Early mortality after implantable cardioverter defibrillator: Incidence and associated factors

Rodrigue Garcia, Serge Boveda, Pascal Defaye, Nicolas Sadoul, Kumar Narayanan, Marie-Cécile Perier, Didier Klug, Laurent Fauchier, Christophe Leclercq, Dominique Babuty, et al.

Original Article

Early Mortality after Implantable Cardioverter Defibrillator: Incidence and Associated Factors

Authors:
Rodrigue GARCIA[a], MD, MSc, Serge BOVEDA[b], MD, PhD, Pascal DEFAYE[c], MD, PhD, Nicolas SADOUL[d], MD, PhD, Kumar NARAYANAN[e,f], MD, Marie-Cécile PERIER[f], MPH, Didier KLUG[g], MD, PhD, Laurent FAUCHIER[h], MD, PhD, Christophe LECLERCQ[i], MD, PhD, Dominique BABUTY[h], MD, PhD, Pierre BORDACHAR[j], MD, PhD, Daniel GRAS[k], MD, Jean-Claude DEHARO[l], MD, PhD, Olivier PIOT[m], MD, Rui PROVIDENCIA[n], MD, Eloi MARIJON[f,n,o], MD, PhD, Vincent ALGALARRONDO[p], MD, PhD; On behalf of the DAI-PP Investigators

Affiliations:
[a]: CHU Poitiers, 86021 Poitiers, France
[b]: Clinique Pasteur, 31076 Toulouse, France
[c]: CHU Michallon, 38700,Grenoble, France
[d]: CHU Brabois, 54500 Vandœuvre-lès-Nancy, France
[e]: Maxcure Hospitals, Hyderabad, 500081 Telangana, India
[f]: Paris Cardiovascular Research Center (Inserm U970), 75015 Paris, France
[g]: CHRU Lille, 59000 Lille, France
[h]: CHU Trousseau, 37170 Chambray-les-Tours, France
[i]: CHU Pontchaillou, 35000 Rennes, France
[j] CHU Haut-Lévêque, 33604 Pessac, France
[k] Hôpital privé du Confluent, 44277 Nantes, France
[l] CHU La Timone, 13005 Marseille, France
[m] Centre Cardiologique du Nord, 93200 Saint Denis, France
[n] Clinique Pasteur, 31076 Toulouse, France; Barts Heart Centre, Barts Health NHS Trust, EC1A 7BE London, UK.
[o] AP-HP – Hôpital Européen Georges Pompidou, 75015 Paris and Université Paris Descartes, 75006 Paris, France
[p] AP-HP - Hospital Bichat Claude Bernard and Université Paris Diderot, 75018 Paris, France

Total word count: 4,029 words (except tables)

Funding: The DAI-PP registry was funded by the French Institute of Health and Medical Research, the ART (Association de Rythmologie Toulousaine), and the French Society of Cardiology.

Corresponding author contact information:
Vincent Algalarrondo
Service de Cardiologie, Hôpital Bichat Claude Bernard
46 rue Henri Huchard
75877, Paris, France
Tel: +33 1 40 25 77 85

Email: vincent.algalarrondo@aphp.fr

Disclosures: Dr Garcia received consulting fees from Abbott and Boston Scientific, alliance BMS/Pfizer and Bayer. Dr. Boveda has served as a consultant for Medtronic, Boston Scientific and LivaNova. Pr Defaye received consulting fees and research grants from Abbott, Microport, Medtronic and Boston Scientific. Pr Klug received consulting fees from Medtronic, Biotronik, Abbott, Microport and Boston Scientific. Pr. Sadoul has served as a consultant for Boston Scientific, Biotronik, Medtronic, LivaNova and St. Jude Medical. Pr Leclercq received research grants from Medtronic, Abbott, Boston scientific and Biotronik. Pr Babuty received research grants from Medtronic and Boston Scientific. Dr Gras received consulting fees from Biotronik, Abbott, Medtronic, and Boston Scientific. Dr Piot received consulting fees or research grants from Microport, Medtronic and Abbott. Pr Marijon received research grants from Abbott, Biotronik, Boston Scientific France, Microport, Medtronic France, Alliance BMS/Pfizer, Boehringer Ingelheim, ZOLL. Dr Algalarrondo received research grants from Abbott, Biotronik, Boston Scientific France, Microport, Medtronic France and Pfizer. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Abstract (249 words)

Background: According to guidelines, implantable cardioverter defibrillator (ICD) candidates must have a "reasonable expectation of survival with a good functional status >1 year". Identifying risk for early mortality in ICD candidates could be challenging. We aimed to identify factors associated with a ≤1-year survival among patients implanted with ICDs.

Methods: The DAI-PP program was a multicenter, observational French study that included all patients who received a primary prevention ICD in the 2002–2012 period. Characteristics of patients who survived ≤1 year following the implantation were compared with those who survived >1 year, and predictors of early death determined.

Results: Out of the 5,539 enrolled patients, survival status at 1 year was known for a total of 5,457, and overall 230 (4.2%) survived ≤1 year. Causes of death were similar in the two groups. Patients with ≤1-year survival had lower rates of appropriate (14 vs. 23%; P=0.004) and inappropriate ICD therapies (2 vs. 7%; P=0.009) than patients who lived >1 year after ICD implantation. In multivariate analysis, older age, higher NYHA class (≥III), and atrial fibrillation

were significantly associated with ≤1-year survival. Presence of all 3 risk factors was associated with a cumulative 22.63% risk of death within 1 year after implantation.

Conclusions: This is the largest study determining the factors predicting early mortality after ICD implantation. Patients dying within the first year had low ICD therapy rates. A combination of clinical factors could potentially identify patients at risk for early mortality to help improve selection of ICD candidates.

Keywords: Implantable cardioverter defibrillator; Guideline; Mortality; Sudden Cardiac Death; Heart failure; Prevention.

Abbreviations

95%CI: 95% confidence interval

HR: Hazard ratio

ICD: implantable cardioverter defibrillator

LVEF: left ventricular ejection fraction

NYHA: New York Heart Association

SCD: Sudden Cardiac Death

Text

Introduction

Efficacy of implantable cardioverter-defibrillators (ICD) for primary prevention of sudden cardiac death (SCD) has been well established through a number of large randomized trials, providing consistent results.[1,2] Current American and European guidelines (ACC/AHA/ESC) for the management of heart failure state that "ICD therapy is recommended (…) in selected patients (…) who have reasonable expectation of meaningful survival for more than 1 year"[3] or "who are expected to survive for at least 1 year with good functional status".[4] Indeed, the competing risk between arrhythmic sudden cardiac death and non-arrhythmic death could potentially reduce the utility of the ICD, more so, as the average age of patients hospitalized for heart failure is 70 or 80 years with frailty and frequent concomitant comorbidity; thereby probably leading to some futile ICD implantations.[5,6]

That being said, accurately identifying subjects at high risk of early mortality is challenging. One-year mortality after ICD implantation ranges from 11 to 30% according to different studies[5] and no criteria have been clearly described to identify high risk patients.

We therefore aimed to describe factors predicting early (≤1 year) mortality among primary prevention ICD recipients in a large, contemporary, real-world French cohort.

Methods

Population

The present analysis is part of the "Defibrillateur Automatique Implantable–Prevention Primaire" (DAI-PP) Program, a multicenter, observational study that enrolled consecutive ICD recipients from 1 January 2002 to 31 December 2012.[6–8] The study was conducted according to the

ethical principles stated in the Declaration of Helsinki, approved by the Institutional Review Board of each participating hospital, registered on ClinicalTrials.gov (NCT01992458), and data file declared to the French data protection committee (Commission Nationale Informatique et Liberté, CNIL, N°913203).

Patients with either ischemic, or non-ischemic cardiomyopathy, receiving an ICD for the primary prevention of SCD were included. Exclusion criteria were secondary prevention ICD implantations and patients with other etiologies (Brugada syndrome, hypertrophic cardiomyopathy …). Primary prevention was defined as no prior history of sudden cardiac arrest and/or ventricular tachycardia/ fibrillation. The choice of ICD type and device settings were left to the discretion of the operator.

As previously described, all variables at the time of the procedure were defined and categorized according to literature or common practice.[9–11] In addition to the New York Heart Association (NYHA) functional class, we noted the etiology of the underlying heart disease (ischemic or non-ischemic cardiomyopathy). Patients were characterized at the time of ICD implantation. Ischemic cardiomyopathy (ICM) was defined as left ventricular ejection fraction (LVEF) <35% with a documented lesion (stenosis >70%) in at least one of the three main coronary arteries, with or without a history of myocardial infarction and/or revascularization. To classify patients as non-ischemic cardiomyopathy, coronary artery disease had to be excluded on coronary angiography. Glomerular filtration rate (GFR), was estimated with the Cockroft–Gault formula and categorized in two categories (≥60 and <60 mL/min); QRS duration was categorized as <120, ≥120 and <150 ms and ≥150 ms. Left ventricular ejection fraction (LVEF) documented during the last 3 months before ICD implantation was collected. Atrial fibrillation (AF) was defined as a history of AF (paroxysmal or persistent), documented on ECG or 24-hour Holter monitoring. Co-morbidities were systematically collected: cancer, chronic obstructive pulmonary disease, chronic renal

failure, chronic liver disease, history of transient ischemic neurological attack, and others (including diabetes mellitus). Medication was also collected at baseline.

Patient follow-up and clinical outcomes

Occurrence of death within the first year of implantation was the assessed outcome. Vital status data were obtained from the hospital or the general practitioner and were systematically corroborated through the French National Institute for Statistics and Economic Research. Causes of death were obtained on Medical Causes of Death (CépiDc–INSERM). The CépiDc–INSERM is an academic public institution focused on the analysis of circumstances and causes of death documented with death certificate and medical records. Causes of deaths were adjudicated by 2 investigators according to the following classification: SCD, cardiovascular non-SCD (including progressive heart failure death and stroke), non-cardiovascular death, ICD complication related death, and "unknown" when the available information did not enable the investigators to appropriately identify the cause of death.

All detected ICD therapies were collected and classified as appropriate or inappropriate. Appropriate ICD therapy was defined as the successful termination of a sustained ventricular tachycardia or ventricular fibrillation episode by single or multiple shocks, antitachycardia pacing or both.

Peri-operative complications were defined as those that appeared before discharge and early complications were defined as those that appeared during the first 30 days after device implantation. They included lead dislodgment, bleeding or hematoma, sepsis, cardiac tamponade, pneumothorax, and death.

Statistical analysis

Preparation of this report was carried out in accordance with the STrengthening the Reporting of Observational studies in Epidemiology (STROBE) statement. Data are summarized using mean (SD) or median (Q1-Q3) for continuous variables when appropriate and n (%) for categorical variables. Comparisons between groups were performed using Student's t-test or Mann-Whitney test for quantitative variables and using a chi-square test for qualitative variables. The Cox proportional hazard model was used to identify variables independently associated with a survival ≤1 year and significant covariates (P<20%) in univariate analysis entered a stepwise multivariate regression. The model was initially adjusted for the following variables: age, sex, NYHA class, LVEF, atrial fibrillation, early complications and device types (single chamber, dual chambers or CRT devices). Kaplan-Meier curves of survival rate across patients according to the number of risk factors were plotted and compared using the log-rank test and the C-statistic was computed. For all analyses, a two-tailed P-value <0.05 was considered statistically significant. All analyses were performed at the Paris Epidemiology Unit of the Cardiovascular Research Centre of the French Institute of Health and Medical Research using SAS 9.4 (Statistical Analysis System, Cary, NC, USA).

Results

Population characteristics at baseline and follow-up

Overall, among the 5,539 patients enrolled in the program, survival status at 1 year was known for a total of 5,457 primary prevention ICD recipients. For the whole population, mean age was 62.5 ± 11years, and 84.9% of patients were male. A total of 3,304 patients (60.2%) presented with ischemic cardiopathy and median ejection fraction was 25 [22; 30] %. 1,258 (22.9%)

patients were implanted with single-chamber ICD, 1,280 (23.3%) with dual-chamber ICD, and 2,952 (53.8%) had cardiac resynchronization therapy associated with ICD.

Mean follow-up was 3.1 ± 2.2 years. Amongst the 5,457 patients included for analysis, 230 (4.2%) patients died within the first year following ICD implantation *vs.* 596 [3.52 per 100 person-years] subsequently. Baseline characteristics of patients according to the 1-year vital status are listed in **Table 1**. When compared to patients who survived more than 1 year, patients who died within the first year following ICD implantation were older, were more likely to be NYHA class III-IV (48% *vs.* 74%, P<0.0001), had lower LVEF, longer QRS duration, higher rate of atrial fibrillation, lower renal function, were more likely to have a concomitant respiratory failure and to receive a cardiac resynchronization therapy (**Table 1**).

Follow-up and survival analysis

Peri-operative complications were more common in patients who died early compared to those who did not (18.3 vs. 13.2% respectively; P=0.03) (see **Table 2**). In the same way, sepsis after implantation was more frequent in the group of patients who died within the first year of implantation compared to those who did not (5.1 vs. 2.7% respectively; P=0.04).

Causes of death were similar in the two groups, with the leading cause of death being related to terminal heart failure (52% in the group with early mortality vs. 48% in the other group).

Patients who died early had less appropriate and inappropriate ICD therapies than patients who lived >1 year after ICD implantation (respectively 14 vs. 23%; P=0.004 and 2 vs. 7%; P=0.009).

Similarly, the rate of appropriate schocks was 281.86 (171.37 ; 392.344) per 1000 person-years for patients with early mortality vs. 75.56 (70.91 ; 80.22) per 1000 person-years for the patients who lived longer (p<0.0001 between the two groups).

Prediction of 1-year mortality after implantation

In multivariate analysis, the following factors were independently and significantly associated with early mortality: age ≥70 years, NYHA class III-IV and atrial fibrillation (see **Table 3**). The 1-year survival following ICD implantation was 98.34% for patients with no risk factors and decreased significantly according to the number of the preoperative risk factors, up to 87.27% for patients with all 3 risk factors (see **Figure 1**; log-rank, P<0.0001). The C-statistic of the score to predict the early mortality was 0.68. Finally, the DAI-PP registry was also used to develop the ScREEN score, a multivariate tool that ranged from 0 to 5 and that was able to predict higher CRT response and survival as it increased.[12] When the early mortality was calculated for each value of the ScREEn score, it appeared that early mortality decreased progressively as the ScREEN score increased, that is to say for the highest expected rate of CRT response (see the **e-Table 1**). For the CRT-D population, the C-statistic of the ScREEN score for discriminating early mortality was 0.647. In this specific population, the discrimination of the early mortality score was slightly lower (C-statistic: 0.603). However, if we compare the 2 scores in the population of patients with single or dual chamber ICDs, ScREEN performed worse than the early death score (C-statistics were respectively 0.616 for the ScREEN score and 0.659 for the early death score).

Discussion

In this large, real world observational study of primary prevention ICD recipients, 4.2% of the patients died within the first year following ICD implantation. Early mortality was especially high for patients with older age, advanced NYHA class and atrial fibrillation. Thus it may be possible to identify patients less likely to benefit from primary prevention ICDs due to high competing risk for early mortality.

Avoiding ICD implantation in subjects at risk of early mortality

The 1-year death rate found in our series was comparable to those previously reported in the ICD arm of major randomized trials: 5% for MADIT, 6% for SCD-Heft and 8% for MADIT-II.[13,14] This suggests that even in real world settings, ICD candidates are highly selected based on favorable clinical profile, from the general population of patients suffering from heart failure. We found that early mortality was associated with older age, advanced NYHA class and atrial fibrillation. Nevertheless, these factors might change as patient populations selected for ICD implantation continue to evolve over time and with advances in heart failure medical therapy.[16] Our results confirm previous studies that challenged the usefulness of ICD implantation in patients with advanced NYHA class or older age[15], but we also report that presence of a single prognostic factor affected survival only in a very modest way. Conversely, there was a cumulative effect of each comorbidity on survival, which strengthens the need for comprehensive evaluation and shared decision-making in this patient population.[16] Finally, even in this large cohort, there was no single powerful clinical feature predicting early mortality after ICD implantation as only 12.7% of patients having all the 3 risk factors died within the first year following ICD implantation.

Comparison to previous studies

Our results could be compared with those of previous studies that addressed the question of predicting early deaths in primary prevention ICD candidates. **e-Table 2** summarizes the main findings of these two studies and ours. In 2012, Kramer and colleagues first built a risk score to identify patients at risk of death early after ICD implantation in a population of 2,717 ICD recipients.[17] Of note, their study population was more heterogeneous than ours, as 25.3% of the patients were implanted for secondary prevention of SCD and thus were potentially more prone

to experience recurrences of arrhythmic events and appropriate ICD therapies. The following factors were found to predict early mortality: peripheral arterial disease, age >70 years, creatinine >2.0 mg/dL, and ejection fraction <20%. In another study, Kraaier et al developed and externally validated a 4-variable score, incorporating glomerular filtration rate <30ml/mn/1.73m^2, age (≥75 years), LVEF ≤ 20% and history of atrial fibrillation, that aimed to identify patients at high risk of early death among prophylactic ICD candidates.[18] By applying their score, they identified a subset of patients with high mortality rate (38.9% in the prediction cohort and 46.3% in the validation cohort). Although their one-year mortality rate was more than threefold compared to our high-risk group (12.7%), the diagnostic accuracies of all these scores have been low (positive predictive values < 50%) and therefore cannot be readily recommended for use in daily practice to contraindicate ICD implantation for the identified patients.

The residual risk of early mortality after ICD implantation

The abovementioned risk factors for early mortality notwithstanding, there is still likely to be some residual risk for early death even among well selected candidates for ICD implantation. The fact that early mortality rates have been largely consistent across studies reflects to some extent an element of non-modifiable risk for death within the first year after ICD implantation which may not be possible to completely eliminate. Nevertheless, this probably impacts only a small proportion of the overall population eligible for ICD implantation and careful candidate selection based on clinical profile can maximize the impact of the ICD.

Limitations

This study is one of the largest to address risk for early mortality after ICD implantation; however, some limitations need be mentioned. Mortality and risk factors were assessed in a

population already selected for ICD implantation which would have relatively lesser comorbidity. Therefore, it would be interesting to study not only ICD recipients but all potential ICD candidates, that is to say all-comers patients having a reduced ejection fraction, to have an overall picture and risk assessment for early death. Secondly, the retrospective feature of this study did not allow collection of specific data that may help refine risk prediction such as N-terminal pro brain natriuretic peptide or co-morbidities.

Conclusions

Using a large real-world population, we describe factors predicting mortality occurring during the first year after ICD implantation. Clinical selection for primary prevention ICD implantation for heart failure in contemporary real-world practice seems largely appropriate with <5% mortality within the first year. Elderly patients (≥70 years) with advanced NYHA class (III-IV) and atrial fibrillation appear to constitute a particularly high-risk group for early mortality and warrant careful decision-making in this scenario.

Acknowledgements: We thank the investigators of the enrolling centers for participating in the study and sharing their data, as well as research associates Frankie Beganton, Nicolas Estrugo, Sandrine Hervouet, Nathalie de Carsin, Radu Mosei, Frederic Treguer, Juliette Tennenbaum, Raoul Hubac-Coupet, Alexandre Bendavid, and Marine Sroussi for collecting the data, and the Arrhythmia Group of the French Society of Cardiology for supporting this project. Finally, we thank Eric Duong for his careful reading of the manuscript.

References

[1] A.J. Moss, W. Zareba, W.J. Hall, H. Klein, D.J. Wilber, D.S. Cannom, J.P. Daubert, S.L. Higgins, M.W. Brown, M.L. Andrews, Multicenter Automatic Defibrillator Implantation Trial II Investigators, Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction, N. Engl. J. Med. 346 (2002) 877–883.

[2] G.H. Bardy, K.L. Lee, D.B. Mark, J.E. Poole, D.L. Packer, R. Boineau, M. Domanski, C. Troutman, J. Anderson, G. Johnson, S.E. McNulty, N. Clapp-Channing, L.D. Davidson-Ray, E.S. Fraulo, D.P. Fishbein, R.M. Luceri, J.H. Ip, Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators, Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure, N. Engl. J. Med. 352 (2005) 225–237.

[3] C.W. Yancy, M. Jessup, B. Bozkurt, J. Butler, D.E. Casey, M.H. Drazner, G.C. Fonarow, S.A. Geraci, T. Horwich, J.L. Januzzi, M.R. Johnson, E.K. Kasper, W.C. Levy, F.A. Masoudi, P.E. McBride, J.J.V. McMurray, J.E. Mitchell, P.N. Peterson, B. Riegel, F. Sam, L.W. Stevenson, W.H.W. Tang, E.J. Tsai, B.L. Wilkoff, American College of Cardiology Foundation, American Heart Association Task Force on Practice Guidelines, 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, J. Am. Coll. Cardiol. 62 (2013) e147-239.

[4] S.G. Priori, C. Blomström-Lundqvist, A. Mazzanti, N. Blom, M. Borggrefe, J. Camm, P.M. Elliott, D. Fitzsimons, R. Hatala, G. Hindricks, P. Kirchhof, K. Kjeldsen, K.-H. Kuck, A. Hernandez-Madrid, N. Nikolaou, T.M. Norekvål, C. Spaulding, D.J. Van Veldhuisen, ESC Scientific Document Group, 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), Eur. Heart J. 36 (2015) 2793–2867.

[5] A.L. Bui, T.B. Horwich, G.C. Fonarow, Epidemiology and risk profile of heart failure, Nat. Rev. Cardiol. 8 (2011) 30–41.

[6] W. Escande, S. Boveda, P. Defaye, C. Leclercq, N. Sadoul, M.-C. Perier, J.-C. Deharo, L. Fauchier, E. Marijon, O. Piot, DAI-PP Investigators, Outcomes in Guideline-Based Versus Off-Guideline Primary Prevention Implantable Cardioverter-Defibrillator Recipients, J. Am. Coll. Cardiol. 70 (2017) 1302–1303.

[7] V. Algalarrondo, R. Perault, M.-C. Bories, K. Narayanan, R. Garcia, N. Combes, M.-C. Perier, P. Defaye, N. Sadoul, D. Gras, D. Klug, P. Bordachar, L. Fauchier, J.-C. Deharo, C. Leclercq, S. Boveda, E. Marijon, D. Babuty, Prophylactic implantable cardioverter defibrillators for primary prevention: From implantation to heart transplantation, Arch. Cardiovasc. Dis. 111 (2018) 758–765.

[8] N. Amara, S. Boveda, P. Defaye, D. Klug, F. Treguer, D. Amet, M.-C. Perier, D. Gras, V. Algalarrondo, A. Bouzeman, O. Piot, J.-C. Deharo, L. Fauchier, D. Babuty, P. Bordachar, N. Sadoul, E. Marijon, C. Leclercq, DAI-PP Investigators, Implantable cardioverter-defibrillator therapy among patients with non-ischaemic vs. ischaemic cardiomyopathy for primary prevention of sudden cardiac death, Eur. Eur. Pacing Arrhythm. Card. Electrophysiol. J. Work. Groups Card. Pacing Arrhythm. Card. Cell. Electrophysiol. Eur. Soc. Cardiol. (2017).

[9] P. Defaye, S. Boveda, D. Klug, F. Beganton, O. Piot, K. Narayanan, M.-C. Périer, D. Gras, L. Fauchier, P. Bordachar, V. Algalarrondo, D. Babuty, J.-C. Deharo, C. Leclercq, E. Marijon, N. Sadoul, Dual- vs. single-chamber defibrillators for primary prevention of sudden cardiac death: long-term follow-up of the Défibrillateur Automatique Implantable-Prévention Primaire registry, Eur. Eur. Pacing Arrhythm. Card. Electrophysiol. J. Work. Groups Card. Pacing Arrhythm. Card. Cell. Electrophysiol. Eur. Soc. Cardiol. (2017).

[10] T. Perrin, A. Mechulan, S. Boveda, F. Beganton, P. Defaye, N. Sadoul, O. Piot, D. Klug, D. Gras, M.-C. Perier, V. Algalarrondo, P. Bordachar, D. Babuty, L. Fauchier, C. Leclercq, E. Marijon, J.-C. Deharo, DAI-PP Investigators, Does defibrillation testing influence outcomes after CRT-D implantation? A cause-of-death analysis from the DAI-PP study, Int. J. Cardiol. 221 (2016) 951–956.

[11] M.S. Ascoeta, E. Marijon, P. Defaye, D. Klug, F. Beganton, M.-C. Perier, D. Gras, V. Algalarrondo, J.-C. Deharo, C. Leclercq, L. Fauchier, D. Babuty, P. Bordachar, N. Sadoul, S. Boveda, O. Piot, DAI-PP Investigators, Impact of early complications on outcomes in patients with implantable cardioverter-defibrillator for primary prevention, Heart Rhythm. 13 (2016) 1045–1051.

[12] R. Providencia, E. Marijon, S. Barra, C. Reitan, A. Breitenstein, P. Defaye, N. Papageorgiou, R. Duehmke, S. Winnik, R. Ang, D. Klug, D. Gras, T. Oezkartal, O.R. Segal, J.-C. Deharo, C. Leclercq, P.D. Lambiase, L. Fauchier, P. Bordachar, J. Steffel, N. Sadoul, O. Piot, R. Borgquist, S. Agarwal, A. Chow, S. Boveda, DAI-PP Investigators, Usefulness of a clinical risk score to predict the response to cardiac resynchronization therapy, Int. J. Cardiol. 260 (2018) 82–87.

[13] G.H. Bardy, K.L. Lee, D.B. Mark, J.E. Poole, D.L. Packer, R. Boineau, M. Domanski, C. Troutman, J. Anderson, G. Johnson, S.E. McNulty, N. Clapp-Channing, L.D. Davidson-Ray, E.S. Fraulo, D.P. Fishbein, R.M. Luceri, J.H. Ip, Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators, Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure, N. Engl. J. Med. 352 (2005) 225–237.

[14] A.J. Moss, W. Zareba, W.J. Hall, H. Klein, D.J. Wilber, D.S. Cannom, J.P. Daubert, S.L. Higgins, M.W. Brown, M.L. Andrews, Multicenter Automatic Defibrillator Implantation Trial II Investigators, Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction, N. Engl. J. Med. 346 (2002) 877–883.

[15] P. Santangeli, L. Di Biase, A. Dello Russo, M. Casella, S. Bartoletti, P. Santarelli, G. Pelargonio, A. Natale, Meta-analysis: age and effectiveness of prophylactic implantable cardioverter-defibrillators, Ann. Intern. Med. 153 (2010) 592–599.

[16] L.A. Allen, L.W. Stevenson, K.L. Grady, N.E. Goldstein, D.D. Matlock, R.M. Arnold, N.R. Cook, G.M. Felker, G.S. Francis, P.J. Hauptman, E.P. Havranek, H.M. Krumholz, D. Mancini, B. Riegel, J.A. Spertus, American Heart Association, Council on Quality of Care and Outcomes Research, Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Cardiovascular Radiology and Intervention, Council on Cardiovascular Surgery and Anesthesia, Decision making in advanced heart failure: a scientific statement from the American Heart Association, Circulation. 125 (2012) 1928–1952.

[17] D.B. Kramer, P.A. Friedman, L.M. Kallinen, T.B. Morrison, D.J. Crusan, D.O. Hodge, M.R. Reynolds, R.G. Hauser, Development and validation of a risk score to predict early mortality in recipients of implantable cardioverter-defibrillators, Heart Rhythm. 9 (2012) 42–46.

[18] K. Kraaier, M.F. Scholten, J.G.P. Tijssen, D.A.M.J. Theuns, L.J.L.M. Jordaens, A.A.M. Wilde, P.F.H.M. van Dessel, Early mortality in prophylactic implantable cardioverter-defibrillator recipients: development and validation of a clinical risk score, Eur. Eur. Pacing Arrhythm. Card. Electrophysiol. J. Work. Groups Card. Pacing Arrhythm. Card. Cell. Electrophysiol. Eur. Soc. Cardiol. 16 (2014) 40–46.

Figure legend

Figure 1: Multivariate Kaplan-Meier curves of survival during the first year post ICD implantation according to the number of risk factors (age ≥70 years, NYHA class III-IV and atrial fibrillation).

Table 1: Baseline characteristics comparison between patients who died within the first year following ICD implantation vs. patients who did not.

Variables	Patients with survival >1 year	Patients with survival ≤1 year	P-value
Number of patients	N = 5227	N = 230	
Age (year)	62.3 ± 11.2	66.9 ± 9.6	<0.0001
Male sex	4428 (84.7)	205 (89.1)	0.07
Ischemic cardiomyopathy	3111 (60.1)	145 (64.2)	0.22
NYHA class:			
I	460 (10.7)	7 (3.7)	<0.0001
II	1788 (41.5)	42 (22.1)	
III	1915 (44.5)	110 (57.9)	
IV	141 (3.3)	31 (16.3)	
Chronic kidney disease	443 (11.17)	35 (24.65)	<0.0001
Neoplasia	297 (7.49)	12 (8.45)	0.67
Stroke	197 (4.97)	12 (8.45)	0.06
Chronic respiratory failure	477 (12.03)	28 (19.72)	0.006

Hepatocellular failure	71 (1.79)	1 (0.70)	0.52
Diabetes	167 (28.74)	3 (23.08)	0.77
Creatinine clearance (ml/min)			
< 30	240 (7.9)	35 (24.3)	<0.0001
30 - 60	915 (30.2)	60 (41.7)	
> 60	1876 (61.9)	49 (34.0)	
Sinus rhythm	3409 (76.5)	122 (63.5)	<0.0001
QRS width, ms			
<120	1119 (30.9)	38 (20.4)	0.004
120 - 150	1270 (35.1)	83 (44.6)	
>150	1231 (34.0)	65 (35.0)	
LVEF (%), median (IQR)	25 (22; 30)	25 (20; 30)	0.002
Medication			
B-blockers	3199 (85.42)	116 (70.73)	<0.0001
Amiodarone	824 (22.00)	57 (34.76)	0.0001
Digoxine	208 (5.55)	10 (6.10)	0.77
Sotalol	21 (0.56)	0	1.00
Antiplatelets	2134 (56.98)	98 (59.76)	0.48
ACEi/ARB-II	3084 (82.35)	119 (72.56)	0.001
Loop diuretics	2526 (67.45)	136 (82.93)	<0.0001
Spironolactone	1220 (32.58)	49 (29.88)	0.47
oral anticoagulation	1301 (34.74)	77 (46.95)	0.001
ICD type			
CRT	2764 (53.3)	160 (70.2)	<0.0001
Dual chamber	1219 (23.5)	32 (14.0)	
Single chamber	1200 (23.2)	36 (15.8)	

Results are expressed as mean ± SD, median (IQR) or number of patients (%).

Table 2: Follow-up comparison between patients who died within the first year following ICD implantation vs. patients who did not.

Variables	**N**	**Patients with survival >1 year**	**Patients with survival ≤1 year**	**P-value**
Number of patients	5457	5227	230	
Peri-operative complications	5143			
Lead dysfunction		134 (2.72)	8 (3.57)	0.45
Bleeding/Hematoma		241 (4.90)	8 (3.57)	0.37
Sepsis		47 (0.96)	3 (1.34)	0.48
Tamponade		4 (0.08)	0	1.00

Pneumothorax		38 (0.77)	3 (1.34)	0.42
Other		187 (3.80)	14 (6.25)	0.06
Post-implantation Complications	5297			
Lead dysfunction		327 (6.43)	10 (4.67)	0.30
Sepsis		138 (2.71)	11 (5.14)	0.04
Other		46 (0.90)	3 (1.40)	0.45
ICD therapies				
Appropriate shock	5286	1149 (22.67)	31 (14.29)	0.004
Inappropriate shock	5278	350 (6.91)	5 (2.33)	0.009
Causes of death	826			
Sudden death		43 (7.21)	21 (9.13)	
Other cardiovascular cause		287 (48.15)	120 (52.17)	
Non-cardiovascular		148 (24.83)	49 (21.30)	0.28
ICD complication		8 (1.34)	6 (2.61)	
Unknown		110 (18.46)	34 (14.78)	

Table 3: Multivariate analysis of the preoperative variables significantly associated with a ≤ 1-year survival.

Variables	HR (IC95%)	P-value	Number of patients n,(%)	Early mortality prevalence (%)
Age ≥70 years	1.80 (1.34; 2.43)	0.0001	1617 (29.66)	6.12
NYHA class III-IV	2.74 (1.95; 3.84)	<0.0001	2197 (48.89%)	6.42
Atrial fibrillation	1.53 (1.12; 2.09)	0.008	1115 (24.00%)	6.28

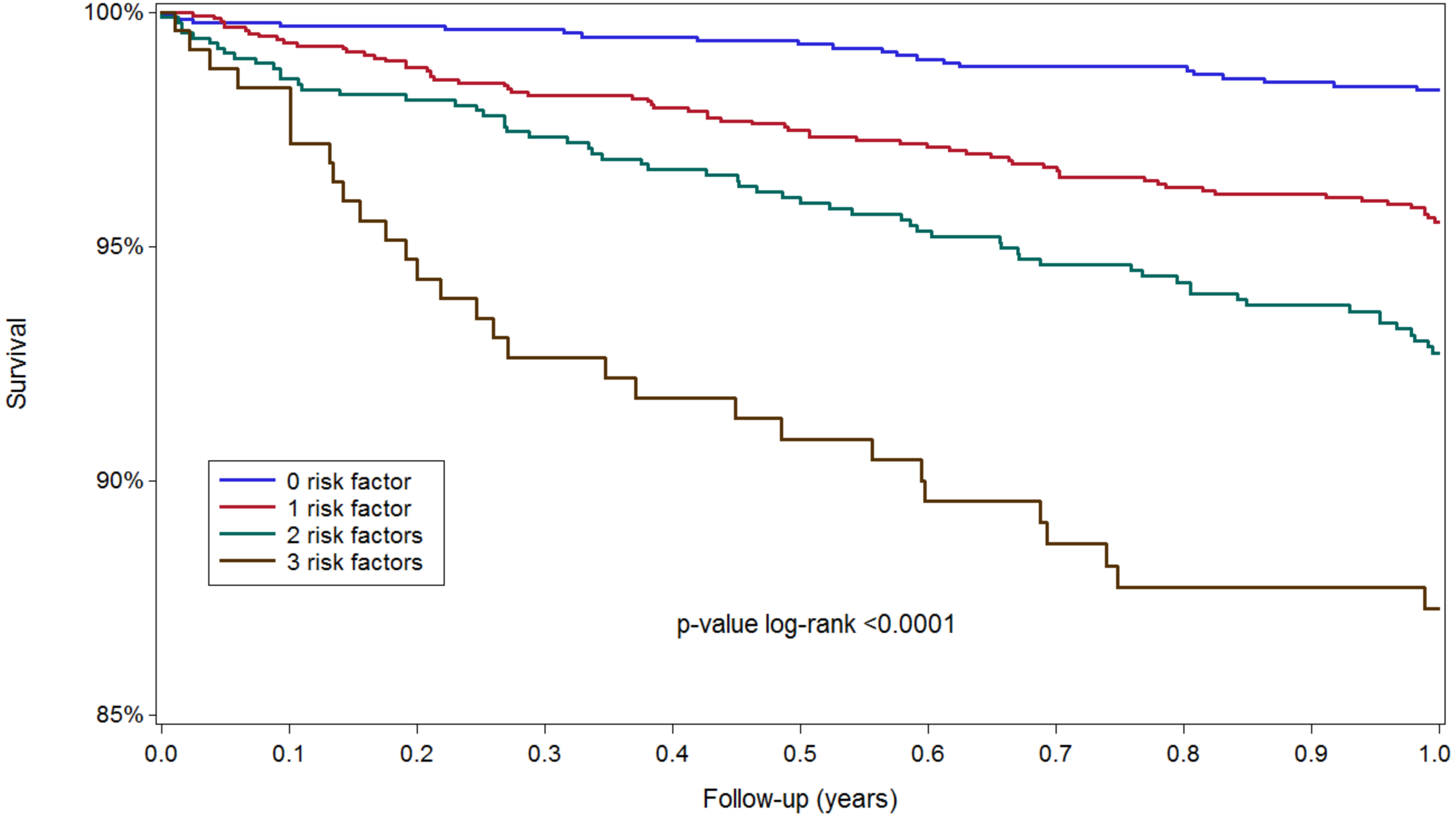
Number of risk factors: 0 1 2 3			1405 (33.51) 1596 (38.06) 937 (22.35) 255 (6.08)	1.49 1.55 6.62 11.76

Results are expressed as Hazard ratio (HR) and 95% confidence interval (95%CI)

Table 4: Main publications that studied the early mortality after ICD implantation (<1year) in primary prevention ICD candidates and that built a risk score.

Reference	Patients' characteristics	Early mortality rate	Risk score	Early mortality / score value
Kraaier K [18]	N: 861 Age: 62.7 ± 10.2 y Men: 79% PP: 100% iCMP: 67% LVEF: 24.2 ± 8.6%	4.8%	Age ≥75 year History of AF LVEF ≤ 20% GFR < 30 mL/min/1.73 m^2	0 pt: 3.0% 1 pt: 3.8% 2 pts: 10.9% ≥3 pts: 38.9%
Kramer DB [17]	N: 2,717 Age: 65 ± 15 y Men: 77% PP: 75% iCMP: 58.1% LVEF: 31%	4.2%	PAD Age ≥70 years Creatinine ≥2.0 mg/dL LVEF ≤ 20%	0 pt: 1.7% 1 pt: 4.0% 2 pts: 6.9% 3 pts: 15.5% ≥4 pts: 18.2%
Garcia R	N: 5,457 Age: 62.5 ± 11y Men: 84.9% PP: 100% iCMP: 60.2% LVEF: 25%	4.2%	Age ≥70 years AF NYHA class III-IV	0 pt: 1.49% 1 pt: 1.55% 2 pts: 6.62 3 pts: 11.76%

N: number of patients; PP: proportion of patients implanted for Primary Prevention; iCMP: ischemic cardiomyopathy; LVEF: Left Ventricular Ejection Fraction; pt/ pts: point / points; AF: atrial fibrillation; GFR: glomerular filtration rate; PAD: peripheral artery disease;


100%
95%
90%
85%
Survival
0 risk factor
1 risk factor
2 risk factors
3 risk factors
p-value log-rank <0.0001
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
Follow-up (years)