A validated risk model for 1-year mortality after primary prevention implantable cardioverter defibrillator placement

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Objective We sought to determine survival for patients with heart failure after an implantation of an implantable cardioverter defibrillator (ICD) for primary prevention in the United States and to develop a simple model that would predict mortality risk.

Background Clinical trials have found that patients with heart failure with a 1-year mortality risk near 20% may not benefit from an ICD.

Methods We identified patients from the ICD Registry of the National Cardiovascular Disease Registries who underwent ICD implantation for primary prevention from 2007 to 2009. Two risk scores for mortality were developed in 2 cohorts: one limited to those with a B-type natriuretic peptide (BNP) value and a second for all patients. The scores were obtained from derivation datasets and tested in a validation sets using logistic regression models and classification and regression trees.

Results In a primary prevention population with BNP available (18,725) the 6 variables most predictive of 1-year mortality were age ≥75, BNP ≥700 pg/mL, chronic lung disease, dialysis, blood urea nitrogen ≥30 mg/dL, and systolic blood pressure <120 mmHg. Patients with zero risk factors had a 3.3% one-year mortality compared to a 66.7% one-year mortality for those with all 6 risk factors. Those with ≥3 risk factors (24.0% of the population) had a 25.8% one-year mortality. A second score using a larger cohort that did not consider BNP identified similar risk factors.

Conclusions A simple validated risk score can identify patients at high and low risk for death within a year after ICD placement. A large fraction of those currently implanted with an ICD in the United States have a high 1-year mortality and may not benefit from ICD therapy. (Am Heart J 2015;170:281-289.e2)

Implantable cardioverter defibrillators (ICDs) improve survival for selected patients with heart failure and reduced left ventricular ejection fraction. High-risk patients with a predicted life expectancy of less than a year (1-year survival <50%) are not considered candidates per published guidelines[1]; the SCD-HeFT and MADIT-2 trials found that patients with expected 1-year mortality risk >20% are unlikely to benefit.[2,3]

Building upon this prior work we sought to determine the distribution of all-cause mortality following an implantation of an ICD in the United States. In particular we sought to determine the fraction of patients with 1-year mortality over 20%. While studies have examined mortality following an ICD implantation in the Medicare population[4] we used the Social Security Death Index which allowed inclusion of all ages within the National Cardiovascular Disease Registry (NCDR) ICD Registry.[5,6]

Methods

We used the data from the ICD Registry which was created in 2006 in response to a mandate from the Centers of Medicare and Medicaid Services that required that all hospitals report data on ICD implantations for primary prevention.[5] Although hospitals are required to enter data only for Medicare beneficiaries, the majority of institutions register all ICD recipients and 79% of all patients in the registry come from these hospitals.[5] Institutions submit data using a standardized questionnaire to submit clinical information, including patient characteristics, device used, and hospital course. Only hospitals achieving 95% completeness of specific data

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elements were included in the data analysis. The data are subject to quality-control checks of missing or improperly coded items and an annual random audit is conducted through site visits.[7]

The authors are solely responsible for the design and conduct of this study, all analyses, the drafting and editing of the manuscript, and its final contents.

Patient populations

First risk score (primary prevention population with B-type natriuretic peptide available). We identified patients who underwent ICD implantation for primary prevention from 2007 to 2009 in the United States and were reported to the ICD Registry (N = 303,285). We excluded 31,713 patients from facilities that did not report all their ICD implantations in a specific quarter to the registry. In addition we excluded patients with a pre-existing ICD (67,261), cardiac arrest (8,467), left ventricular ejection fraction unknown or higher than 35% (15,182), use of an epicardial lead (2,491) and prior cardiac transplant (586). We also excluded 5,140 patients that could not be matched to survival data from the Social Security Death Index. This left 172,985 patients. For the primary analysis we further limited the population to those without New York Heart Association (NYHA) class IV, without CRT-D, and with a B-type natriuretic peptide (BNP) data available (N = 18,725). These patients were split into derivation (n = 9,399) and validation (n = 9,320) cohorts.

Second risk score: all patients

We repeated the analyses using the larger cohort of 172,985 patients, in which Patients with New York Heart Association class IV, CRT-D, and BNP missing were not excluded. This risk score did not consider BNP given that it was missing in a large fraction. This group was also split into derivation (n = 86,602) and validation (n = 86,683) cohorts.

Primary outcome

The outcome was death within the year following ICD implantation determined by linking the patient's social security number with the Social Security Death Index Data.

Statistical analysis

Patient characteristics were compared between patients who did and did not die within one year of the procedure using the chi-square test for categorical variables and unbalanced t-test for continuous variables. PR interval was missing in more than 5% and was excluded as a potential risk factor. All other variables had missing values in less than 0.5% of cases. To obviate case-wise deletion in the regression analyses, missing values were imputed as the most common category for the categorical values and the median value for continuous variables. In the model analyses, significant variables associated with the death within one year of the procedure were identified through the stepwise selection method in a multivariable logistic regression model. We then used a Classification and Regression Tree (CART) analysis to develop a risk algorithm with the selected significant variables.[8,9] CART is a non-parametric, empiric statistical method that produces easily interpretable decision trees that can be applied in clinical care. With the CART analyses, 6 predictors associated with 1-year mortality in the derivation cohort were found in the first 3 branches. For continuous variables CART determined the threshold to optimize classification; these thresholds were rounded to the nearest 5 or 10-U level. In cases where CART identified multiple thresholds (for different branches) we chose an intermediate threshold. To simplify the process, a scoring system was then created that assigned one point to each parameter identified in the CART prediction algorithm, which provides a risk group of 1-year survival with a score from 0 to 6. In order to identify a very low risk group we also examined those with 0 risk factors using a lower age cutoff (≤65). In secondary analyses, we examined the larger cohort with BNP frequently missing to determine the stability and predictive value of the top 6 risk factors.

We validated the scoring system for 1-year mortality developed in the derivation cohort in the remaining half of the dataset (validation cohort). Areas under the receiving operating characteristic curve (AUC) were determined for both derivation and validation cohorts. The performance of the risk score was also evaluated in subgroups of those electively admitted for an ICD (yes/no) and those receiving CRT (yes/no). The statistical level of .05 was used for significance. The CART analyses were performed using R version 2.13.1 and all other analyses were performed using the SAS statistical package version 9.2 (SAS Institute, Cary, NC).

Source of funding and conduct of the study

All analyses were approved by the Yale University Human Investigation Committee. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the manuscript, and its final contents. No extramural funding was used to support this work.

Results

Patient characteristics

Patient characteristics of the 172,985 patients are listed in Tables I and II. The mean patient age was 67 ± 13 years, 27% were female and 20% were non-white. Differences in clinical characteristics between derivation and validation cohorts were minimal.

Mortality

A total of 15,239 (8.8%) died within one year of ICD implantation. Patients who died were older, had more comorbid diseases (Table I), lower left ventricular ejection