Mortality risk score in primary prevention implantable cardioverter defibrillator recipients with non-ischaemic or ischaemic heart disease

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Aims
To assess survival and to construct a baseline mortality risk score in primary prevention implantable cardioverter defibrillator (ICD) patients with non-ischaemic or ischaemic 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-ischaemic and ischaemic 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-ischaemic 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 ischaemic 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
Utilization of an easily applicable baseline risk score can create an individual patient-tailored estimation on mortality risk to aid clinicians in daily practice.

Keywords
Implantable cardioverter defibrillator • Mortality • Primary prevention • Risk score • Ischaemic heart disease • Cardiomyopathy

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 randomized 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-ischaemic and ischaemic 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 USA.11–13 So far, data on the survival of primary prevention ICD patients are limited to post hoc analyses of large randomized 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-ischaemic or ischaemic heart disease.

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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). Ischaemic 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). 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 categorized according to literature or common practice. Age was categorized in ≥70 years or <70 years; a history of nsVT was defined as a run of 3–30 ventricular ectopic beats at a rate >120 b.p.m.; renal clearance was estimated with the formula of Cockroft–Gault and categorized 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); QRS duration was categorized as ≥130 ms or <130 ms; LVEF was categorized as ≤25% or >25%; 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 and body mass index was defined as ≥30 or <30 kg/m².

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 was performed. Used systems were manufactured by Biotronik (Berlin, Germany), Medtronic (Minneapolis, MN, USA), Boston Scientific (Natick, MA, USA, formerly CPI, Guidant (St Paul, MN, USA)), and St Jude Medical/Ventritex (St Paul, MN, USA).

Defibrillators were programmed as follows: a ventricular arrhythmia monitor zone was programmed in all patients (150–188 b.p.m.). No therapy was programmed in this zone until during follow-up arrhythmias were detected. Ventricular arrhythmias faster than 188 b.p.m. 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 b.p.m., device shocks were the initial therapy. Furthermore, atrial arrhythmia detection was set to >170 b.p.m. with SVT discriminators enabled. Settings were adapted, only when clinically indicated (i.e. haemodynamic well-tolerated VT at high rate; VT in the monitor zone).

Long-term follow-up

Patient check-up was scheduled every 3–6 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 VT 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 healthcare system, all patients are followed by the implanting centre. Since periodical follow-up was performed every 3–6 months, patients without data on the past 6 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-ischaemic vs. ischaemic heart disease) were assessed using logistic regression. Missing values were imputed using the single imputation procedure. 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. First, the variables were studied in univariate logistic regression models, with all-cause mortality as outcome. Variables with a P-value less than 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 less than 0.25. With the variables’ regression coefficient in this multivariate model, a simple risk stratification score was defined 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 endpoint 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. 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, USA). 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 monogenic 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, 308–1271 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 summarized in Table 1.

Seven hundred and four (68%) of all 1036 patients had ischaemic heart disease. The remaining 332 (32%) patients were considered non-ischaemic. Ischaemic 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, 308–1271 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 1 year, 17% (95% CI 13–20%) at 3 years, and 27% (95% CI 22–32%) at 6 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.

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**Table 1** Baseline characteristics

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

ACE, angiotensin-converting enzyme; AT, angiotensin; CHF, congestive heart failure; LVEF, left ventricular ejection fraction; nsVT, non-sustained ventricular tachycardia.

\(^a\)Renal clearance was determined with the formula of Cockroft–Gault.

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 summarized in Table 1.

Seven hundred and four (68%) of all 1036 patients had ischaemic heart disease. The remaining 332 (32%) patients were considered non-ischaemic. Ischaemic 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.

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

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.
Mortality risk score in non-ischaemic heart disease

Univariate and subsequent multivariate logistic regression identified the following variables as suitable for the construction of a predictive model: (i) poor renal function, (ii) poor LVEF, (iii) history of AF, and (iv) high age. The strongest predictor of mortality was a renal clearance $\leq 60$ mL/min (odds ratio 5.4, 95% CI 1.7–17.5), when compared with 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-ischaemic heart disease facilitates the stratification in three risk categories: (i) low risk (0–2 points); (ii) intermediate risk (2.5–4 points); and (iii) high risk (4.5–8 points).

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 1, 3, and 6 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 1 year, 11% (95% CI 2–19%) at 3 years, and 18% (95% CI 6–31%) at 6 years follow-up. Finally, in the population with a risk score $\geq 4.5$ 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 patient-years. For this group, survival was 8% (95% CI 3–12%) at 1 year, 26% (95% CI 17–35%) at 3 years, and 46% (95% CI 30–62%) at 6 years follow-up.

Mortality risk score in ischaemic heart disease

In ICD patients with ischaemic heart disease, the multivariate logistic model contained the following variables: (i) poor renal function, (ii) history of smoking, (iii) diabetes, (iv) poor LVEF, (v) high age, and (vi) long QRS duration. Similar to the non-ischaemic population, the strongest predictor of mortality was a renal clearance $\leq 60$ mL/min (odds ratio 4.5, 95% CI 2.1–9.7), when compared with 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: (i) low risk (0–2 points); (ii) intermediate risk (3–7 points); and (iii) high risk (8–13 points).

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

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

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Regression coefficient</th>
<th>Odds ratio (95% CI)</th>
<th>P-value</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal clearance*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\leq 60$ mL/min</td>
<td>1.694</td>
<td>5.444 (1.696–17.472)</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>61–90 mL/min</td>
<td>0.837</td>
<td>2.309 (0.722–7.381)</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>LVEF $\leq 25%$</td>
<td>0.991</td>
<td>2.694 (1.321–5.493)</td>
<td>0.006</td>
<td>2.5</td>
</tr>
<tr>
<td>History of AF</td>
<td>0.481</td>
<td>1.693 (0.853–3.360)</td>
<td>0.132</td>
<td>1</td>
</tr>
<tr>
<td>Age $\geq 70$ years</td>
<td>0.401</td>
<td>1.493 (0.715–3.117)</td>
<td>0.286</td>
<td></td>
</tr>
</tbody>
</table>

CI, confidence interval; LVEF, left ventricular ejection fraction.

*Renal clearance was determined with the formula of Cockroft–Gault.

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

<table>
<thead>
<tr>
<th>Risk score</th>
<th>Patients</th>
<th>Patient-years</th>
<th>Events</th>
<th>Event rate per 100 patient-years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>0–2</td>
<td>91</td>
<td>256</td>
<td>1</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>2.5–4</td>
<td>91</td>
<td>226</td>
<td>8</td>
</tr>
<tr>
<td>High risk</td>
<td>4.5–8</td>
<td>150</td>
<td>372</td>
<td>35</td>
</tr>
<tr>
<td>Total</td>
<td>332</td>
<td>854</td>
<td>44</td>
<td></td>
</tr>
</tbody>
</table>
survival was 4% (95% CI 0–10%) in ischaemic low risk patients and 66% (95% CI 49–82%) in the high risk population (Figure 3).

### Discussion

In the current study on the long-term follow-up and the construction of an easy-to-use mortality risk score in non-ischaemic and ischaemic primary prevention ICD patients, the findings can be summarized as follows: (i) cumulative mortality was ~5% per year; (ii) non-ischaemic and ischaemic patients demonstrated an equal survival; (iii) non-ischaemic and ischaemic ICD recipients exhibited a different risk profile in the prediction of mortality; (iv) 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: (i) determine if the patient has ischaemic or non-ischaemic heart disease to determine the risk factors, influencing mortality risk (Table 2 or Table 4); (ii) add the risk score points, associated with patient’s risk factors; (iii) allocate patient as low, intermediate, or high risk for mortality and estimate event rate (Table 3 or Table 5).

### Mortality

In the current analysis, 138 patients (13%) died during a median follow-up of 721 days (interquartile range 308–1271 days). Cumulative mortality after 1, 3, and 6 years was 6, 17, and 27%, respectively, and was not different in non-ischaemic or ischaemic ICD recipients. Previously, few trials have been conducted on a population containing non-ischaemic, as well as ischaemic patients. Bardy et al.7 show a beneficial effect of defibrillator implantation in ICD recipients with non-ischaemic or ischaemic heart disease and congestive heart failure. 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 ischaemic heart disease only, demonstrate an annual death rate of 7.0–8.5%.9,10 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-ischaemic 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.1,23 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.23–27 Furthermore, renal failure has previously been noted as one of the strongest predictors of mortality in a population with cardiac disease.26,28 Characteristics increasing risk for mortality in ischaemic patients were more diverse: renal failure, a history of smoking, diabetes, poor LV function, high age, and prolonged QRS duration. Risk

![Figure 2](image_url)

**Figure 2** Risk stratification for all-cause mortality in non-ischaemic cardiomyopathy. Kaplan–Meier curve for cumulative all-cause mortality in patients with non-ischaemic heart disease with low, intermediate, or high risk.
stratification in the ischaemic ICD recipients of MADIT II revealed similar risk factors, as described by Goldenberg et al.27 Addition-
ally, a sub-analysis of the MUSTT exposed these factors as predic-
tors of mortality in the non-ICD treated arm.25

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 ischaemic heart disease.25

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

<table>
<thead>
<tr>
<th>Risk score</th>
<th>Patients</th>
<th>Patient-years</th>
<th>Events</th>
<th>Event rate per 100 patient-years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>0–2</td>
<td>127</td>
<td>291</td>
<td>3</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>3–7</td>
<td>416</td>
<td>993</td>
<td>31</td>
</tr>
<tr>
<td>High risk</td>
<td>8–13</td>
<td>161</td>
<td>337</td>
<td>60</td>
</tr>
<tr>
<td>Total</td>
<td>704</td>
<td>1621</td>
<td>94</td>
<td>5.8 (4.7–7.1)</td>
</tr>
</tbody>
</table>

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

Goldenberg et al.27 constructed a model with five factors in the post-myocardial infarction population of the MADIT II. 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 state-
ments on risk for mortality, prior to defibrillator implantation in daily practice. Its utilization could greatly increase survival esti-
ration for the clinician as well as the patient. Of note that the pro-
posed risk score does require validation. Furthermore, clinicians
have shown concern that the population, eligible for primary pre-
vention ICD treatment, is of such magnitude that provision of ICD
therapy will strain financial resources and the pool of trained per-
sonnel.29,30 In current daily practice, the choice on the most effi-
cient 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 implant-
tation. These findings could aid clinicians in current daily practice
in their choices for the optimal allocation of ICD treatment.

Limitations

This was a non-randomized prospective observational study, per-
formed to assess the long-term follow-up in non-ischaemic or
ischaemic primary prevention ICD patients outside the setting of
a clinical trial. Since patients were collected over a period of
11 years, expanding guidelines for the implantation of defibrillators,
treatment of acute myocardial infarction, and pharmacological anti-
arrhythmic therapy could have created a heterogeneous popu-
lation.11,14 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 treat-
ment. Finally, the constructed risk score requires external
validation.

Conclusion

Non-ischaemic and ischaemic primary prevention ICD recipients
demonstrate similar survival during long-term follow-up but
exhibit different factors that influence risk for mortality. Utilization 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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References