Improvements in implantable cardioverter defibrillator patient stratification

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Chapter 4

Mortality Risk Score in Primary Prevention Implantable Cardioverter Defibrillator Recipients with Non Ischemic or Ischemic Heart Disease.

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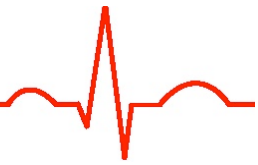
Abstract

Aims: To assess survival and to construct a baseline mortality risk score in primary prevention implantable cardioverter defibrillator (ICD) patients with non-ischemic or ischemic heart disease.

Methods and results: Since 1996, data of all consecutive patients who received an ICD system in the Leiden University Medical Center were collected and assessed at implantation. For the current study, all 1036 patients (age 63 (SD 11) years, 81% male) with a primary indication for defibrillator implantation were evaluated and followed for 873 (SD 677) days. During follow-up, 138 patients (13%) died. Non-ischemic and ischemic patients demonstrated similar survival but exhibited different factors that influence risk for mortality. A risk score, consisting of simple baseline variables could stratify patients in low, intermediate and high risk for mortality. In non-ischemic patients, annual mortality was 0.4% (95% CI 0.0-2.2%) in low risk and 9.4% (95% CI 6.6-13.1%) in high risk patients. In ischemic patients, mortality was 1.0% (95% CI 0.2-3.0%) in low risk and 17.8% (95% CI 13.6-22.9%) in high risk patients.

Conclusion: Utilisation of an easily applicable baseline risk score can create an individual patient-tailored estimation on mortality risk to aid clinicians in daily practice.



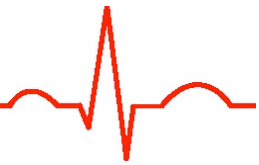
Introduction

Sudden cardiac death, mainly caused by ventricular arrhythmias degenerating into ventricular fibrillation, is responsible for 50% of all cardiac mortality worldwide.[1-3] Large randomised trials have shown a beneficial effect of an implantable cardioverter defibrillator (ICD), initially in survivors of life-threatening arrhythmias,[4-6] but more recently also as primary prevention of sudden arrhythmic death in selected non-ischemic and ischemic patients at high risk.[7-10] Since the implementation of primary prevention in the international guidelines, implantation rates have increased drastically to 160 000 yearly in the United States.[11-13] So far, data on the survival of primary prevention ICD patients are limited to post-hoc analyses of large randomised trials requiring specific patient characteristics for inclusion. This could cause the results to be less applicable to the more diverse, presently indicated population outside the setting of a clinical trial. Since 1996, all ICD recipients in the Leiden University Medical Center have been assessed and followed up. This cohort offers a unique opportunity to study mortality and to identify baseline parameters that influence risk. Furthermore, an easy-to-use and clinically applicable algorithm is created to aid clinicians in patient tailored survival estimations for patients with non-ischemic or ischemic heart disease.

Methods

Patients and study protocol

From 1996 to 2007, all consecutive patients who received an ICD system in the Leiden University Medical Center were prospectively collected in the departmental Cardiology Information System (EPD-Vision®, Leiden University Medical Center). Characteristics at baseline, data of the implant procedure, and data of all follow-up visits were recorded. For the current study, patients with a primary indication for defibrillator implantation were evaluated.



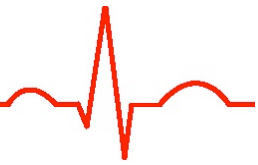
Eligibility for ICD implantation in this population was based on international guidelines for primary prevention which, due to evolving guidelines, might have changed over time. In the majority of patients, indication for an ICD was made in the presence of a depressed left ventricular ejection fraction [LVEF] with or without non sustained ventricular tachycardia (nsVT).[14, 15] Ischemic heart disease was defined as the presence of significant coronary artery disease (a diameter stenosis of at least 50% in at least one coronary artery).[16] Patients with congenital structural or monogenetic heart disease (associated with an increased risk of sudden arrhythmic death) were excluded from the analysis.

Definitions of variables

All tested variables were acquired at defibrillator implantation and were defined and categorised according to literature or common practice. Age was categorised in ≥ 70 years or < 70 years;[17] a history of nsVT was defined as a run of 3 to 30 ventricular ectopic beats at a rate > 120 beats per minute;[18] renal clearance was estimated with the formula of Cockroft-Gault and categorised in normal or stage 1 renal failure (> 90 ml/min), stage 2 renal failure (60-90 ml/min), or stage 3-5 renal failure (≤ 60 ml/min);[19] QRS duration was categorised as ≥ 130 ms or < 130 ms; LVEF was categorised as ≤ 25% or > 25%;[20] atrial fibrillation (AF) was defined as a history of AF, as documented on ECG; a history of smoking was defined if a patient had a positive answer when asked for past or present smoking;[21] and body mass index was defined as ≥ 30 kg/m^2 or < 30 kg/m^2.[22]

Device implantation

All defibrillator systems used were implanted transvenously and without thoracotomy. During the implant procedure testing of sensing and pacing thresholds and defibrillation threshold testing was performed. Used systems were manufactured by Biotronik (Berlin, Germany), Medtronic



(Minneapolis, MN, United States), Boston Scientific (Natick, MA, United States, formerly CPI, Guidant [St. Paul, MN, United States]) and St. Jude Medical/Ventritex (St. Paul, MN, United States).

Defibrillators were programmed as follows: a ventricular arrhythmia monitor zone was programmed in all patients (150-188 bpm) No therapy was programmed in this zone until during follow-up arrhythmias were detected. Ventricular arrhythmias faster than 188 bpm were initially attempted to be terminated with two bursts of ATP and, after continuation of the arrhythmia, with defibrillator shocks. In the case of a ventricular arrhythmia faster than 210 bpm, device shocks were the initial therapy. Furthermore, atrial arrhythmia detection was set to >170 bpm with SVT discriminators enabled. Settings were adapted, only when clinically indicated (i.e. hemodynamic well tolerated ventricular tachycardia at high rate; ventricular tachycardia in the monitor zone).

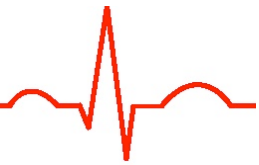
Long-term follow-up

Patient check-up was scheduled every three-six months. Device interrogation printouts were checked for appropriate and inappropriate ICD therapy (ATP or shocks). Therapies were classified as appropriate when they occurred in response to ventricular tachycardia or ventricular fibrillation and as inappropriate when triggered by sinus or supraventricular tachycardia, T-wave oversensing, or electrode dysfunction. Furthermore, follow-up included all-cause mortality.

In the Dutch health care system, all patients are followed by the implanting centre. Since periodical follow-up was performed every three to six months, patients without data on the past six months were considered as lost to follow-up.

Statistical analysis

Continuous data are expressed as mean with standard deviation (SD) or median with 25th and 75th percentile where appropriate; dichotomous data are presented as numbers and percentages.



Event rates for all-cause mortality were analyzed by method of Kaplan-Meier. Differences in event rates (non-ischemic vs. ischemic heart disease) were assessed using logistic regression. Missing values were imputed using the single imputation procedure.[23] Last follow-up data were acquired in November 2008.

To obtain a risk score, composed of robust, reproducible and non clinician driven variables, the use of medication at baseline was not used in its construction. All other baseline variables were entered as categorical variables. Firstly, the variables were studied in univariate logistic regression models, with all-cause mortality as outcome. Variables with a p-value <0.10 were further evaluated in a multivariate logistic model, using backward stepwise selection. At each step, the least significant variable was discarded from the model, until all variables in the model reached a p-value <0.25. With the variables' regression coefficient in this multivariate model, a simple risk stratification score was designed by giving a base regression coefficient the value of one point on the risk score and giving all variables the associating score, according to their multiplication of this base regression coefficient and rounding it of to the nearest whole or half number. Subsequently, the patient specific values for the predictors in the score were summed to obtain a score for each patient. The ability of the score to discriminate between patients who did and patients who did not reach the end-point was estimated by the area under the curve of the receiver operator curve. After the determination of the individual risk score per patients, cut offs were determined for a population at low, intermediate and high risk of mortality. These cut-offs were chosen to optimize the discriminative effect of the model without making groups too small. Bootstrap with 1000 resamples was used for internal validation and to assess the stability of variable selection.[24] In the calculation of the 95% confidence interval (95% CI) for event rates, a Poisson distribution of the observed number of events was presumed. All analyses (except bootstrapping analysis) were performed with SPSS for Windows, version 14.0 (SPSS, Chicago, IL). For the bootstrapping analysis, R (version 2.9.1) was used.

Results

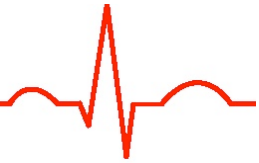
Baseline characteristics

Since 1996, data of 1086 consecutive patients receiving an ICD for primary prevention and without diagnosed congenital heart disease or monogenetic heart disease (associated with an increased risk of sudden arrhythmic death) were prospectively collected. Fifty patients (4.6%) were lost to follow-up. The remaining 1036 ICD recipients were included in the analysis. Median follow-up time was 721 days (interquartile range, 308 to 1271 days). The majority of patients (81% men, mean age 63 (SD 11) years) had a depressed LVEF (29 (SD 12) %), wide QRS (131 (SD 35) ms) and poor renal function (renal clearance 78 (SD 35) ml/min). Medication included beta blockers in 73%, ACE inhibitors or AT antagonists in 85% and diuretics for congestive heart failure in 75%. Baseline characteristics are summarised in Table 1. Seven-hundred-and-four (68%) out of all 1036 patients had ischemic heart disease. The remaining 332 (32%) patients were considered non-ischemic. Ischemic ICD recipients were more often male (87% vs. 66%, $p<0.001$), had a higher age (64 (SD 11) vs. 61 (SD 12) years, $p<0.001$) and shorter QRS duration (126 (SD 34) vs. 140 (SD 36) ms, $p<0.001$), as is shown in Table 1.

Follow-up

During a median follow-up time was 721 days (interquartile range, 308 to 1271 days), 138 patients (13%) died. Total follow-up was 2475 patient-years. Survival analysis showed a cumulative mortality of 6% (95% CI 4-7%) at one year, 17% (95% CI 13-20%) at three years and 27% (95% CI 22-32%) at six years follow-up. Stratification by type of underlying disease did not demonstrate differences in survival (Figure 1) (odds ratio, adjusted for age: 1.0, 95% CI 0.7-1.5).

A total of 6575 episodes of ventricular arrhythmia, causing appropriate device therapy, was noted in 220 (21%) patients. These consisted of 6220 arrhythmia episodes being terminated



by ATP in 148 (14%) patients and 355 episodes being terminated by ICD shocks in 113 (11%) patients.

Table 1. Baseline characteristics

	All (n=1036)	Non-ischemic (n=332)	Ischemic (n=704)	p-value	Patients with missing data
Clinical parameters					
Male gender (%)	835 (81)	220 (66)	615 (87)	<0.001	0
Age, mean (SD), years median (interquartile range), years	63 (11) 64 (56; 71)	61 (12) 64 (55; 70)	64 (11) 65 (57; 72)	<0.001	0
History of nsVT (%)	287 (28)	96 (29)	191 (27)	0.5	0
Renal clearance, mean (SD), ml/min*	78 (35)	80 (37)	77 (34)	0.3	41 (4)
QRS-duration, mean (SD), ms	131 (35)	140 (36)	126 (34)	<0.001	8 (1)
LVEF, mean (SD), %	29 (12)	29 (14)	29 (11)	0.7	59 (6)
History of atrial fibrillation (%)	283 (27)	107 (32)	176 (25)	0.015	2 (0)
Diabetes (%)	226 (22)	54 (16)	172 (24)	0.003	35 (3)
History of smoking (%)	491 (47)	146 (44)	345 (49)	0.130	63 (6)
Body mass index, mean (SD), kg/m^2	26 (4)	26 (4)	26 (4)	0.3	51 (5)
Implantable cardioverter defibrillator					
Single chamber	50 (5%)	17 (5%)	33 (5%)	0.8	0
Dual chamber	409 (40%)	83 (25%)	326 (46%)	<0.001	0
Cardiac resynchronization therapy	577 (56%)	232 (70%)	345 (49%)	<0.001	0
Medication					
Beta-blocker (%)	647 (63)	212 (64)	435 (62)	0.5	0
Sotalol (%)	112 (11)	27 (8)	85 (12)	0.057	0
ACE inhibitors / AT antagonist (%)	879 (85)	284 (86)	595 (85)	0.7	0
Statins (%)	681 (66)	106 (32)	575 (82)	<0.001	0
Diuretics for CHF (%)	781 (75)	271 (82)	510 (72)	<0.001	0
Amiodarone (%)	149 (14)	44 (13)	105 (15)	0.5	0

** Renal clearance was determined with the formula of Cockroft-Gault.*
ACE = angiotensin-converting enzyme; AT = angiotensin; CHF = congestive heart failure; LVEF = left ventricular ejection fraction; nsVT = non sustained ventricular tachycardia

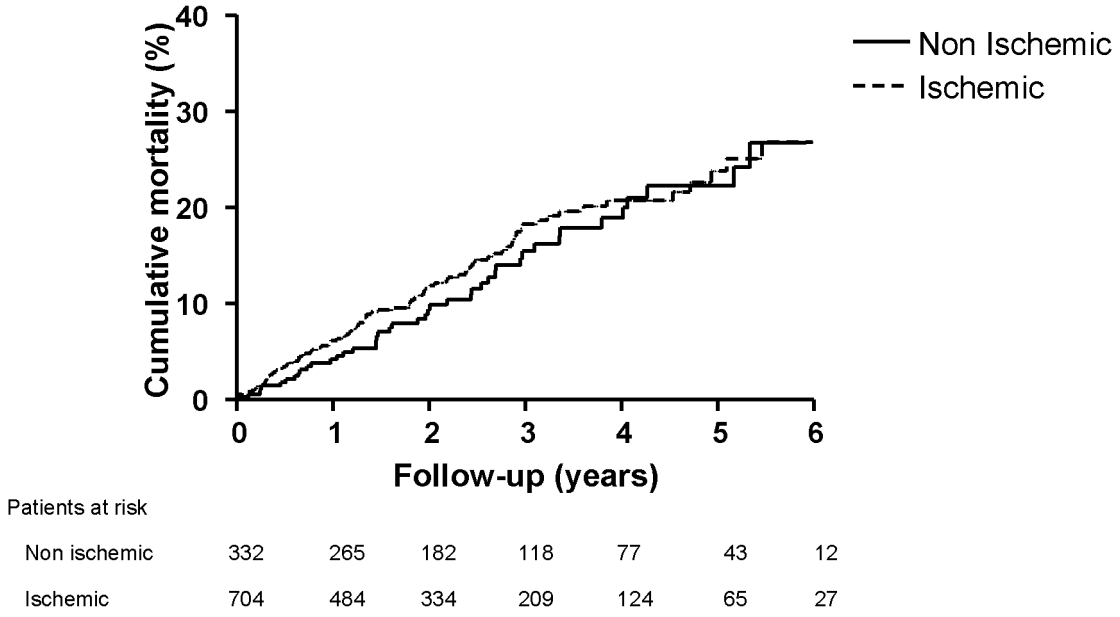


Figure 1: All-cause mortality. Kaplan-Meier curve for cumulative all-cause mortality in patients with non-ischemic heart disease vs. ischemic heart disease.

Mortality risk score in non-ischemic heart disease

Univariate and subsequent multivariate logistic regression identified the following variables as suitable for the construction of a predictive model: (1) poor renal function, (2) poor LVEF, (3) history of AF and (4) high age. The strongest predictor of mortality was a renal clearance ≤60 ml/min (odds ratio 5.4, 95% CI 1.7-17.5), when compared to renal clearance > 90 ml/min (Table 2). Bootstrap analysis showed that renal clearance, LVEF, a history of AF and high age were selected in 97%, 95%, 60%, and 49% respectively. As base regression coefficient, 0.4 was used. For each variable, the appropriate risk score was determined by calculating the multiplications of this base regression coefficient (Table 3). The area under the receiver operator curve of the acquired risk score was reasonably good: 0.76 (95% CI 0.69 – 0.82). Application of this risk score on the study population with non-ischemic heart disease facilitates the stratification in three risk categories: (1) low risk (0-2 points); (2) intermediate risk (2.5-4 points); and (3) high risk (4.5-8 points).

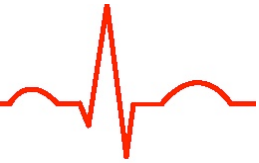


Table 2. Multivariate logistic regression model and corresponding risk score for patients with non-ischemic heart disease.

	Regression coefficient	Odds ratio (95% CI)	P-value	Score
Renal clearance*			.007	
≤60 ml/min	1.694	5.444 (1.696 – 17.472)		4
61-90 ml/min	0.837	2.309 (0.722 – 7.381)		2
LVEF ≤ 25%	0.991	2.694 (1.321 – 5.493)	.006	2.5
History of atrial fibrillation	0.481	1.693 (0.853 – 3.360)	.132	1
Age ≥ 70 yrs	0.401	1.493 (0.715 – 3.117)	.286	1

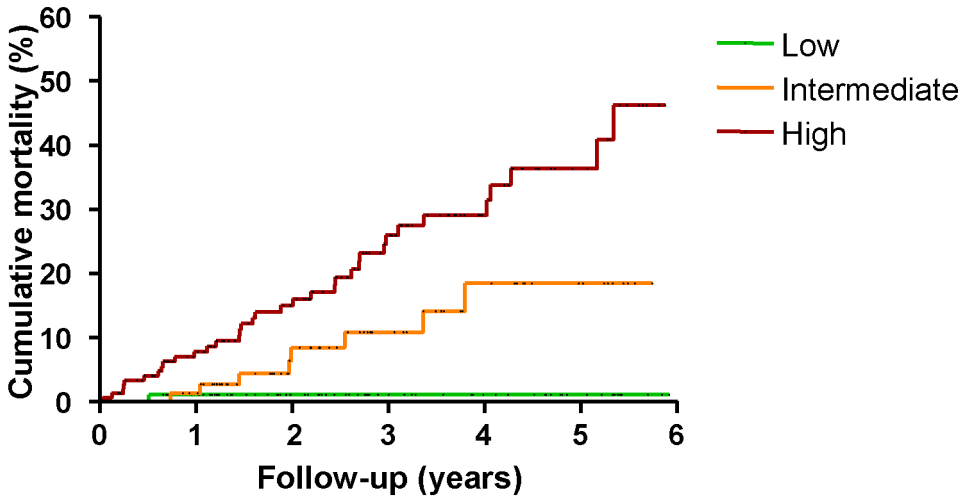
** Renal clearance was determined with the formula of Cockroft-Gault.*
CI = Confidence interval; LVEF = left ventricular ejection fraction

Table 3. Risk stratification and corresponding event rates for mortality in patients with non-ischemic heart disease.

	Risk score	Patients	Patient-years	Events	Event rate per 100 patient-years (95% CI)
Low risk	0-2	91	256	1	0.4 (0.0-2.2)
Intermediate risk	2.5-4	91	226	8	3.5 (1.5-7.0)
High risk	4.5-8	150	372	35	9.4 (6.6-13.1)
Total		332	854	44	5.2 (3.7-6.9)

In patients with low risk for all-cause mortality (91/332, 27%), one patient (1%) died during 256 patient-years, corresponding to an event-rate of 0.4 (95% CI 0.0-2.2) per 100 patient-years (Table 4). Survival analysis showed a cumulative mortality of 1% (95% CI 0-3%) at one year, three years and at six years follow-up (Figure 2). In the population with intermediate risk (91/332, 27%), eight patients (9%) died during 226 patient-years. Therefore, the calculated event rate is 3.5 (95% CI 1.5-7.0) per 100 patient-years. Survival analysis showed a survival of 1% (95% CI 0-4%) at one year, 11% (95% CI 2-19%) at three years and 18% (95% CI 6-31%) at six

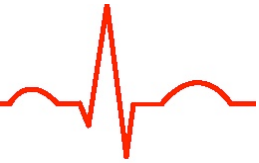
years follow-up. Finally, in the population with a risk score ≥ 4.5 points (150/332, 45%), 35 patients died during 372 patients-years, which corresponds to an event rate of 9.4 (95% CI 6.6-13.1) per 100 patients-years. For this group, survival was 8% (95% CI 3-12%) at one year, 26% (95% CI 17-35%) at three years and 46% (95% CI 30-62%) at six years follow-up.



Patients at risk

Low	91	77	54	35	27	17	6
Intermediate	91	73	46	31	20	12	4
High	150	117	84	54	32	16	4

Figure 2: Risk stratification for all-cause mortality in non-ischemic cardiomyopathy. Kaplan-Meier curve for cumulative all-cause mortality in patients with non-ischemic heart disease with low, intermediate, or high risk.



Mortality risk score in ischemic heart disease

In ICD patients with ischemic heart disease, the multivariate logistic model contained the following variables: (1) poor renal function, (2) history of smoking, (3) diabetes, (4) poor LVEF, (5) high age and (6) long QRS duration. Similar to the non-ischemic population, the strongest predictor of mortality was a renal clearance ≤60 ml/min (odds ratio 4.5, 95% CI 2.1-9.7), when compared to renal clearance > 90 ml/min (Table 4). Bootstrapping analysis showed that renal clearance, history of smoking, diabetes, LVEF, high age, and long QRS duration were selected in 100%, 100%, 98%, 99%, 97%, and 84% respectively. The area under the receiver operator curve of the acquired risk score was reasonably good: 0.81 (95% CI 0.76 – 0.87). Using 0.4 as the base regression coefficient, the risk score for each variable was determined. Stratification resulted in three risk categories: (1) low risk (0-2 points); (2) intermediate risk (3-7 points); and (3) high risk (8-13 points).

Table 4. Multivariate logistic regression model and corresponding risk score for patients with ischemic heart disease.

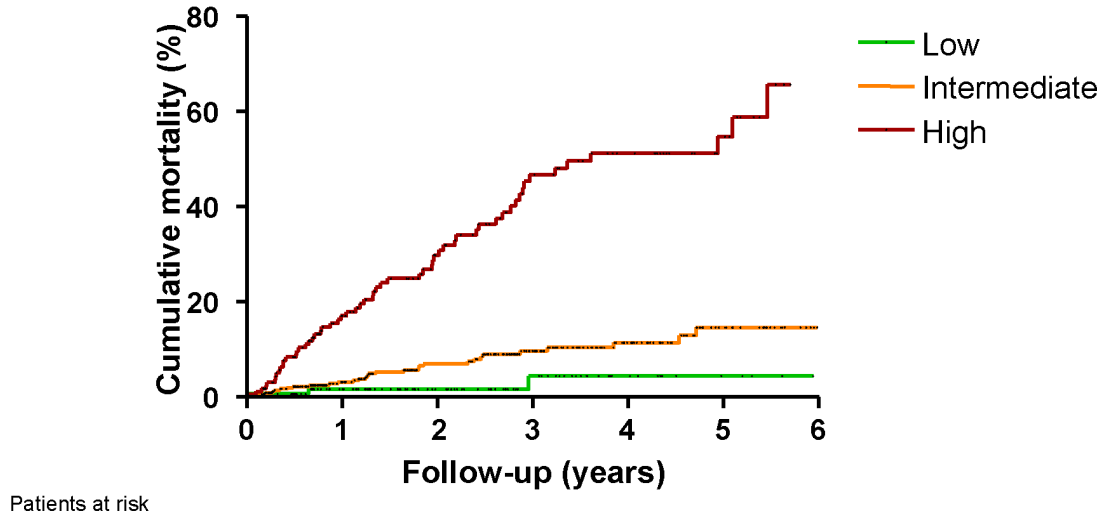
	Regression coefficient	Odds ratio (95% CI)	P-value	Score
Renal clearance*			.000	
≤60 ml/min	1.509	4.523 (2.119 – 9.657)		4
61-90 ml/min	0.388	1.474 (0.667 – 3.256)		1
History of smoking	1.146	3.145 (1.884 – 5.252)	.000	3
Diabetes	0.889	2.434 (1.466 – 4.041)	.001	2
LVEF ≤ 25%	0.870	2.388 (1.465 – 3.892)	.000	2
Age ≥ 70 yrs	0.788	2.200 (1.283 – 3.773)	.004	2
QRS duration ≥ 130 ms	0.498	1.694 (1.035 – 2.772)	.036	1

** Renal clearance was determined with the formula of Cockroft-Gault.*
CI = Confidence interval; LVEF = left ventricular ejection fraction

As can be seen in Table 5, event rates varied from 1.0 (95% CI 0.2-3.0) per 100 patient-years in the low-risk group, to 17.8 (95% CI 13.6-22.9) per 100 patient-years in the high risk group. Six-year mortality was 4% (95% CI 0-10%) in ischemic low risk patients, and 66% (95% CI 49-82%) in the high risk population.

Table 5. Risk stratification and corresponding event rates for mortality in patients with ischemic heart disease.

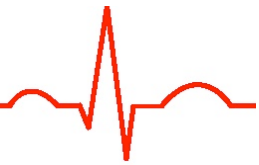
	Risk score	Patients	Patient-years	Events	Event rate per 100 patient-years (95% CI)
Low risk	0-2	127	291	3	1.0 (0.2-3.0)
Intermediate risk	3-7	416	993	31	3.1 (2.1-4.4)
High risk	8-13	161	337	60	17.8 (13.6-22.9)
Total		704	1621	94	5.8 (4.7-7.1)



Patients at risk

Low	127	91	58	35	19	11	7
Intermediate	416	292	209	135	80	42	19
High	161	104	68	41	27	14	3

Figure 3: Risk stratification for all-cause mortality in ischemic cardiomyopathy. Kaplan-Meier curve for cumulative all-cause mortality in patients with ischemic heart disease with low, intermediate, or high risk.



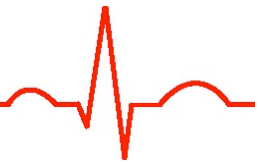
Discussion

In the current study on the long-term follow-up and the construction of an easy-to-use mortality risk score in non-ischemic and ischemic primary prevention ICD patients, the findings can be summarised as follows: 1) Cumulative mortality was approximately 5% per year; 2) Non-ischemic and ischemic patients demonstrated an equal survival; 3) Non-ischemic and ischemic ICD recipients exhibited a different risk profile in the prediction of mortality; 4) A baseline risk score can easily estimate an individual patient's risk for mortality.

Using the presented risk score, a patient, considered for primary prevention ICD treatment, could be stratified as follows: 1) determine if the patient has ischemic or non-ischemic heart disease to determine the risk factors, influencing mortality risk (Table 2 or Table 4); 2) add the risk score points, associated with patient's risk factors; 3) allocate patient as low, intermediate or high risk for mortality en estimate event-rate (Table 3 or Table 5).

Mortality

In the current analysis, 138 patients (13%) died during a mean follow-up of median follow-up time was 721 days (interquartile range, 308 to 1271 days). Cumulative mortality after one, three and six year was 6%, 17% and 27% respectively and was not different in non-ischemic or ischemic ICD recipients. Previously, few trials have been conducted on a population containing non-ischemic, as well as ischemic patients. Bardy and co-workers show a beneficial effect of defibrillator implantation in ICD recipients with non-ischemic or ischemic heart disease and congestive heart failure.[25] In their population, crude annual death rates reach up to 5.7% which are comparable to our annual crude death rate of 5.6%. Other large trials assessing the effect of an ICD in patients with ischemic heart disease only, demonstrate an annual death rate of 7.0% to 8.5%.[26, 27] These higher rates can be explained by the poor patient characteristics, required to be



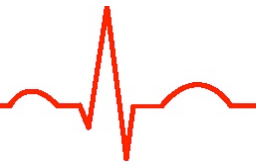
eligible for inclusion. The study population might therefore not prove to be completely representative for the "real life" population considered for defibrillator implantation.

Risk factors

The current study reveals different factors influencing risk for mortality for either type of heart disease. For all-cause mortality in non-ischemic patients, a history of AF, depressed LVEF, poor renal function and high age are predictors of mortality during follow-up. A depressed LV function has proven to be one of the most powerful markers of cardiac death in patients without an ICD, causing it to be the current main criterion for primary prevention defibrillator eligibility.[28, 29] Furthermore, AF, renal failure and high age have been described in the prediction of death in a population with, as well as without an ICD.[30-34] Furthermore, renal failure has previously been noted as one of the strongest predictors of mortality in a population with cardiac disease.[35, 36] Characteristics increasing risk for mortality in ischemic patients were more diverse: renal failure, a history of smoking, diabetes, poor LV function, high age and prolonged QRS duration. Risk stratification in the ischemic ICD recipients of MADIT II revealed similar risk factors, as described by Goldenberg et al.[37] Additionally, a sub-analysis of the MUSTT exposed these factors as predictors of mortality in the non-ICD treated arm.[38]

Risk score

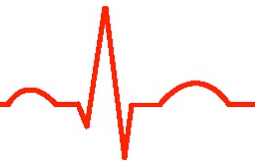
Previous studies constructing a risk score were mainly limited to patients in the setting of large clinical trials, requiring specific characteristics to be eligible for inclusion, and followed patients for a relatively short time. This might cause the findings to be less applicable to the more diverse population, currently receiving an ICD for primary prevention in a "real life" population. In a sub-study of the MUSTT, Buxton and co-workers constructed a model containing eight factors in patients with ischemic heart disease.[39] Since the MUSTT study was designed to test the ability of



electrophyiologically (EP) guided therapy to reduce risk of arrhythmic events, all included patients underwent EP testing. Inducibility of VT at EP testing was one of the factors, found to increase risk for all-cause mortality. In the current study, as in the present population receiving ICD treatment, not all patients underwent EP testing, therefore making it hard to assess its prognostic value. The power of the presented model to correctly identify patients in the MUSTT was 0.78, which is comparable to the 0.81 in the current study. Goldenberg and co-workers constructed a model with five factors in the post-myocardial infarction population of the MADIT II.[40] This model, containing New York Heart Association functional class, AF, a wide QRS, high age and renal failure, shows substantial resemblance with the model constructed in the current study.

Clinical implications

The results of this study imply that the large population, currently indicated for ICD treatment, can be easily stratified for mortality risk. The proposed risk score can prove an easily applicable mean to aid clinicians in making individual patient-tailored statements on risk for mortality, prior to defibrillator implantation in daily practice. Its utilisation could greatly increase survival estimation for the clinician, as well as the patient. Of note that the proposed risk score does require validation. Furthermore, clinicians have shown concern that the population, eligible for primary prevention ICD treatment, is of such magnitude that provision of ICD therapy will strain financial resources and the pool of trained personnel.[41, 42] In current daily practice, the choice on the most efficient allocation of ICD treatment is mostly based on the life expectancy of the patient. With the current study, a group of patients, currently indicated for ICD treatment, can be identified who have a very short life expectancy, regardless of ICD implantation. These findings could aid clinicians in current daily practice in their choices for the optimal allocation of ICD treatment.

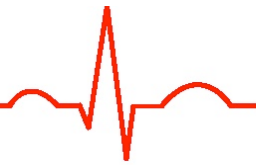


Limitations

This was a non-randomised prospective observational study, performed to assess the long-term follow-up in non-ischemic or ischemic primary prevention ICD patients outside the setting of a clinical trial. Since patients were collected over a period of eleven years, expanding guidelines for the implantation of defibrillators, treatment of acute myocardial infarction, and pharmacological antiarrhythmic therapy could have created a heterogeneous population.[43, 44] The currently constructed risk score does not take pharmacological treatment in consideration since inclusion of these clinician driven variables would lead to a less robust and reproducible score. Furthermore, since no control group was assessed, no statements can be made on the effect of ICD treatment. Finally, the constructed risk score requires external validation.

Conclusion

Non-ischemic and ischemic primary prevention ICD recipients demonstrate similar survival during long-term follow-up but exhibit different factors that influence risk for mortality. Utilisation of an easily applicable baseline risk score can create an individual patient-tailored estimation on mortality risk to aid clinicians in daily practice.



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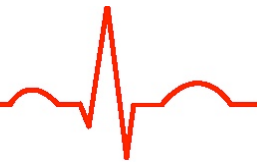

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