

# Comparison of pharmacological treatment alone vs. treatment combined with implantable cardioverter defibrillator therapy in patients older than 75 years

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## Abstract

**Aims** Implantable cardioverter defibrillator (ICD) reduces mortality in selected patients. However, its role in patients older than 75 years is not well established.

**Methods and results** We performed a retrospective, non-randomized study using a historical cohort from a single centre. Between January 2008 and July 2014, we assessed patients aged  $\geq 75$  years with left ventricular ejection fraction  $\leq 35\%$ , identifying 385 patients with a Class I or IIa recommendation for ICD implantation. At the decision of the patient or attending cardiologists, 92 patients received an ICD. To avoid potential confounding factors, we used propensity-score matching. Finally, 126 patients were included (63 with ICD). The mean age was  $79.1 \pm 3.1$  years (86.5% male). As compared with the medical therapy group, the ICD patients had a lower percentage of chronic obstructive pulmonary disease (19.0% vs. 38.1%,  $P < 0.05$ ) and more frequent use of beta-blockers (BBs) (85.7 vs. 70.0%,  $P < 0.05$ ). Other treatments were otherwise similar in both groups. There were no differences related to age, aetiology, or other co-morbidities. During follow-up ( $39.2 \pm 22.4$  months), total mortality was 46.0% and cardiovascular events (death or hospitalization) occurred in 66.7% of the patients. A multivariate analysis revealed that only BB therapy was shown to be an independent protective variable with respect to mortality [hazard ratio 0.4 (0.2–0.7)]. ICD therapy did not reduce overall mortality or the rate of cardiovascular events.

**Conclusions** According to our results, the use of ICD, as compared with medical therapy, in patients older than 75 years did not demonstrate any benefit. Well-designed randomized controlled studies in patients older than 75 years are needed to ascertain the value of ICD therapy.

**Keywords** Elderly; Implantable cardioverter defibrillator; Heart failure; Low ejection fraction

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## Introduction

Implantable cardioverter defibrillator (ICD) therapy has been shown to reduce mortality in high-risk patients, aiding in both primary and secondary prevention of sudden cardiac death (SCD). Randomized controlled trials have demonstrated the superiority of the ICD over optimal medical therapy in patients with left ventricular dysfunction of ischaemic or non-ischaemic origin.<sup>1–6</sup> According to a recently published registry from the USA, 40% of new ICDs

and cardiac resynchronization therapy defibrillators (CRT-D) are implanted in patients older than 70 years and  $>10\%$  in octogenarians.<sup>7</sup> However, the benefit and safety of the ICD in the elderly are still a matter of debate owing to controversial results of observational studies and the lack of randomized trials in patients of this age group.<sup>8–17</sup> This study analyses the role of ICD in a population of elderly patients with left ventricular dysfunction, seeking to provide a potential indication for the implantation of this type of device.

## Methods

### Patients

Of all the patients consecutively referred to the echocardiography laboratory for a transthoracic echocardiogram between January 2008 and July 2014, we identified 802 subjects aged  $\geq 75$  years with left ventricular ejection fraction (LVEF) of  $\leq 35\%$ . From this group, we selected all cases with a potential indication for ICD according to the Class I or IIa recommendations contained in the 2008 Guidelines of the American Heart Association (AHA)/American College of Cardiology (ACC).<sup>18</sup> We excluded all patients with poor clinical condition that limited survival or functional capacity, according to the European Society of Cardiology and ACC/AHA recommendations (poor clinical condition defined as patients with serious co-morbidities who are unlikely to survive substantially  $>1$  year with good functional status). We defined patients as having poor clinical condition according to explicit comments and data obtained from the electronic health records of the attending physician. We identified 385 patients with a potential indication for ICD implantation at inclusion or during follow-up. Patients were divided into two groups: those in whom an ICD device had been implanted (ICD group, 92 patients) and those with a potential indication for ICD but who had not received the device owing to the decision of the patient or at the advice of the physician in charge (non-ICD group, 293 patients). In order to avoid potential confounding factors, we performed a propensity-score (PS)-matched analysis. Patient matching was performed at a 1:1 ratio using the nearest neighbour function. In the end, 126 patients were included in our study (63 with ICD and 63 PS-matched controls without ICD).

### Study design and treatment protocol

We collected the baseline characteristics of the patients and a number of clinically relevant events occurring during follow-up. Data were obtained from the electronic health records and through telephone interviews with the patients or their families. Patients in the ICD group had received an ICD or CRT-D; both types of device had been implanted according to standard techniques under mild sedation and local anaesthesia. The ICD-group patients attended a follow-up visit 1 month after device implantation and then every 3 months for device check-up. The non-ICD group received regular medical supervision depending on their symptoms and the indications of their physician. All patients had at least one visit every 6 months. This investigation was carried out in accordance with the principles outlined in the Declaration of Helsinki.

### Outcomes

The primary endpoint was death from any cause. Secondary endpoints were a composite of death from any cause and unplanned hospitalization due to heart failure (HF) or ventricular tachycardia (cardiovascular events), whichever occurred first. Hospitalization for HF was defined as admission to a health care facility lasting  $>24$  h for worsening of symptoms of HF and followed by specific HF treatment (regardless of the cause of decompensation).

### Complications of device implantation

We collected all the possible complications during or after device implantation, including pocket infection, pocket haematoma with intervention (or without intervention, although with increased hospital stay in all cases), pericardial effusion, pneumothorax, pulmonary oedema, stroke, coronary venous dissection, coronary sinus perforation, lead revision, and extracardiac stimulation.

### Statistical analysis

Data were subjected to descriptive statistical analysis via frequency measurements (absolute frequencies and percentages) for qualitative variables, and using means and standard deviations for quantitative variables. The magnitude of the effects of the variables was expressed in the form of odds ratio (OR) and 95% confidence intervals (95% CI).

Comparative analysis between the ICD and non-device groups and a univariate analysis of the quantitative variables were performed using Student *t*-test when the distribution was normal and Mann–Whitney *U*-test when it was not. The qualitative variables were analysed using  $\chi^2$  or Fisher exact test.

As observational studies do not allow for randomization, and in order to control for potential confounding factors, we performed a PS-matched analysis between the ICD and non-ICD groups. The PS was calculated using a binary logistic regression model, taking the ICD group as the dependent variable and adopting a parsimonious approach. In a first step, all the following variables were included in the univariate analysis: age, gender, hypertension, diabetes mellitus, obesity, chronic kidney disease, chronic obstructive pulmonary disease (COPD), peripheral vascular disease, any degree of cognitive impairment, any degree of functional disability, ischaemic origin of reduced EF, previous HF admission, sinus rhythm, wide QRS complex, LVEF, and New York Heart Association (NYHA) Class I or II (vs. III, IV, or not available) at onset of follow-up. All variables with a *P*-value  $< 0.2$  were entered into a multivariate binary logistic regression model, which served to estimate the PS of every patient. Patient matching

was performed at a 1:1 ratio with the nearest neighbour method (calliper =  $0.2 \times \text{SD} [\text{logitPs}]$ ).

We then performed a multivariate analysis (Cox regression) to identify significant predictors of cardiovascular events and mortality. Of the baseline variables collected, we selected those that had the potential to act as confounding factors. The criteria for this selection were their clinical and biological plausibility as well as the statistical criterion of Mickey, excluding all those variables for which the univariate analysis returned a  $P$ -value of  $>0.20$ . The results are expressed as hazard ratio (HR) and 95% CI.

## Results

### Baseline characteristics

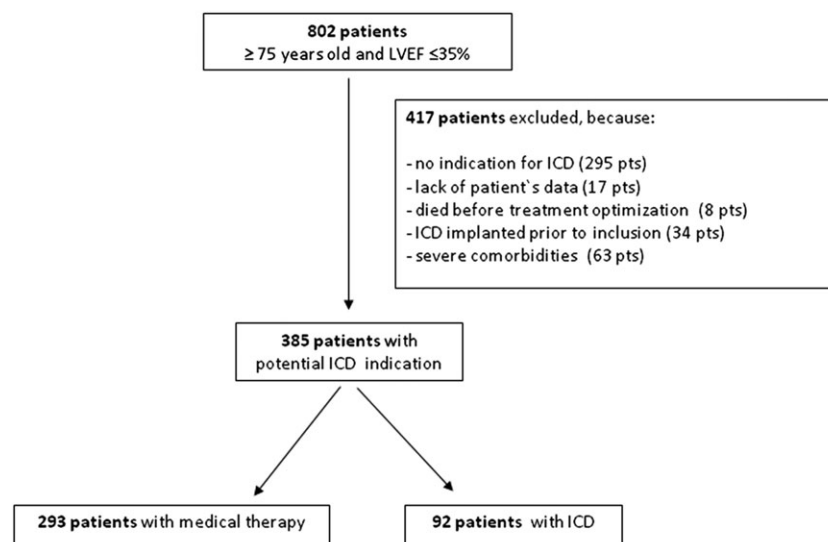
During the study period, 802 consecutive patients with LVEF  $\leq 35\%$  were assessed for eligibility. We excluded 417 patients owing to the following reasons: absence of a potential indication for ICD (295), lack of patient data (17), death before optimization of medical treatment,<sup>8</sup> ICD implanted prior to inclusion (34), or presence of severe co-morbidities including dementia, dependence for activities of daily living, disabling osteoarthritis, or additional diseases leading to a life expectancy of  $<1$  year (63). Ultimately, 385 patients met the criteria for a potential ICD indication (mean age of  $81.6 \pm 4.8$  years). After the initial evaluation and in accordance with the decision of the physician in charge and the opinion of the patient, 92 subjects underwent ICD implantation (23.9% of the 385 patients fulfilling the criteria

for potential ICD indication) (Figure 1). Among these patients, 46 received a CRT-D. In 77.2% of the patients receiving ICD/CRT-D, the indication was for primary prevention.

Table 1 shows the baseline characteristics of all patients with a potential indication for ICD implantation ( $n = 385$ ). The majority (71.4%) were male, and the mean LVEF was  $27.7 \pm 6.5\%$ . Compared with the non-device group, the ICD group had significantly lower age ( $78.5 \pm 2.9$  vs.  $82.6 \pm 4.9$  years,  $P < 0.001$ ), lower LVEF ( $25.0 \pm 7.3\%$  vs.  $28.5 \pm 6.0\%$ ,  $P = 0.01$ ), higher incidence of male gender (87.0% vs. 66.6%,  $P < 0.001$ ), and lower incidence of COPD (14.1% vs. 26.3%,  $P = 0.01$ ) and sleep apnoea syndrome (1.6% vs. 15.9%,  $P = 0.02$ ). ICD-group patients were in a worse functional class than were non-device subjects (NYHA III–IV 29.2% vs. 12.7%,  $P = 0.006$ ). Also, a comparison of the medical treatment received by the ICD and non-ICD patients is shown in Table 1. We observed a significantly higher percentage of patients receiving treatment with beta-blockers (BBs), angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and mineralocorticoid receptor antagonists.

In order to control for potential confounding factors, we performed a PS-matched analysis (patient matching was performed at a 1:1 ratio). Finally, 126 patients were included in our study (63 with ICD and 63 without ICD). Among ICD patients, 26 received a CRT-D. The mean age was  $79.1 \pm 3.1$  years (86.5% male). Table 2 shows the baseline characteristics of our study population. As compared with the medical therapy group, the ICD patients had a lower percentage of COPD (19.0% vs. 38.1%,  $P = 0.017$ ), with higher use of BB (85.7 vs. 70.0%,  $P = 0.026$ ). Other treatments were otherwise similar in both groups. There were no differences in relation to age, aetiology, or other co-morbidities.

**Figure 1** Flow chart for patients. Flow chart for 802 subjects aged  $\geq 75$  years with a left ventricular ejection fraction (LVEF)  $\leq 35\%$ , between January 2008 and July 2014. ICD, implantable cardioverter defibrillator.



**Table 1** Baseline characteristics in the two study groups (*n* = 385)

	ICD <i>n</i> = 92	No ICD <i>n</i> = 293	<i>P</i>
Age (years, $\pm$ SD)	78.5 $\pm$ 2.9	82.6 $\pm$ 4.9	<0.001
Sex (M/F, %)	87/13	67/33	<0.001
LVEF (% $\pm$ SD)	25.0 $\pm$ 7.3	28.5 $\pm$ 6.0	0.011
HBP ( <i>n</i> , %)	75 (81.5)	235 (80.2)	0.780
Diabetes ( <i>n</i> , %)	29 (31.5)	106 (36.2)	0.412
COPD ( <i>n</i> , %)	13 (14.1)	77 (26.3)	0.012
Previous stroke ( <i>n</i> , %)	12 (13.0)	48 (16.4)	0.434
Peripheral vascular disease ( <i>n</i> , %)	20 (21.7)	56 (19.1)	0.584
CKD ( <i>n</i> , %)	45 (48.9)	116 (39.6)	0.115
Ischaemic LVSD ( <i>n</i> , %)	58 (63.0)	163 (55.6)	0.143
NYHA ( <i>n</i> , %)			0.006
I–II	61 (70.1)	235 (86.7)	
III	26 (29.2)	35 (12.3)	
IV	0 (0)	1 (0.4)	
Sinus rhythm ( <i>n</i> , %)	53 (57.6)	175 (61.0)	0.567
QRS > 120 ms ( <i>n</i> , %)	74 (82.2)	160 (55.9)	<0.001
Beta-blocker ( <i>n</i> , %)	79 (87.8)	199 (69.8)	<0.001
ACEi and ARB ( <i>n</i> , %)	78 (84.8)	213 (72.7)	0.015
MRAs ( <i>n</i> , %)	59 (65.6)	141 (49.5)	0.007
Ivabradine ( <i>n</i> , %)	7 (7.8%)	20 (7.0%)	0.809
Diuretic ( <i>n</i> , %)	81 (90.0)	235 (82.5)	0.074
Digoxin ( <i>n</i> , %)	17 (18.9)	46 (16.1)	0.547
Amiodarone ( <i>n</i> , %)	26 (28.9)	34 (11.9)	<0.001
Sotalpor ( <i>n</i> , %)	4 (4.4)	2 (0.7%)	0.026

ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; HBP, high blood pressure; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; LVSD, left ventricular systolic dysfunction; M/F, male/female; MRAs, mineralocorticoid receptor antagonists; NYHA, New York Heart Association; SD, standard deviation.

**Table 2** Baseline characteristics in the study population (propensity score; *n* = 126)

	ICD <i>n</i> = 63	No ICD <i>n</i> = 63	<i>P</i>
Age (years, $\pm$ SD)	79.0 $\pm$ 2.8	79.1 $\pm$ 3.4	0.954
Sex (M/F, %)	54/9	55/8	0.794
LVEF (% $\pm$ SD)	26.2 $\pm$ 7.0	26.7 $\pm$ 6.5	0.680
HBP ( <i>n</i> , %)	50 (79.4)	54 (85.7)	0.347
Diabetes ( <i>n</i> , %)	17 (27.0)	27 (42.9)	0.061
COPD ( <i>n</i> , %)	12 (19.0)	24 (38.1)	0.017
SAS ( <i>n</i> , %)	1 (1.6)	10 (15.9)	0.02
Previous stroke ( <i>n</i> , %)	10 (15.9)	9 (14.3)	0.659
Ischaemic stroke	9 (14.3)	8 (12.7)	
Haemorrhagic stroke	1 (1.6)	1 (1.6)	
Peripheral vascular disease ( <i>n</i> , %)	14 (22.2)	15 (23.8)	0.832
Carotid artery disease	2 (3.2)	3 (4.8)	
Lower extremity artery disease	7 (11.1)	12 (19.0)	
Abdominal aorta aneurysm	5 (7.9)	0 (0.0)	
CKD ( <i>n</i> , %)	31 (49.2)	26 (41.3)	0.371
eGFR			
45–60 mL/min/1.73 m <sup>2</sup> ( <i>n</i> , %)	14 (22.2)	14 (22.2)	
30–44 mL/min/1.73 m <sup>2</sup> ( <i>n</i> , %)	13 (20.6)	7 (11.1)	
<30 mL/min/1.73 m <sup>2</sup> ( <i>n</i> , %)	4 (6.3)	5 (7.9)	
Ischaemic LVSD ( <i>n</i> , %)	40 (63.5)	38 (60)	0.272
NYHA ( <i>n</i> , %)			0.668
I–II	50 (79.4)	48 (76.2)	
III	13 (20.6)	15 (23.8)	
IV	0 (0)	0 (0)	
Sinus rhythm ( <i>n</i> , %)	35 (55.6)	37 (58.7)	0.719
QRS > 120 ms ( <i>n</i> , %)	48 (76.2)	50 (79.4)	0.668
Beta-blocker ( <i>n</i> , %)	54 (85.7)	44 (70.0)	0.026
ACEi and ARB ( <i>n</i> , %)	54 (85.7)	51 (81.0)	0.473

(Continues)

Table 2 (continued)

	ICD <i>n</i> = 63	No ICD <i>n</i> = 63	<i>P</i>
MRAs ( <i>n</i> , %)	40 (63.5)	34 (54.0)	0.272
Ivabradine ( <i>n</i> , %)	5 (7.9%)	6 (9.5%)	0.752
Diuretic ( <i>n</i> , %)	57 (90.5)	49 (77.8)	0.038
Digoxin ( <i>n</i> , %)	10 (15.9)	9 (14.3)	0.803
Amiodarone ( <i>n</i> , %)	19 (30.2)	4 (6.3)	<0.001
Sotalpor ( <i>n</i> , %)	2 (3.2)	0 (0)	0.094

ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; HBP, high blood pressure; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; LVSD, left ventricular systolic dysfunction; M/F, male/female; MRAs, mineralocorticoid receptor antagonists; NYHA, New York Heart Association; SAS, sleep apnoea syndrome; SD, standard deviation.

## Outcomes

### Device related

Six of the 92 patients receiving an ICD (6.5%) presented clinically significant complications in relation with the implantation procedure: four local haematomas that required prolonged hospitalization, one seroma, and one acute pulmonary oedema. Routine check-up of the ICDs was performed at our institution in 87/92 patients in the ICD group. Of these, 21 had received appropriate therapies (16 ICD shock, 18 antitachycardia pacing, 13 both). Seven patients had received inappropriate therapies, and four more patients had had both appropriate and inappropriate shocks. In total, 23 patients had received ICD shocks, 16 of which were appropriate and seven inappropriate. Mortality in patients without any

form of ICD therapy was 31.6% (19/60). In contrast, mortality for patients receiving appropriate ICD therapies was 61.9% (13/21) (*P* = 0.016). Mortality in patients with appropriate shocks was 75.0% (12/16).

### Study population

After a mean and median follow-up of  $39.2 \pm 22.4$  and 38.1 months, respectively, the total mortality in our study population (126 patients) was 46.0%, and cardiovascular events (mortality, hospitalization for HF or for ventricular arrhythmias) occurred in 66.7%. Twenty-four per cent of all mortalities were of a demonstrated cardiac origin (Table 3).

We performed a multivariate analysis (Cox regression) in our study population to identify significant predictors of total mortality. Previous HF, LVEF, COPD, cerebrovascular

Table 3 Mortality and cardiovascular events in the study population (propensity score)

	Total ( <i>n</i> , %) <i>n</i> = 126	ICD ( <i>n</i> , %) <i>n</i> = 63	No ICD ( <i>n</i> , %) <i>n</i> = 63	<i>P</i>
Total mortality	58 (46.0)	24 (38.1)	34 (54.0)	0.073
Cardiac mortality	14 (11.1)	7 (11.1)	7 (11.1)	1.0
Mortality of non-cardiac or unknown origin	44 (34.9)	17 (27.0)	27 (42.8)	0.061
Hospitalization for HF	55 (43.7)	32 (50.8)	23 (36.5)	0.105
Hospitalization for ventricular arrhythmia	6 (4.8)	6 (9.5)	0 (0)	0.003
Total cardiac events	84 (66.7)	46 (73.0%)	38 (60.3)	0.130

HF, heart failure; ICD, implantable cardioverter defibrillator; NS, non-significant.

Table 4 Total mortality [univariate and multivariate analysis in study population (*n* = 126)]

	Univariate analysis		Multivariate analysis	
	OR	95% CI	OR	95% CI
Previous HF	1.935	1.136–3.294		NS
Cerebrovascular disease	2.261	1.251–4.086	2.188	1.182–4.049
ICD	0.486	0.286–0.825		NS
Beta-blockers	0.403	0.232–0.701	0.425	0.243–0.743
LVEF	0.935	0.900–0.970	0.939	0.903–0.976
COPD	2.115	1.249–3.579	2.041	1.172–3.553
NYHA	1.949	1.117–3.402		NS

CI, confidence interval; COPD, chronic obstructive pulmonary disease; HF, heart failure; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; NS, not significant; NYHA, New York heart Association class; OR, odds ratio.

Included variables in the multivariate analysis: age, implantable cardioverter defibrillator, beta-blocker therapy, previous heart failure, LVEF, chronic obstructive pulmonary disease, cerebrovascular disease, rhythm, and New York heart Association class.



disease, NYHA class, ICD, and BB therapy were found to be related to mortality in the univariate analysis. However, Cox multivariate regression analysis of total mortality revealed that BB therapy was the only independent variable predicting reduced mortality (OR 0.425, CI [0.243–0.976]). This beneficial effect was not demonstrated with ICD therapy (Table 4).

We conducted a similar study in relation to the secondary endpoint (a composite of death from any cause, or unplanned hospitalization for HF or ventricular tachycardia). After a Cox regression multivariate analysis, no variable showed a protective effect related to the secondary endpoint (Table 5).

## Discussion

Several randomized trials of ICD in selected populations have shown that the implantation of these devices reduces mortality.<sup>4–6</sup> However, the populations recruited for these randomized controlled trials had a mean age of no more than 60–65 years, with relative low co-morbidity. Given that a substantial number of patients with severe left ventricular systolic dysfunction in daily clinical practice are aged  $\geq 75$  years<sup>19</sup> and have a higher proportion of co-morbidities, polypharmacy, and frailty (>70% of patients with HF older than 80 years met the criteria for frailty),<sup>20</sup> these differences are relevant when interpreting the results of randomized clinical trials about ICD. However, specific data regarding the benefit of ICD in elderly patients remain limited and controversial.

In a substudy of the Multicenter Automatic Defibrillator Implantation Trial II published by Huang *et al.*, 204 elderly patients with a mean age of  $79 \pm 3$  years were identified (59% received an ICD). Mortality reduction rates were similar in both the younger and elderly subgroups.<sup>21</sup> Furthermore, combined data from four randomized controlled trials on ICD implantation for primary prevention suggest that ICD reduces all-cause mortality in patients older than 75 years (HR 0.73).<sup>22</sup> Similarly, several articles have been published showing a positive role of ICD in the elderly. However, this and other studies are observational registries, or studies that

compare senior ICD recipients with their younger counterparts rather than with patients of the same age group receiving optimized medical therapy.<sup>9–13,15,16</sup>

In contrast to the aforementioned results, a subgroup analysis of the Sudden Cardiac Death in Heart Failure Trial found that ICD therapy did not reduce mortality in patients older than 65 years.<sup>5</sup> Moreover, another meta-analysis published by Santangeli *et al.*, based on combined data from five randomized controlled trials on ICD implantation for primary prevention, showed contradictory results about the benefit of ICD in elderly patients depending on the methodology used.<sup>23</sup> In addition, in the meta-analysis of the three secondary-prevention ICD trials (Antiarrhythmics versus Implantable Defibrillators, Cardiac Arrest Study Hamburg, and Canadian Implantable Defibrillator Study), the 252 patients aged  $\geq 75$  years did not experience any significant reduction in total or arrhythmic mortality with the ICD.<sup>24</sup> Also, a higher mortality in the elderly in spite of equivalent rates of appropriate ICD therapies has been described in several database analyses published in recent years.<sup>8,17,25</sup> That is, in spite of the fact that older ICD recipients have similar arrhythmic events and SCD rate as their younger counterparts, all-cause and non-cardiac mortality rates tend to be significantly higher in the elderly, likely because of higher proportion of frailty, co-morbidities, and so on, leading to a major increase in mortality risk among those patients  $\geq 75$  years old, which probably attenuated the benefit of ICD.<sup>14,26,27</sup>

Additionally, the substudy published by Huang *et al.* may have a significant limitation, as the study populations excluded high-risk and senile patients, and thus do not represent actual clinical practice.<sup>21</sup> Owing to their rigorous inclusion criteria, such as a cut-off point of 65 years for elderly patients, the trials tend to represent a relatively small and young study population. In routine practice, however, physicians often manage an elderly population and must decide whether to advise the implantation of an ICD/CRT-D on the basis of the guideline recommendations or, alternatively, to optimize pharmacological treatment as the sole therapy.

In our study, we assessed the benefit of ICD in a very elderly population with a potential indication for ICD implantation. As our study was not randomized, some differences regarding baseline characteristics and medical therapy were observed between the two study groups. To adjust for possible biases, we performed a PS-matched analysis with a subsequent multivariate analysis (Cox regression). This analysis of total mortality showed that BB therapy was the only independent variable that behaved as a protective factor. Moreover, no variable showed a protective effect related to the secondary endpoint, likely owing to a high incidence of HF admissions associated with a very-high-risk population. Although ICD implantation in patients older than 75 years is safe, with a relatively low complication rate (6.5%, similar to other published series<sup>28</sup>), elderly patients, when compared with their medically treated counterparts, may not

**Table 5** Total cardiovascular events [multivariate analysis in study population ( $n = 126$ )]

	OR	95% CI
ICD	1.646	1.033–2.622
MRAs	1.608	1.060–2.860
Diabetes	2.096	1.280–3.430
COPD	1.741	1.060–2.860

CI: confidence interval; COPD: chronic obstructive pulmonary disease; ICD: implantable cardioverter defibrillator; MRAs: mineralocorticoid receptor antagonists; OR: odds ratio.

Included variables in the multivariate analysis: age, ICD, MRAs, beta-blockers therapy, previous heart failure, diabetes, cerebrovascular disease, COPD, New York Heart Association class.

benefit from ICD in terms of primary endpoint-free survival or lower mortality rates. We consider that our results can be explained by the fact that senior patients are usually frail and present higher rates of co-morbidities and at more advanced stages. These factors increase mortality in the elderly population and could dilute the clinical benefit of ICD therapy. Furthermore, consistent with our results, patients with appropriate ICD shocks presented a higher mortality rate than those without ICD shocks (65% vs. 32%), suggesting that having ICD therapy indicates poor prognosis owing to an unfavourable clinical status, and the procedure does not necessarily save lives. On the other hand, optimal adjustment of medical treatment in accordance with current clinical recommendations would have a greater clinical impact. We know that nowadays, in a significant number of very elderly patients with low EF, BB therapy is not used as a therapeutic option.<sup>29</sup> In real-world practice, the very elderly populations like the ones studied here are frequently managed by general practitioners and usually have a high burden of co-morbidities or polypharmacy, which may interfere with BB treatment. In addition, the fear of possible side effects of medication also reduces the proportion of elderly patients with BB. However, the use of BB also brings benefits in elderly patients. Regarding this, our group has recently published the reduction of mortality with BB in this subgroup of patients.<sup>30</sup> Awareness among professionals of the benefits of using BB treatment in this kind of patients is needed in order to promote BB use when there is no formal contraindication.

Some recently published studies also showed no mortality-related benefit of the device in other population subgroups. In particular, the Danish Study to Assess the Efficacy of ICDs in Patients with Non-ischemic Systolic Heart Failure on Mortality trial showed no benefit in patients with symptomatic systolic HF not caused by coronary artery disease,<sup>31</sup> especially in those patients older than 70 years.<sup>32</sup> Data such as those shown in this trial or in our work call into question a broad indication for device implantation. Therefore, we consider it

necessary to perform specific controlled clinical trials to determine the role of ICD in elderly patients.

## Study limitations

Some limitations of our study should be taken into account. First, the study population is relatively small. This small sample size may have influenced the statistical results. In addition, ours is a retrospective, non-randomized study using a historical cohort from a single centre. Another limitation is the relatively short follow-up period, which could mask a long-term benefit of ICD. Nevertheless, this last issue is less relevant owing to the lower life expectancy of elderly patients.

## Conclusions

The role of ICD in the elderly is still unclear owing to controversial data in the literature. According to our results, ICD did not confer benefits over medical treatment in terms of survival or cardiovascular event rate. Nevertheless, well-designed randomized controlled studies to ascertain the value of ICD in senior patients are undoubtedly needed.

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## Conflict of interest

None declared.

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