Journal of Interventional Cardiac Electrophysiology (2022) 64:573–580
https://doi.org/10.1007/s10840-021-01017-8

Implantable cardioverter-defibrillators in elderly patients: outcome and predictors of mortality

Massimiliano Marini[1] · Marta Martin[1] · Mattia Strazzanti[1] · Silvia Quintarelli[1] · Fabrizio Guarracini[1] · Alessio Coser[1] · Sergio Valsecchi[2] · Roberto Bonmassari[1]

Received: 4 March 2021 / Accepted: 30 May 2021 / Published online: 1 July 2021

Abstract

Purpose The implantable cardioverter-defibrillator (ICD) is the therapy of choice for the prevention of sudden cardiac death. The number of elderly patients receiving ICDs is increasing. This study aimed to assess the outcome of patients according to their age at the time of implantation, and to identify variables potentially associated with patient survival.

Methods Between June 2009 and December 2019, we retrospectively enrolled all consecutive patients in whom ICD implantation had been performed for primary or secondary prevention at our center.

Results During the study period, 670 patients underwent ICD implantation. We stratified the population into four age-classes: Class 1 (23%) (pts aged less than 60 years), Class 2 (28%) (pts aged between 60 and 70 years), Class 3 (39%) (pts aged between 70 and 80 years) and Class 4 (9%) (pts aged 80 years or older). Over a median follow-up of 42 months, the rate of deaths in Class 4 was higher than in Classes 1 and 2 (log-rank test, $P<0.01$), but was comparable to that in Class 3 ($P=0.407$). With increasing age, we observed more complications at the time of implantation and during follow-up. On multivariate analysis, higher NYHA class, creatinine level and CHA_2DS_2-VASc score were identified as independent predictors of death, while age was not associated with worse prognosis. Higher body mass index, higher NYHA class and CHA_2DS_2-VASc score were also confirmed as independent predictors of hospitalizations or death due to any cause.

Conclusion This study showed good survival in ICD patients in all age-groups, including those aged ≥80 years. The CHA_2DS_2-VASc score seems to be a stronger predictor of death than age.

Keywords Implantable defibrillator · Elderly · Mortality

1 Introduction

International guidelines recommend the use of implanted cardioverter-defibrillator (ICD) in the primary and secondary prevention of sudden cardiac death. The number of ICD devices has been increasing year by year [1] and, as life expectancy increases, more elderly patients meet the criteria for ICD implantation. In elderly patients, the benefit of ICD therapy on arrhythmic death may be attenuated by non-arrhythmic mortality. However, US guidelines [2] and ESC guidelines [3] do not place any specific age limit on ICD implantation; only US guidelines state that ICD implantation is “rarely appropriate” in nonagenarians. Clinical evidence on the use of ICDs in the elderly is limited. Indeed, they are poorly represented in many clinical trials, and the mean age of patients in randomized controlled trials of ICDs is 63 years [4]. Moreover, in elderly patients with severe cardiac disease, it is difficult to assess 1-year survival, and the effectiveness of ICD therapy is hard to predict.

The aims of this study were to describe the clinical practice of ICD implantation at our center, to assess the medium-term outcome of patients according to their age at the time of implantation, and to identify variables potentially associated with patient survival.

2 Methods

We retrospectively enrolled all consecutive patients in whom ICD implantation had been performed for primary or secondary prevention of sudden cardiac death from June 2009 to December 2019 at our center. Patients were required to

✉ Massimiliano Marini
massimiliano.marini@apss.tn.it

1 Department of Cardiology, S. Chiara Hospital, Trento, Italy

2 Boston Scientific, Milan, Italy

have standard indications for ICD implantation. Informed consent was obtained from all patients. At the time of ICD implantation, the baseline evaluation included demographics and medical history, clinical examination, 12-lead electrocardiogram, echocardiographic evaluation of left ventricular ejection fraction, assessment of NYHA class, and estimation of the CHA_2DS_2-VASc score. Devices and pacing leads were implanted by means of standard techniques. Optimization of device programming and pharmacological treatments were based on clinical evaluation by the attending physicians. During follow-up, patients returned for regular clinic visits and the following information was retrospectively collected: mortality due to any cause, ICD interventions, hospitalization.

2.1 Statistical analysis

Descriptive statistics are reported as means ± standard deviation for normally distributed continuous variables, or medians with 25th to 75th percentiles in the case of skewed distribution. Categorical data were expressed as percentages. One-way analysis of variance was performed to test for differences between age-classes. Rates of all-cause death and the combined endpoint of cardiovascular hospitalization or death were summarized by constructing Kaplan-Meier curves, and the distributions of the groups were compared by means of a log-rank test (level of significance adjusted for multiple testing by Bonferroni correction). Cox regression was used to analyze possible predictors of death and the combined endpoint of cardiovascular hospitalization or death due to any cause. In the regression models, age was included as a continuous variable. All variables associated to a P value <0.05 on univariate analysis were entered into the multivariate regression analysis. In order to present the predicted probability of all-cause death, a combined score was proposed, based on converting the regression coefficient for each predictor of the multivariate model to integers. We organized the risk factors into categories, we determined the reference values for each variable, how far each category is from the reference category in regression units, and the number of points for each of the categories of each variable. The final score was calculated as the sum of points for all variables. A P value <0.05 was considered significant for all tests. All statistical analyses were performed by means of R: a language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria).

3 Results

3.1 Study population

From June 2009 to December 2019, a total of 670 patients with a standard indication for ICD underwent implantation at our center. A single-chamber ICD was implanted in 284 (42%) patients, a dual-chamber ICD in 99 (15%), and a subcutaneous ICD in 27 (4%). The remaining 260 (39%) patients had concomitant biventricular pacing indications and received a cardiac resynchronization therapy ICD. For the aims of the analysis, we stratified the study population into four age-classes: patients younger than 60 years (Class 1–156 (23%)), patients aged between 60 and 70 years (Class 2–189 (28%)), patients aged between 70 and 80 years (Class 3–264 (39%)), and patients aged 80 years or more (Class 4–61 (9%)). Table 1 shows baseline clinical variables stratified by age-class. With increasing age, we observed worse functional class, a more frequent history of cardiovascular events, and greater prevalence of cardiovascular and non-cardiovascular complications. We also noted a more frequent use of single-chamber and subcutaneous ICDs in Class 1 patients, and of cardiac resynchronization therapy in patients of other classes. Periprocedural complications were reported in 18 (3%) patients (Table 2).

3.2 Follow-up

During a median follow-up of 42 months [25th–75th percentile: 18–72], 6 patients were lost to follow-up (1%) and 122 (18%) patients died of any cause. The Kaplan–Meier estimates of time to death, stratified by age-class, demonstrated considerable differences in survival (overall log-rank test, $P<0.001$; Fig. 1). Specifically, the actuarial rate of survival at 8 years ranged from 91% in Class 1 to 48% in Class 4. The rate of death in Class 4 was higher than in Classes 1 and 2 (log-rank test, $P<0.01$ for pairwise comparisons), but was comparable to that in Class 3 (log-rank test, $P=0.407$). Cardiovascular hospitalizations were reported in 284 (42%) patients, and the combined endpoint of cardiovascular hospitalization or death due to any cause was reported in 321 (48%) patients. Considerable differences among age-classes were observed in the time to cardiovascular hospitalization or death (overall log-rank test, $P<0.001$; Fig. 2). Specifically, the actuarial rate of patients free from events at 8 years ranged from 41% in Class 1 to 10% in Class 4. The rate of events in Class 4 was higher than in the other classes (log-rank test, $P<0.01$ for pairwise comparisons). During follow-up, system-related complications were reported in 58 (9%) patients (Table 2). With increasing age, we observed more complications at the time of implantation and during follow-up. Analysis of the ICD therapies delivered during follow-up showed differences among age-classes (Table 2). Specifically, patients in Class 3 reported fewer episodes than patients in Classes 1 and 2.

3.3 Predictors of clinical events

Baseline parameters were evaluated by means of univariate and multivariate analyses in order to assess their ability

Table 1 Demographics and baseline clinical parameters of the study population, by age-class

Parameter	Age Class 1 <60 yrs. (*n* = 156)	Age Class 2 ≥60 & <70 yrs. (*n* = 189)	Age Class 3 ≥70 & <80 yrs. (*n* = 264)	Age Class 4 ≥80 yrs. (*n* = 61)
Male gender, n (%)	124 (79)	155 (82)	215 (81)	46 (75)
Body Mass Index, Kg/m2	28 ± 22	27 ± 5	27 ± 23	32 ± 45
Left ventricular ejection fraction ≤35%, n (%)	99 (63)	137 (72)	195 (74)	44 (72)
NYHA Class *	1.9 ± 0.6	2.1 ± 0.4	2.1 ± 0.4	2.1 ± 0.4
Previous myocardial infarction, n (%) *	45 (29)	84 (44)	127 (48)	32 (52)
History of atrial fibrillation, n (%) *	30 (19)	68 (36)	150 (57)	42 (69)
Arterial hypertension, n (%) *	49 (31)	116 (61)	195 (74)	46 (75)
Diabetes, n (%) *	19 (12)	40 (21)	70 (27)	13 (21)
Vascular disease, n (%) *	5 (3)	28 (15)	52 (20)	14 (23)
Dyslipidemia, n (%) *	58 (37)	105 (56)	172 (65)	33 (54)
Previous transient ischemic attack/Stroke, n (%) *	5 (3)	16 (8)	37 (14)	7 (11)
Creatinine, mg/dl	0.99 ± 0.04	1.07 ± 0.25	1.11 ± 0.32	1.00 ± 0.12
CHA_2DS_2-VASc Score *	1.4 ± 1.0	2.6 ± 1.3	3.9 ± 1.3	4.4 ± 1.2
$CHADS_2$ score *	1.1 ± 0.9	1.7 ± 1.0	2.5 ± 1.2	2.9 ± 1.0
Secondary prevention, n (%)	80 (51)	80 (42)	113 (43)	29 (48)
Single-chamber, n (%) *	81 (52)	92 (49)	89 (34)	22 (36)
Dual-chamber, n (%)	22 (14)	20 (11)	43 (16)	14 (23)
Cardiac resynchronization therapy, n (%) *	29 (19)	76 (40)	130 (49)	25 (41)
Subcutaneous ICD, n (%) *	24 (15)	1 (0.5)	2 (0.8)	0 (0)

*$p < 0.05$

to predict the occurrence of death during follow-up, as reported in Table 3. On multivariate analysis, higher NYHA class, creatinine level and CHA_2DS_2-VASc score were confirmed as independent predictors of death. Age at the time of implantation was not associated with worse prognosis. We built a combined mortality risk score, based on the predictors of the multivariate model, i.e. NYHA class, creatinine level and CHA_2DS_2-VASc score. In Table 4 we reported the risk factors categories and the number of points assigned to each category. The final score (the sum of points for all variables) ranges from 0 to 25. The distribution of patients according to the combined score, together with the probability of events associated with score values is reported in Fig. 3. Table 5 reports the results of the univariate and multivariate analyses for the prediction of the combined endpoint of cardiovascular hospitalization or death due to any cause. On multivariate analysis, higher body mass index, higher NYHA class and CHA_2DS_2-VASc score were confirmed as independent predictors of events. Age was not associated with higher rates of events.

Table 2 Events reported at the time of implantation and during follow-up, by age-class

Number of patients (%)	Age Class 1 <60 yrs. (n = 156)	Age Class 2 ≥60 and < 70 yrs. (n = 189)	Age Class 3 ≥70 and < 80 yrs. (n = 264)	Age Class 4 ≥80 yrs. (n = 61)
All complications, n (%) *	14 (9)	13 (7)	33 (13)	11 (18)
- Periprocedural complications, n (%)	2 (1)	6 (3)	6 (2)	4 (7)
- System-related complications during follow-up, n (%)	13 (8)	9 (5)	28 (11)	8 (13)
Therapies delivered: *	48 (31)	60 (32)	48 (18)	17 (28)
- Anti-tachycardia pacing, n (%)	16 (10)	21 (11)	16 (6)	5 (8)
- Anti-tachycardia pacing and shock, n (%)	3 (2)	9 (5)	5 (2)	3 (5)
- Shock, n (%)	29 (19)	30 (16)	27 (10)	9 (14)

*$p < 0.05$

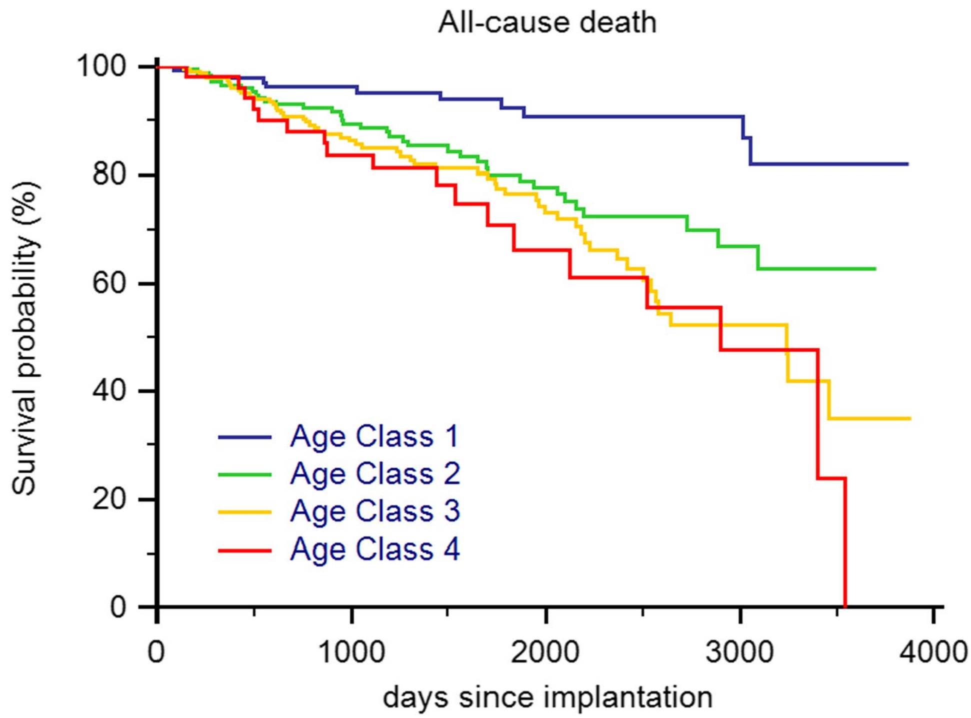

Fig. 1 Kaplan-Meier estimates of time to death, stratified by age-class (overall log-rank test **P** < 0.001).

4 Discussion

This analysis of the clinical practice of ICD implantation in our center showed that age was not an independent predictor of mortality and cardiovascular events. Although belonging to older age-groups was associated with higher rates of death, patients in their eighties did not seem to have a worse prognosis than those in their seventies, who currently constitute the largest patient group undergoing ICD implantation [5].

The incidence of sudden cardiac death is known to increase progressively with age until 80–85 years [6]' when it reaches a plateau. The relative contribution of non-arrhythmic mortality in the elderly may therefore mask the

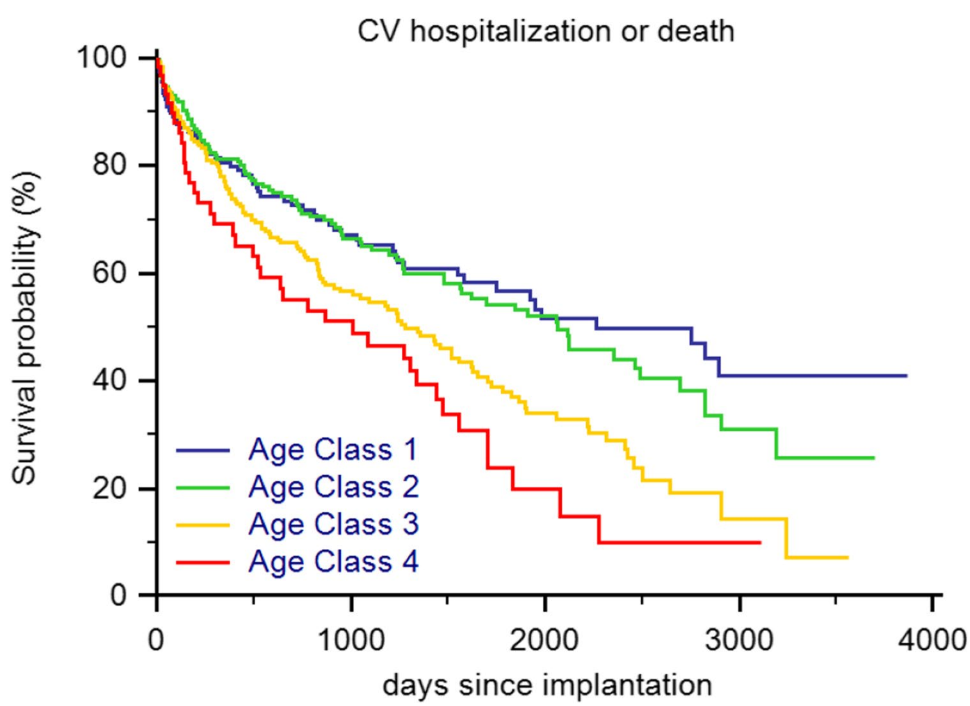

Fig. 2 Kaplan-Meier estimates of time to cardiovascular hospitalization or death, stratified by age-class (overall log-rank test, $P < 0.001$)

Table 3 Univariate and multivariate analyses of factors predicting death in the study population

	Univariate analysis			Multivariate analysis		
	HR	95% CI	P	HR	95% CI	P
Age	1.05	1.03–1.07	<0.001	1.02	0.99–1.05	0.063
Male gender	1.12	0.69–1.80	0.649	–	–	–
Body Mass Index	0.97	0.92–1.03	0.327	–	–	–
Left ventricular ejection fraction ≤35%	1.72	1.10–2.68	0.018	1.01	0.63–1.64	0.953
NYHA Class	2.14	1.48–3.09	<0.001	1.76	1.15–2.70	0.009
Previous myocardial infarction	1.74	1.22–2.48	0.002	1.30	0.90–1.88	0.160
History of atrial fibrillation	1.33	1.05–1.68	0.016	1.17	0.93–1.48	0.187
Arterial hypertension	1.95	1.31–2.91	0.001	–	–	–
Diabetes	1.84	1.26–2.70	0.002	–	–	–
Dyslipidemia	1.19	0.83–1.70	0.345	–	–	–
Creatinine	1.05	1.03–1.07	<0.001	1.04	1.02–1.06	<0.001
CHA_2DS_2-VASc score	1.45	1.30–1.61	<0.001	1.23	1.06–1.44	0.008

benefits of ICD therapy. Nonetheless, in agreement with some previous studies [7–9], the prognosis of our ICD patients was good in all groups, with about half of patients aged ≥80 years at the time of implantation still alive after 8 years. This result is positive in view of the increasing life expectancy of the general population. Indeed, according to the figures of the Italian National Institute of Statistics (ISTAT), in our region the life expectancy of people aged 85 years was 5.6 years for males and 7.2 years for females in 2010, while in 2017 it was 6.2 years for males and 7.6 years for females [10]. However, the clinical effectiveness of the ICD in the elderly remains unclear and would require a specific randomized study. Indeed, most randomized studies have included a low percentage of octogenarians, and others have purposely excluded patients above the age of 80 [11].

In our study, the variables that appeared to play a major role in predicting mortality were the severity of heart failure and the presence of comorbidities. In particular, an index such as the CHA_2DS_2-VASc score, which summarizes multiple variables, can be useful in determining the patient's life expectancy at the time of defining the indication for ICD implantation. Several risk scores have been developed in order to identify ICD patients at high risk of all-cause mortality. In the MADIT II population, Goldenberg et al. [12] identified age > 70 years old, atrial fibrillation, impaired renal function, NYHA II, and QRS duration >120 ms as risk factors for non-arrhythmic mortality; the accuracy of this score was also confirmed in another study by Anné et al. [13]. An algorithm developed by Kraaier et al. included age > 75, low ejection fraction, atrial fibrillation and renal dysfunction; patients with three of these risk factors and those with more than three had 1-year mortality rates of 38.9 and 46.3%, respectively [14]. Ferretto et al. studied an ICD population aged >75 years and found that age alone was not a predictor of 1-year mortality, while low ejection fraction and moderate-to-severe renal failure predicted high 1-year non-arrhythmic death [15]. With increasing age, we observed a worsening of the functional status and an increase in complications, such as the prevalence of atrial fibrillation, a history of myocardial infarction and the presence of non-cardiovascular conditions. All these variables are taken into account in the CHA_2DS_2-VASc score, which is widely used for thromboembolic risk assessment in atrial fibrillation cohorts. Recently, its prognostic performance has been investigated in patients with atrial fibrillation [16, 17] and with coronary artery disease [18], suggesting that the score can be used as a quick surrogate marker for predicting outcomes beyond thromboembolic risk. Our findings seem to confirm this result in patients of all ages with indications for ICD implantation. We also proposed a score for the prediction of the probability of all-cause death, based on the predictors of the multivariate model. The inclusion of all independent predictors allowed to identify, based on baseline clinical variables, subgroups of patients with an extremely high probability of death after implantation.

Table 4 Mortality risk score based on the predictors of the multivariate model. Risk factors categories and number of points assigned to each category

NYHA class	Points	Creatinine (mg/dl)	Points	CHA_2DS_2-VASc score	Points
- I	0	- <1.3	0	- 0	0
- II	2	- 1.3–2.5	2	- 1	1
- III	5	- 5.0	4	- 2	2
- IV	8	- 10	6	- 3	3
		- >10	8	- 4	4
				- 5	5
				- 6	6
				- 7	7
				- 8	8
				- 9	9

The final score is the sum of points for all variables (range: 0–25)

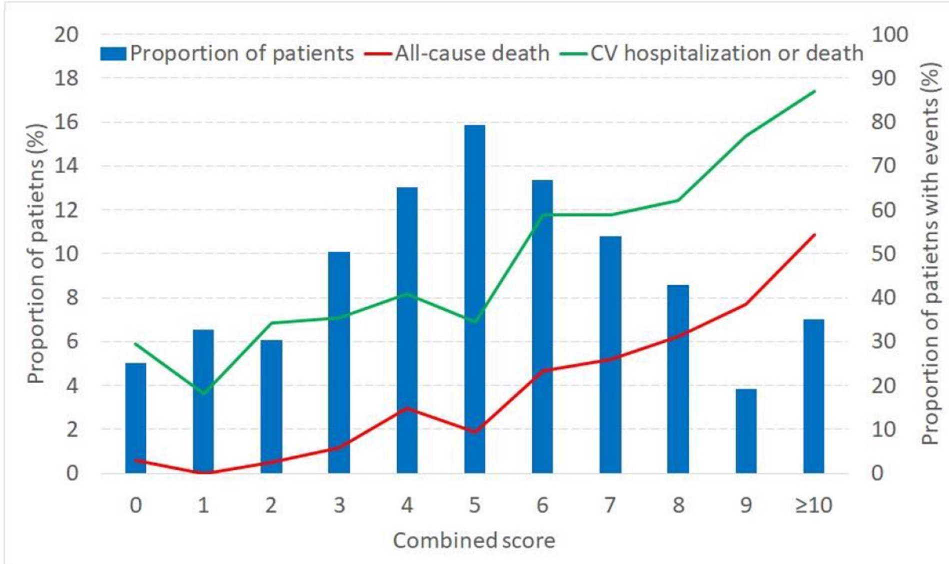

Fig. 3 Distribution of patients according to the combined score and probability of events associated with score values

Our analysis of patient characteristics by age-group provided insights into how patients are considered for ICD implantation in current clinical practice, and which devices are assigned to them. Indeed, in young patients (<60 years old), who present ICD indication for the secondary prevention of sudden death, with preserved systolic function and with no need for pacing or CRT, the most frequently adopted device was a single-chamber ICD. In some cases, a subcutaneous ICD was also adopted, since this is usually preferred in order to preserve the venous system of patients with longer life expectancy [19]. In contrast, patients in the 60-year-old age-group more frequently had heart failure, reduced ejection fraction, ICD indications for primary prevention and a need for resynchronization therapy. In these patients, the most frequently adopted devices were single-chamber ICDs and biventricular ICDs. Patients in the 70-year-old age-group were substantially equivalent to the younger ones in terms of ICD indication, but more often received a dual-chamber ICD because of the need for anti-bradycardia pacing. Obviously, in this group, the prevalence of atrial fibrillation and other comorbidities increases significantly, with higher values of CHA_2DS_2-VASc score. Patients aged 80 years or more, despite having more frequent atrial fibrillation and a history of myocardial infarction, seemed not much more compromised than those in the 70-year-old age-group. This can probably be ascribed to the selection of less compromised patients by the operators.

Data from the ALTITUDE registry showed that the frequency of ICD therapy in the elderly group was lower and that the death was more likely to be due to pump failure [20]. In our study, the proportion of patients in whom therapies were delivered during follow-up was equivalent in all

Table 5 Univariate and multivariate analyses of factors predicting cardiovascular hospitalization or death in the study population

	Univariate analysis			Multivariate analysis		
	HR	95% CI	P	HR	95% CI	P
Age	1.02	1.01–1.03	<0.001	1.00	0.98–1.02	0.903
Male gender	1.00	0.76–1.32	0.998	–	–	–
Body Mass Index	1.00	1.00–1.01	0.003	1.01	1.00–1.01	0.005
Left ventricular ejection fraction ≤35%	1.17	0.91–1.50	0.217	–	–	–
NYHA Class	1.64	1.29–2.07	<0.001	1.36	1.02–1.81	0.038
Previous myocardial infarction	1.37	1.11–1.71	0.005	1.28	0.99–1.67	0.061
History of atrial fibrillation	1.37	1.19–1.59	<0.001	1.24	1.03–1.48	0.091
Arterial hypertension	1.39	1.10–1.74	0.006	–	–	–
Diabetes	1.53	1.19–1.95	<0.001	–	–	–
Dyslipidemia	1.26	1.01–1.57	0.043	–	–	–
Creatinine	1.02	1.01–1.04	0.003	1.00	0.98–1.02	0.493
CHA_2DS_2-VASc score	1.45	1.30–1.61	<0.001	1.19	1.07–1.33	0.001

Age is included as a continuous variable in the model groups, except for those in the 70-year-old age-group, who reported fewer interventions. This could be ascribed to the higher proportion of biventricular pacing in this group and to its known effect on the burden of arrhythmias, as a consequence of left ventricular reverse remodeling [21].

The risk of possible complications should be carefully considered when defining the indication for ICD therapy. Tsai et al. [22] studied the influence of age on perioperative complications among 150,264 ICD patients. Co-morbidities, such as renal failure, severe heart failure, atrial fibrillation, third-degree heart block, female gender, and implantation by non-electrophysiologists, were stronger predictors of complications than age. Other studies have confirmed that age is not an independent risk factor for increased ICD-related complications (operative, in-hospital or long-term) [23]. In our experience, complications seemed to occur in a non-negligible percentage of the population, and this aspect must certainly be considered in the evaluation of the risk/benefit balance of ICD therapy. This is particularly important in patients aged 80 years or more, who appeared to be more prone to complications in the perioperative phase and during follow-up. We believe this should be considered when evaluating the cost-effectiveness of therapy in this patient group. Indeed, patients aged 80 years or more also had a higher rate of cardiovascular hospitalizations, and this certainly determines a higher cost for the healthcare system.

4.1 Limitations

This study was not intended to investigate the efficacy of ICD therapy in the elderly, which would require a randomized clinical trial. In addition, the cause of death was not determined in the study population. The main limitation of the present study is the retrospective design of the analysis. The availability of additional data on non-cardiovascular comorbidities would have improved the analysis and possibly allowed to identify further important predictors of outcome. Moreover, some variability in the selection or management of patients during the inclusion period may have influenced the results. However, the study was carried out in a single center, the operators in charge of patient selection, device implantation and clinical management did not change during the study period, and all the patients included were consecutive and came from the same region.

5 Conclusions

In summary, with the selection criteria adopted in current clinical practice, we recorded good survival in ICD patients of all age-groups, including those aged 80 years or more, and an equivalent need for anti-tachycardia therapies. Patient selection criteria should not be strictly based on chronological age, but on a more comprehensive assessment of the patient's condition and clinical history. To cite the French author Jules Renard, "*it is not how old you are, but how you are old*". According to our findings, a synthetic parameter such as the CHA_2DS_2-VASc score could serve this purpose. Physicians' familiarity with this score makes it an easy-to-use clinical tool for improving the appropriateness of ICD adoption.

Author contribution Massimiliano Marini: conception and design of the research, drafting of the manuscript.

Marta Martin, Mattia Strazzanti, Silvia Quintarelli, Fabrizio Guarracini, Alessio Coser: acquisition of data, critical revision of the manuscript.

Sergio Valsecchi: statistical analysis.

Roberto Bonmassari: supervision.

All authors read and approved the final version of the manuscript.

Declarations

Conflict of interest S. Valsecchi is an employee of Boston Scientific, Inc. No other conflicts of interest exist.

References

1. Raatikainen MJP, Arnar DO, Merkely B, Nielsen JC, Hindricks G, Heidbuchel H, et al. A decade of information on the use of cardiac implantable electronic devices and interventional electrophysiological procedures in the European Society of Cardiology Countries: 2017 report from the European heart rhythm association. Europace. 2017;19:ii1–ii90.
2. Russo AM, Stainback RF, Bailey SR, Epstein AE, Heidenreich PA, Jessup M, et al. ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR 2013 appropriate use criteria for implantable cardioverter-defibrillators and cardiac resynchronization therapy: a report of the American College of Cardiology Foundation appropriate use criteria task force, Heart Rhythm Society, American Heart Association, American Society of Echocardiography, Heart Failure Society of America, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. J Am Coll Cardiol. 2013;61:1318–68.
3. Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, et al. 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). Europace. 2015;17:1601–87.
4. Connolly SJ, Hallstrom AP, Cappato R, Schron EB, Kuck KH, Zipes DP, et al. Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials. AVID, CASH and CIDS studies. Antiarrhythmics vs implantable defibrillator study. Cardiac arrest study Hamburg. Canadian implantable defibrillator study. Eur Heart J. 2000;21:2071–8.

5. Proclemer A, Zecchin M, D'Onofrio A, Boriani G, Ricci RP, Rebellato L, et al. Registro Italiano pacemaker e Defibrillatori - Bollettino Periodico 2018. Associazione Italiana di Aritmologia e Cardiostimolazione [the pacemaker and implantable Cardioverter-defibrillator registry of the Italian Association of Arrhythmology and Cardiac Pacing - annual report 2018]. G Ital Cardiol (Rome). 2020;21:157–69.
6. Bogle BM, Ning H, Mehrotra S, Goldberger JJ, Lloyd-Jones DM. Lifetime risk for sudden cardiac death in the community. J Am Heart Assoc. 2016;5:e002398.
7. Koplan BA, Epstein LM, Albert CM, Stevenson WG. Survival in octogenarians receiving implantable defibrillators. Am Heart J. 2006;152:714–9.
8. Kong MH, Al-Khatib SM, Sanders GD, Hasselblad V, Peterson ED. Use of implantable cardioverter-defibrillators for primary prevention in older patients: a systematic literature review and meta-analysis. Cardiol J. 2011;18:503–14.
9. Pellegrini CN, Lee K, Olgin JE, Turakhia MP, Tseng ZH, Lee R, et al. Impact of advanced age on survival in patients with implantable cardioverter defibrillators. Europace. 2008;10:1296–301.
10. Provincia Autonoma di Trento Home Page. http://www.statistica.provincia.tn.it (accessed on Sept 2019).
11. Barra S, Providência R, Paiva L, Heck P, Agarwal S. Implantable cardioverter-defibrillators in the elderly: rationale and specific age-related considerations. Europace. 2015;17:174–86.
12. Goldenberg I, Vyas AK, Hall WJ, Moss AJ, Wang H, He H, et al. Risk stratification for primary implantation of a cardioverter-defibrillator in patients with ischemic left ventricular dysfunction. J Am Coll Cardiol. 2008;51:288–96.
13. Anné W, Theuns DA, Schaer B, Van Belle Y, Szili-Torok T, Smith T, et al. ICDs at higher age and clinical risk factors. Neth Heart J. 2014;22:279–85.
14. Kraaier K, Scholten MF, Tijssen JG, Theuns DA, Jordaens LJ, Wilde AA, et al. Early mortality in prophylactic implantable cardioverter-defibrillator recipients: development and validation of a clinical risk score. Europace. 2014;16:40–6.
15. Ferretto S, Zorzi A, Dalla Valle C, Migliore F, Leoni L, De Lazzari M, et al. Implantable cardioverter-defibrillator in the elderly: predictors of appropriate interventions and mortality at 12-month follow-up. Pacing Clin Electrophysiol. 2017;40:1368–73.
16. Naccarelli GV, Panaccio MP, Cummins G, Tu N. CHADS2 and CHA2DS2-VASc risk factors to predict first cardiovascular hospitalization among atrial fibrillation/atrial flutter patients. Am J Cardiol. 2012;109:1526–33.
17. Lahewala S, Arora S, Patel P, Kumar V, Patel N, Tripathi B, et al. Atrial fibrillation: utility of CHADS2 and CHA2DS2-VASc scores as predictors of readmission, mortality and resource utilization. Int J Cardiol. 2017;245:162–7.
18. Huang FY, Huang BT, Pu XB, Yang Y, Chen SJ, Xia TL, et al. CHADS2, CHA2DS2-VASc and R2CHADS2 scores predict mortality in patients with coronary artery disease. Intern Emerg Med. 2017;12:479–86.
19. Botto GL, Forleo GB, Capucci A, Solimene F, Vado A, Bertero G, et al. The Italian subcutaneous implantable cardioverter-defibrillator survey: S-ICD, why not? Europace. 2017;19:1826–32.
20. Saxon LA, Hayes DL, Gilliam FR, Heidenreich PA, Day J, Seth M, et al. Long-term outcome after ICD and CRT implantation and influence of remote device follow-up: the ALTITUDE survival study. Circulation. 2010;122:2359–67.
21. Di Biase L, Gasparini M, Lunati M, Santini M, Landolina M, Boriani G, et al. Antiarrhythmic effect of reverse ventricular remodeling induced by cardiac resynchronization therapy: the InSync ICD (implantable Cardioverter-defibrillator) Italian registry. J Am Coll Cardiol. 2008;52:1442–9.
22. Tsai V, Goldstein MK, Hsia HH, Wang Y, Curtis J, Heidenreich PA, et al. Influence of age on perioperative complications among patients undergoing implantable cardioverter-defibrillators for primary prevention in the United States. Circ Cardiovasc Qual Outcomes. 2011;4:549–56.
23. Reynolds MR, Cohen DJ, Kugelmass AD, Brown PP, Becker ER, Culler SD, et al. The frequency and incremental cost of major complications among medicare beneficiaries receiving implantable cardioverter-defibrillators. J Am Coll Cardiol. 2006;47:2493–7.