years versus 64.1 ± 13.1 years, $p = < 0.001$), had lower a LVEF (28.3 ± 9.5% versus 38 ± 14.4%, $p < 0.0001$) and a worse prognosis ($p = 0.002$, Fig. 3a).

Device types were implanted as follows: single chamber (VVI, $n = 665$), dual chamber (DDD, i = 965), and cardiac resynchronization therapy defibrillator devices (CRT, $n = 1113$). Five subcutaneous ICDs were counted as VVI devices. Figure 3b shows total survival rates, differentiated

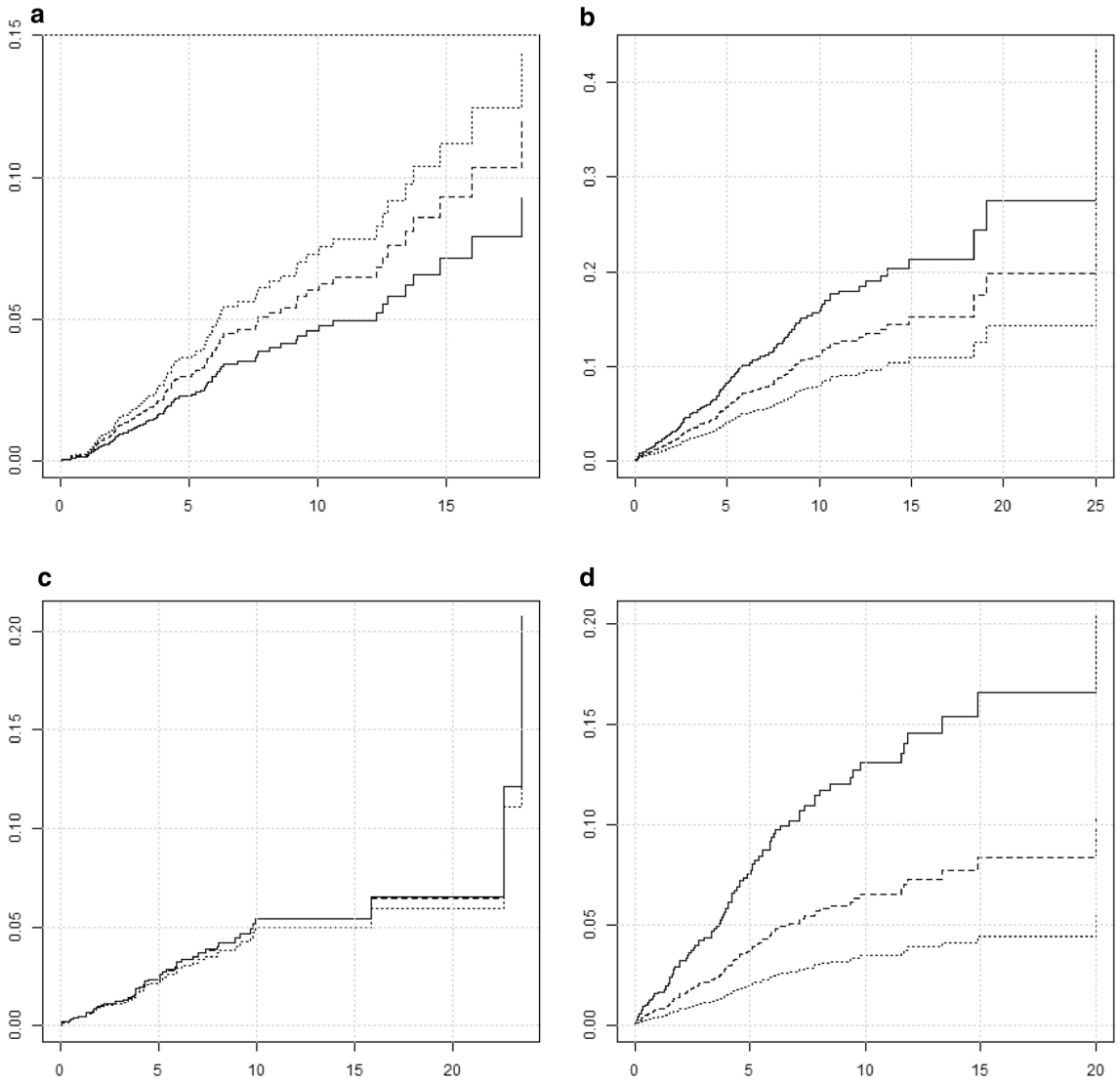


Fig. 5 a–d Age, sex, LVEF and GFR adjusted competitive risk regression hazard function (cpmrsk) in patients after ICD implantation for death from cancer (**a**), from heart failure (**b**) from infection (**c**) and from sudden death and (**d**). *X*-axis: observation times (years); *Y*-axis: probability of death; solid lines: 25% quantiles; dashed lines: 50% quantiles; dotted lines: 75% quantiles

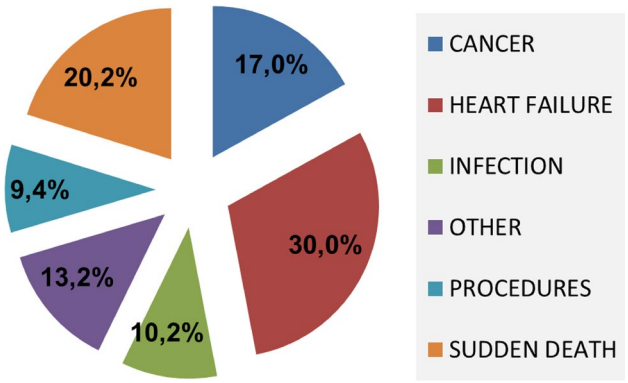


Fig. 6 Percentage of causes of 713 classified deaths after ICD implantation

between ICD types at the first implantation. Patients with CRT were significantly older (68.7 ± 10 years versus 64.6 ± 12 years, $p < 0.0001$), had a significantly lower LVEF at baseline (27.3 ± 8.1% versus 33 ± 13.1%, $p = < 0.001$) and eGFR (61.7 ± 23 versus 69.4 ± 25 /1.73 m^2, $p < 0.0001$) and had a worse prognosis compared to those with single chamber and dual chamber devices ($p < 0.001$). There was no difference between relative percentage of classified death according to ICD type ($p = 0.65$, supplementary Table III).

In addition we separately analyzed three etiologies: rhythm disorders ("pure" electrical, $n = 37$, 1.4%), ischemic ($n = 1423$, 51.8%), and non-ischemic cardiomyopathies ($n = 1266$, 46.2%). 17 patients (0.62%) could not be classified. When these groups were compared by Kaplan–Meier Analysis, zero mortality was found for pure electrical disease patients. Patients with ischemic cardiomyopathy had the worst prognosis ($p < 0.001$, Fig. 3c).

536 (20%) of the patients had atrial fibrillation (AF) at baseline (missing baseline rhythm information $n = 128$). Kaplan–Meier analysis on the influence of atrial fibrillation showed that mortality was higher in the presence of AF, $p < 0.001$, Fig. 4a). 578 patients (201%) are women. They showed a significantly lower survival rate compared to men ($p = 0.002$, Fig. 4b). We looked on possible contemporary trends in prognosis, which may occur during an observation period of 30 years. Survival analysis comparing implants from the years 1990–2009 ($n = 1290$) and 2010–2020 ($n = 1453$) showed significant changes in prognosis, becoming evident after 5 years ($p = 0.001$, Fig. 4c).

A multivariate Cox regression analysis on the influence of sex, age, LVEF, eGFR, heart rate (HR), atrial fibrillation (AF), and coronary artery disease (CAD) showed independent associations on prognosis for female sex, age, LVEF, and eGFR (Table 3).

Analysis of the specific causes of death

An analysis of the specific causes of death showed the following: a total of 852 deaths were observed. In 139 of them (16%), we found no further clarification of the terminal event. The remaining 713 deaths could be classified according to the modes of death. Patient's characteristics in relation to classification of death are shown in Table 2. A stacked histogram showed the time course of each classified death (supplementary Figure I).

Cancer with a fatal outcome was found in 121 patients and accounted for 17% of classified deaths (Table 2, Figs. 5 and 6, supplementary figures I and II). Bronchial carcinomas were the predominant entity ($n = 36$, 30%). Details of cancer diagnoses are listed in in supplementary table I. Competitive risk analysis with age, sex, LVEF, and GFR as covariates showed a median 10 year cancer death risk of 6.5% (1st quartile: 5%, 3rd quartile: 7.5%; Fig. 5a). The timely distribution of the four most important malignant diagnoses (pancreas, mamma, colon plus rectum, and bronchial carcinoma) in the first 12 observation years are shown in supplementary figure II.

The leading cause of death was CHF in 30% of classified cases ($n = 214$; Table 2, Figs. 5 and 6). Competitive risk analysis with age, sex, LVEF, and GFR as covariates showed a median 10 year CHF death risk of 12% (1st quartile: 8%, 3rd quartile: 16%; Fig. 5b).

73 patients died from infections (10% of classified deaths, Table 2, Figs. 5 and 6). There were fewer women than men in the infection group (Table 2, $p < 0.03$). In two patients, an infected device was found to be the source. Five patients had endocarditis, and 30 developed lethal pneumonia. One patient died due to spondylodiscitis, one due to urosepsis. Thirty-two deaths were due to fulminant sepsis where a specific focus of infection could not be found. Competitive risk analysis with age, sex, LVEF, and GFR as covariates showed a median 10 year infection death risk of 5% (1st quartile: %, 3rd quartile: 5.5%; Fig. 5c).

We observed various other causes of death ($n = 94$, 13.2% of classified deaths, Table 2, Fig. 6). A total of 30 deaths were of neurological cause, and the majority ($n = 20$) were caused by ischemic stroke. Ten patients died from progressive dementia, one died from intracranial hemorrhage, and one from amyotrophic lateral sclerosis. Twenty-seven patients developed terminal renal failure and died during dialysis. Eight patients died from brain hematoma due to household falls. 15 patients deceased from gastrointestinal causes: bleeding $n = 5$, liver cirrhosis $n = 6$, mesenterial infarction $n = 3$ and gastric perforation $n = 1$. Eight patients died from terminal chronic obstructive pulmonary disease (COPD), two from lethal aortic dissection, two from pulmonary embolism, and two patients commenced suicide.

In total, 67 patients (10% of classified deaths) died in a timely association to various medical procedures (Table 3, Fig. 6 and complementary Table II). The majority of these fatalities occurred during vascular surgery (24% of cases), MitraClip procedures (16% of cases), and endoscopies (15% of cases). Two deaths occurred early after cardiac catheterization and two after placement of a central line. In one patient the use of sedation for placement of the central line was suspected to be related to the event. Significantly more life years were lost associated with procedures compared to other classifications (12.1 versus 9.3 years except SD, $p = 0.02$).

A total 144 patients (20.2% of classified death) died suddenly (Table 2, Figs. 5 and 6). In 74 (53% of SD cases), a postmortem interrogation of devices, including the analysis of stored electrograms, was performed. In 39 (54% of available electrograms), repetitive cycles of VT/VF were found immediately prior to death, in the remaining we found no documented arrhythmias in the device memory. Patients dying suddenly were younger at implant and time of death than the other groups. Significantly more life years were lost associated to SD compared to other classifications (11.9 versus 9.3 years except procedures, $p = 0.02$). Competitive risk analysis with age, sex, LVEF, and GFR as covariates showed a median 10 year sudden death risk of 6.5% (1st quartile: 3.5%, 3rd quartile: 13%; Fig. 5d). A pie chart demonstrating the distribution of causes of classified death was given in Fig. 6.

Discussion

In our cohort of 2743 ICD patients with a mean follow-up of 5.4 years, only 20% of deaths were sudden despite the use of implanted devices. According to the available postmortem interrogations, more than half of SD in our series occurred during ventricular arrhythmias. ICD interventions may have been ineffective in these cases due to inadequate recovery of myocardial output due to preexisting systolic dysfunction or underlying acute myocardial ischemia. In patients with a history of recurring VTs, improved VT ablation techniques may be one strategy to mitigate this issue [7]. SD may have other non-arrhythmic causes. Patients can die from electromechanical dissociation (EMD), resulting in a blank memory of the device, as it occurs in 46% of our postmortem interrogations. The latter can be the result of undersensing of fine ventricular fibrillation [8]. EMD itself can be due to pulmonary embolism, aortic aneurysm rupture, asphyxiation, stroke, and so far undefined mechanisms. Strategies against EMD are still lacking and research in this field should be encouraged.

Our data show that CHF is still the leading cause of death in patients with ICDs and it occurred independently from primary and secondary indications. The lower survival in patients with CRT as compared to patients with regular VVI or DDD ICDs is most likely explained by the higher age, more advanced heart disease, and comorbidities. The availability of disease-modifying drugs for CHF has increased significantly in recent years [20–23] They should be used vigorously and per current guidelines also given their potential beneficial effect on arrhythmic death. Sudden death, cancer, infections, and invasive procedures may become even more important as competitive risks with further advances in medical heart failure therapy.

The death toll from cancer stems predominantly from bronchial carcinomas accounting for nearly one-third of diagnoses. The competitive risk for cancer death was 6% after 10 years. Our result corresponds with a recent meta-analysis of randomized CHF trials, which demonstrated that cancer is a major, yet overlooked cause of non-cardiovascular death in CHF [9]. Overlapping risk factors such as smoking may result in both ischemic CHF and cancer. Several cardiovascular imaging procedures (i.e., coronary angiography, scintigraphy) expose patients to ionizing radiation [10]. We speculate that the peak in the occurrence of bronchial carcinomas after 4 years in our series could be related to the latter. In this context it is to acknowledge, that safer cardiac interventions are under development [11]. Tumor screening—especially for the lung—could be helpful [12], however, such an approach had no influence on total mortality in a recent study [13]. As 28 patients of our series died from cancer in the first 2 years after ICD implantation, pre-implant evaluation and adequate selection of patients is of importance.

Several deaths were observed shortly after medical procedures. Whether there were causal relationships with the procedure itself, the associated anesthesia or the underlying disease could not be finally deduced from our data. Two deaths after coronary angiography and two after placement of central venous lines emphasize the need for critical evaluation of indication of the respective medical procedure, good training, and careful perioperative sedation in this vulnerable patient group.

Infectious death due to pneumonias and/or sepsis in CHF has recently been reported by Drodz et al. [14]. Our results are similar to their findings. New information from our study is that more men than women were prone to fatal infections, this fits to data showing a higher mortality of men in pneumonia and sepsis [15]. The reason for this remains unclear. In some cases, the implanted hardware could be the source of the bacteremia. In fulminant sepsis, this relation may have been overlooked. As a causative factor, a heightened susceptibility to infections may be present in patients with CHF [16]. We hypothesize that implantable devices could also be used to detect preclinical infections, for example, by measuring body temperature [17].

In conclusion, our data show that patients with ICDs are at an increased risk of death from various causes in long-term follow-up and treatment has to be optimized in many directions to improve prognosis. The high rates of non-cardiovascular death or SD despite the implanted device questions the notion whether ICD implantations are always appropriate and extend life. The median of life years lost in our study participants compared to the average German population was 9.7 years. In this regard, the SCD-HeFT trial showed no benefit from ICD on survival in NYHA Class III CHF patients [18]. In the DANISH trial, no effect on total mortality was observed in non-ischemic CHF, especially in elderly candidates for ICD [1]. Perhaps devices in patients who have a poor symptom response to pharmacological therapy are elderly or have severely impaired renal function should be avoided [19]. In any case, the indication for ICD implantation should be made on a critical and individual basis and based on the best available, appropriate, and current evidence for the respective patient.

Limitations

The study was a retrospective analysis and unmeasured confounding cannot be excluded. Loss of follow-up was 11, 16% of deaths could not be classified and LVEF, rhythm and serum creatinine was not collected in all patients at baseline which limits data quality and may have caused unknown bias. However, we do believe the study subset is representative of a real world setting in ambulatory cardiac care. The rates of appropriate and inappropriate ICD interventions were not collected, limiting the evaluation of effectiveness of the implanted devices. Autopsies were performed only rarely, and alternative causes of death could not be excluded. We suggest routine autopsies of device carriers, because they may help to further clarify terminal pathomechanisms, especially non-cardiac causes of SD [24–26]. Our findings stem are derived from a study carried out over a long period of time, and background therapy and medical approaches may have changed over time. However, survival analysis comparing implants before and after 2010 showed significant, albeit disappointingly small changes in prognosis, becoming evident only after 5 years.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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Authors and Affiliations

Herbert Nägele[1] · Eike Gröene[1] · Daniel Stierle[1] · Matthias P. Nägele[2]

✉ Herbert Nägele
herbert.naegele@immanuelalbertinen.de

[1] Heart Center, Cardiology Division, Department of Heart Failure and Device Therapy, Albertinen-Krankenhaus, Süntelstraße 11a, 22457 Hamburg, Germany

[2] Department of Cardiology, University Hospital Zürich, Zurich, Switzerland