Real-World Long-Term Effectiveness of Implantable Cardioverter-Defibrillators in Elderly Patients

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Background: Because it is unclear whether implantable cardioverter-defibrillators (ICDs) are equally effective in patients of all ages, we investigated the association of age with long-term clinical outcomes of patients who underwent ICD implantation.

Methods and Results: A total of 416 consecutive patients (mean age: 69 years) from 4 tertiary hospitals who underwent ICD implantation or were upgraded from an existing permanent pacemaker between January 2011 and November 2022 were enrolled and divided into 3 groups based on age: <65 years (n=158), 65–74 years (n=138), and ≥75 years (n=120). We compared the incidence of all-cause death and adverse cardiovascular events, including cardiac death, appropriate ICD therapy, and heart failure hospitalization. During a median follow-up period of 3.2 years (interquartile range: 1.1–5.6 years), 120 patients died. Older patients had a higher cumulative incidence of all-cause death and composite adverse cardiovascular events. The cumulative incidence of cardiac death and appropriate ICD therapies did not differ significantly; however, the incidence of hospitalization for heart failure increased with age. In multivariate analysis, age was independently associated with all-cause death but not composite adverse outcomes.

Conclusions: Age had a significant effect on subsequent all-cause death, but not on adverse cardiovascular events in patients with ICDs, suggesting that age should not be the only indication considered for ICD implantation.

Key Words: Age-appropriate therapy; Elderly patients; Implantable cardioverter-defibrillators

mplantable cardioverter-defibrillators (ICDs) are effective in preventing sudden cardiac death, as shown by randomized clinical trials that evaluated the efficacy of primary prevention ICDs.¹⁻³ Nonetheless, it is still unclear whether they are equally effective in patients of all ages. One of the reasons for the uncertainty about the effectiveness of ICDs in elderly people is the differences in efficacy and side effects between those reported in landmark clinical trials and those observed in real-world elderly patients. Past trials have enrolled patients with a mean age of approximately 60–65 years,¹⁻³ so the proportion of elderly patients may have been underrepresented in such trials compared with the proportion of such patients treated in real-world practice. Some trials have evaluated

the efficacy of ICDs in elderly patients, ⁴⁻⁹ a population that is the fastest growing worldwide, and for which heart failure (HF) is an increasingly important public health issue. In addition, both the incidence and mortality rate of coronary artery disease have improved substantially over past decades, ¹⁰ so the results of previous trials may not be relevant to current clinical practice. Therefore, we examined the real-world long-term clinical outcomes of consecutive adult patients of all ages with ICDs.

Methods

This retrospective observational study was conducted according to the principles of the Declaration of Helsinki,

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Variables	Overall (n=416)	<65 years (n=158)	65–74 years (n=138)	≥75 years (n=120)	P value	
Age, years	69 (58–76)	54 (46–60)	71 (67–73)	80 (77–83)	<0.001	
Male sex, n (%)	314 (76)	123 (78)	105 (76)	86 (72)	0.485	
Body mass index, kg/m ²	22.3 (19.5–25.1)	23.3 (20.8–27.3)	22.3 (18.9–24.7)	20.7 (18.8–23.7)	<0.001	
Follow-up, years	3.2 (1.1–5.6)	3.7 (1.4-6.6)	3.1 (1.0-5.4)	2.8 (0.9-4.8)	0.006	
Past history, n (%)						
Hypertension	161 (39)	50 (32)	55 (40)	56 (47)	0.037	
Dyslipidemia	144 (35)	53 (34)	58 (42)	33 (28)	0.047	
Diabetes mellitus	122 (29)	33 (21)	48 (35)	41 (34)	0.012	
CAD	160 (38)	49 (31)	65 (47)	46 (38)	0.018	
Atrial fibrillation	127 (31)	35 (22)	40 (29)	52 (43)	0.001	
Echocardiography						
LVEF, %	42 (27.5–61)	45 (27–65)	41 (30–56)	40 (27–56)	0.294	
LVDd, mm	54 (47–61)	52 (46-60)	55 (49–61)	54 (46-63)	0.268	
LVDs, mm	43 (31–53)	39 (29–51)	45 (31–53)	43 (31–56)	0.282	
LAD, mm	42 (36–48)	38 (32–44)	42 (37–48)	44 (39–50)	< 0.001	
IVSTd, mm	10 (8–12)	9 (8–11)	11 (9–13)	11 (9–13)	<0.001	
LVPWTd, mm	10 (9–12)	9.5 (8–11)	10 (9–12)	10 (9–12)	0.011	
Laboratory data						
Hemoglobin, g/dL	13.0±2.3	13.7±2.2	12.7±2.2	12.3±2.0	<0.001	
Cr, mg/dL	1.06 (0.81-1.445)	0.95 (0.79-1.24)	1.11 (0.90–1.55)	1.1 (0.86–1.595)	0.001	
HbA1c, %	5.9 (5.6–6.5)	5.7 (5.4-6.3)	6.0 (5.7–6.7)	6.0 (5.8–6.4)	0.001	
BNP, pg/mL	320.7 (87.7–664.2)	137.8 (32.1–453.9)	375.8 (106.7–640.0)	447.6 (188.7–979.2)	<0.001	
Medications, n (%)						
ACE inhibitors/ARBs	216 (52)	78 (49)	77 (56)	61 (51)	0.522	
β -blockers	318 (76)	104 (66)	116 (84)	98 (82)	<0.001	
Amiodarone	198 (48)	79 (50)	65 (47)	54 (45)	0.670	
Anticoagulant	170 (41)	50 (32)	54 (39)	66 (55)	<0.001	
Device therapy					<0.001	
TV-ICD	244 (59)	100 (63)	85 (62)	59 (49)		
S-ICD	41 (10)	24 (15)	13 (9)	4 (3)		
CRTD	131 (31)	34 (22)	40 (29)	57 (48)		
Secondary prevention	265 (64)	115 (73)	94 (68)	56 (47)	< 0.001	

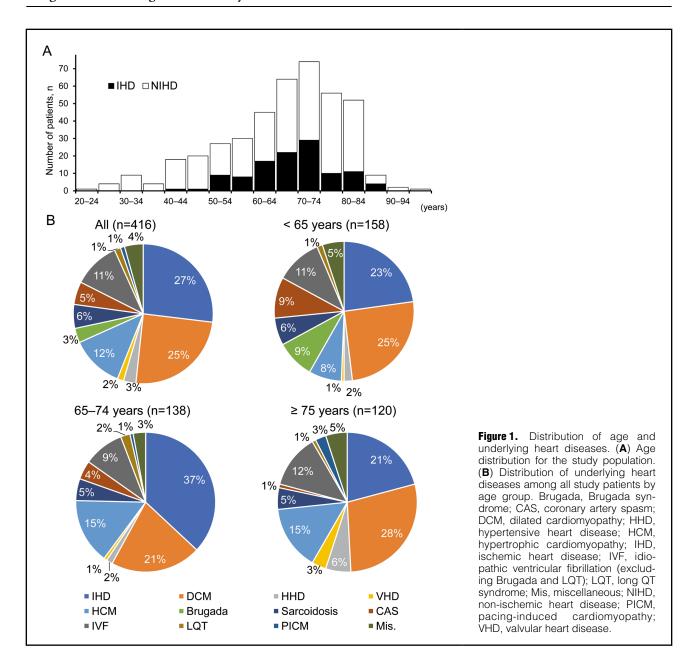
Values are expressed as mean }standard deviation, median (interquartile range), or numbers (proportion, %). ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; BNP, B-type natriuretic peptide; CAD, coronary artery disease; Cr, creatinine; CRTD, cardiac resynchronization therapy with a defibrillator; HbA1c, hemoglobin A1c; IVSTd, interventricular septal thickness at end-diastole; LAD, left atrial diameter; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-diastolic diameter; LVPB, left ventricular end-diastolic diameter; LVPWTd, left ventricular posterior wall thickness at end-diastole; S-ICD, subcutaneous implantable cardioverter-defibrillator.

and was approved by the ethics committees of Kushiro City General Hospital (2022-10), Hakodate Municipal Hospital (2023-103), Sunagawa City Medical Center (2023-5), and the National Hospital Organization Hokkaido Medical Center. Participants were informed of the study through information posted at each institution using the opt-out method. A total of 416 consecutive patients from 4 tertiary hospitals (Kushiro City General Hospital, Hakodate Municipal Hospital, Sunagawa City Medical Center, and National Hospital Organization Hokkaido Medical Center) who underwent ICD implantation or were upgraded from an existing permanent pacemaker between January 2011 and November 2022 were enrolled. The analysis included all types of ICD therapy, including transvenous and subcutaneous ICDs with or without cardiac resynchronization therapy (CRT). The indications for ICD were determined according to the guidelines of the Japanese Circulation Society.^{11–13} All 416 patients were included in this study. Of

them, 10 patients underwent device upgrades from a permanent pacemaker to an ICD, and 12 patients underwent device upgrades from a permanent pacemaker to a CRT defibrillator.

The clinical data of all patients were retrospectively analyzed. Echocardiographic examinations were performed within 2 months before ICD implantation or upgrade from an existing permanent pacemaker.

The primary outcome of this study was all-cause death. Secondary outcomes were adverse cardiovascular events, comprising cardiac death, appropriate ICD therapy, and hospitalization for HF. Non-arrhythmic death, defined as death without experiencing appropriate ICD therapy at any time during follow-up, was also analyzed. Cardiac death was defined as death attributable to a cardiovascular origin. Device detection settings, such as atrial/ventricular sensitivity, were individually determined for each patient. In addition, we also evaluated the ventricular tachycardia/



fibrillation (VT/VF) score and non-arrhythmic mortality score, which are included in the MaDIT-ICD score. However, we excluded non-sustained VT and New York Heart Association (NYHA) category because these data could not be retrieved for all patients.

The reported complications were classified into the following categories: lead-related (lead dislodgement, dissection, or perforation, including tamponade, and need for lead replacement for twitching), access-related (hematoma and pneumothorax), and infection.

Statistical Analysis

Where appropriate, continuous variables are presented as mean±standard deviation or median and interquartile range. We divided the patients into 3 groups based on age: <65 years, 65–74 years, and ≥75 years. Baseline variables were compared among the 3 groups by the chi-square test for categorical data or by one-way analysis of variance

followed by Bonferroni's post hoc test or the Kruskal-Wallis test followed by Dunn's post-test for multiple comparisons. The cumulative incidence of clinical outcomes was estimated using Kaplan-Meier curves, and a log-rank test was performed to calculate the episode-free rate over time. Cox regression analysis was performed to evaluate the influence of age on all-cause death and adverse cardiovascular events. Four models adjusting for the combination of the following variables based on their clinically relevant association with the primary outcome were constructed: Model 1, unadjusted; Model 2, adjusted for sex; Model 3, adjusted for items in Model 2 and hypertension, diabetes mellitus, hemoglobin, and creatinine; and Model 4, adjusted for items in Model 3 and cardiovascular risk factors, including left ventricular ejection fraction (LVEF), left atrial diameter, log B-type natriuretic peptide (BNP), β -blockers and amiodarone use, CRT, and secondary prevention. 15-25 All tests were 2-tailed, and statistical signifi-

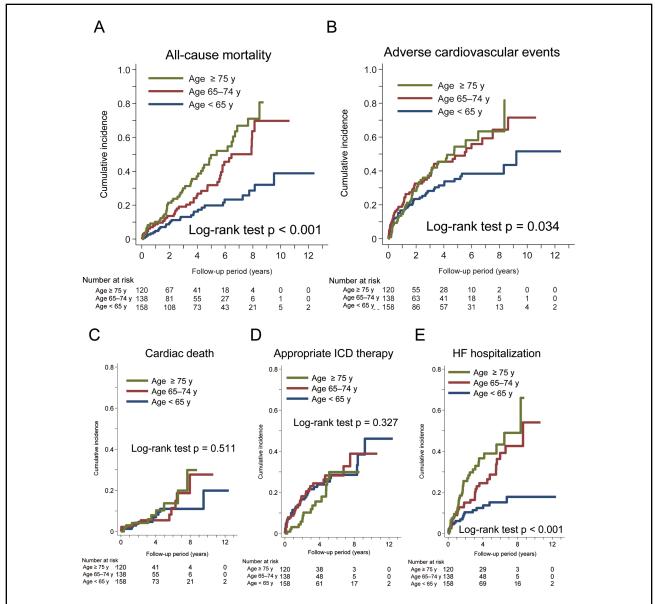


Figure 2. Survival analyses of long-term clinical outcomes based on age: <65 years, 65–74 years, and ≥75 years. (**A**) All-cause death. (**B**) Composite of adverse cardiovascular events: cardiac death, appropriate ICD therapy, and HF hospitalization. (**C**) Cardiac death, (**D**) appropriate ICD therapy, and (**E**) HF hospitalization. HF, heart failure; ICD, implantable cardioverter-defibrillator.

cance was set at P<0.05. All analyses were performed using Stata MP64 version 15 (StataCorp, College Station, TX, USA).

Results

The baseline characteristics of the 416 patients and the frequency distribution of their ages are shown in **Table 1** and **Figure 1A**. The mean patient age was 69 years, and 76% of the patients were male. Patients aged <65 years had lower levels of hemoglobin, creatinine, and hemoglobin A1c and a higher prevalence of diabetes mellitus compared with the other 2 groups. Patients aged ≥75 years had a higher prevalence of atrial fibrillation compared with the other 2 groups. A decrease in body mass index and an

increase in plasma BNP levels were observed with increasing age category. No significant difference in LVEF was observed across the groups. Patients aged <65 years had the lowest baseline treatment rate with β -blockers compared with the other 2 groups. Further, patients aged \geq 75 years had the highest baseline treatment rate with anticoagulants and the lowest proportion of secondary prevention ICDs. The major underlying diseases among all patients included ischemic heart disease (IHD) (27%) and dilated cardiomyopathy (25%) (**Figure 1B**). The incidence of IHD (21%) was lower than that of dilated cardiomyopathy (28%) in the \geq 75-year-old group.

During a median follow-up period of 3.2 years (interquartile range: 1.1–5.6 years), 120 patients (29%) died. Kaplan-Meier analyses revealed that all-cause death

occurred significantly less frequently in patients aged <65 years and tended to occur more frequently in patients aged ≥75 years (Figure 2A). The 1-year Kaplan-Meier event-free estimates were 95% in the <65-year-old group, 91% in the 65–74-year-old group, and 90% in the ≥75-year-old group (log-rank P=0.204). Composite outcomes occurred significantly less frequently in patients aged <65 years and tended to occur more frequently in patients aged ≥75 years (Figure 2B). For each component of the composite outcome, the cumulative incidences of cardiac death and appropriate ICD therapy were comparable between groups (**Figure 2C,D**). A total of 32 cardiac deaths were reported: 30 due to HF and 2 due to electrical storm. Appropriate ICD therapy was administered with antitachycardia pacing in 42 patients and ICD shock in 39 patients (some were previously unsuccessful with antitachycardia pacing). However, HF hospitalization tended to occur most frequently in patients aged ≥75 years (Figure 2E). Cox proportional hazard analyses indicated that age was associated with an increased risk of all-cause death even after full adjustment by major confounders, with a hazard ratio of 1.04 (95% confidence interval (CI) 1.01–1.06, P=0.004) (Table 2). However, this model demonstrated that age was not an independent determinant of adverse cardiovascular events, with a hazard ratio of 1.02 (95% CI 0.99-1.03, P=0.219). As for HF hospitalization, the hazard ratio after full adjustment of major confounders was 1.04 (95% CI 1.01–1.07, P=0.008). Cardiac death and appropriate ICD therapy were not associated with age (**Table 3**).

Kaplan-Meier analyses revealed that non-arrhythmic death occurred significantly more frequently in patients aged ≥75 years (**Supplementary Figure 1**). The patients aged ≥75 years had the lowest VT/VF score and the highest non-arrhythmic mortality score (**Supplementary Tables 1,2**).

Moreover, we divided the study cohort into 2 subgroups according to etiology: IHD and non-IHD (NIHD). We compared all-cause death and composite primary outcomes by age between the IHD and NIHD groups. In patients with IHD, Kaplan-Meier analyses revealed that all-cause death tended to occur more frequently in patients aged ≥75 years (Figure 3A), but adverse cardiovascular events were comparable between groups (Figure 3B). For each component of the composite outcome, the cumulative incidences of cardiac death, appropriate ICD therapy, and HF hospitalization were comparable (Figure 3C–E). In contrast, in patients with NIHD, Kaplan-Meier analyses revealed that all-cause death and adverse cardiovascular

Table 2. Cox Regression Model for All-Cause Death								
	All-cause death							
Incidence of events (%)		120 (29)						
	HR	95% CI	P value					
Model 1	1.05	1.04-1.07	<0.001					
Model 2	1.05	1.04-1.07	< 0.001					
Model 3	1.05	1.03-1.06	<0.001					
Model 4	1.05	1.02-1.08	0.001					

Values are presented as numbers (proportion, %). Model 1 unadjusted; Model 2 adjusted for sex; Model 3 adjusted for items in Model 2 and hypertension, diabetes mellitus, hemoglobin, and Cr; Model 4 adjusted for items in Model 3 and cardiovascular risk factors, including LVEF, LAD, log BNP, β -blockers and amiodarone use, CRTD, and secondary prevention. Cl, confidence interval; HR, hazard ratio. Other abbreviations as in Table 1.

events tended to occur more frequently in patients aged ≥75 years (**Figure 4A,B**). For each component of the composite outcome, the cumulative incidences of cardiac death and appropriate ICD therapy were comparable between the groups (**Figure 4C**–**E**). However, HF hospitalization tended to occur in patients with a higher age.

We compared the all-cause death and composite outcomes between the IHD and NIHD groups for each age group. All-cause death and adverse cardiovascular events occurred more frequently in patients with IHD (Supplementary Figure 2A,B). When divided into 3 groups based on age, there were no significant differences, except for adverse cardiovascular events, in patients aged <65 years (Supplementary Figure 2C–H).

As no consensus has been reached on whether ion channel diseases should be included in the category of cardiomy-opathy, ²⁶⁻²⁸ we performed a Cox regression analysis that excluded inherited cardiac arrhythmias^{29,30} (Supplementary Figures 3,4). In the NIHD group excluding hereditary arrhythmias, the cumulative incidences of all-cause death and cardiovascular events were similar to those in the NIHD group including hereditary arrhythmias (Supplementary Figure 3A,B). For each component of the composite outcome, the cumulative incidences of cardiac death, appropriate ICD therapy, and HF hospitalization were comparable (Supplementary Figure 3C–E). No significant differences in all-cause death and composite outcomes were observed

Table 3. Cox Regression Model for Adverse Events													
	Adve	Adverse cardiovascular events			Cardiac death		Appropriate ICD therapy		Н	HF hospitalization			
Incidence of event (%)		150 (36)			32 (8)			80 (19)			86 (21)		
	HR	95% CI	P value	HR	95% CI	P value	HR	95% CI	P value	HR	95% CI	P value	
Model 1	1.02	1.01-1.03	0.001	1.04	1.01-1.07	0.016	1.00	0.98-1.01	0.635	1.05	1.02-1.07	<0.001	
Model 2	1.02	1.01-1.04	0.001	1.04	1.01-1.07	0.017	1.00	0.98-1.01	0.653	1.05	1.03-1.07	<0.001	
Model 3	1.02	1.00-1.03	0.008	1.03	0.99-1.06	0.235	1.00	0.98-1.01	0.790	1.04	1.02-1.06	<0.001	
Model 4	1.01	0.99-1.04	0.210	1.03	0.96-1.10	0.468	0.99	0.96-1.02	0.401	1.05	1.01-1.08	0.013	

Values are presented as numbers (proportion, %). Model 1 unadjusted; Model 2 adjusted for sex; Model 3 adjusted for items in Model 2 and hypertension, diabetes mellitus, hemoglobin, and Cr; Model 4 adjusted for items in Model 3 and cardiovascular risk factors, including LVEF, LAD, log BNP, β -blockers and amiodarone use, CRTD, and secondary prevention. HF, heart failure; ICD, implantable cardioverter-defibrillator. Other abbreviations as in Tables 1,2.

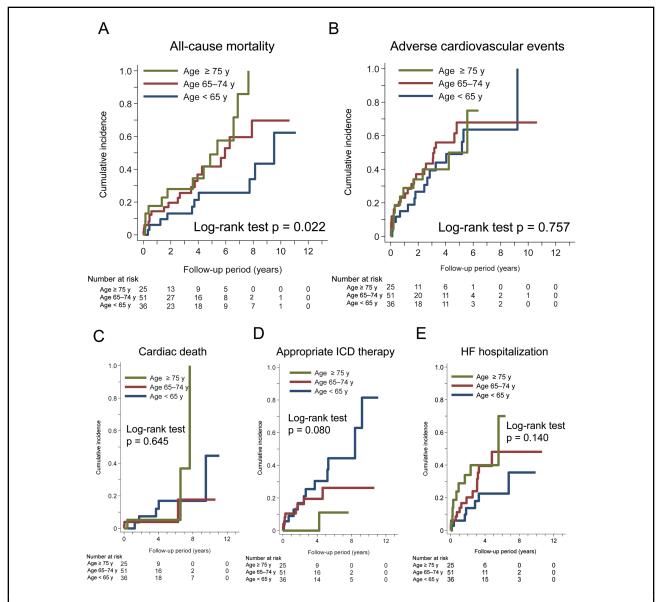


Figure 3. Survival analyses for the long-term clinical outcomes of ischemic heart disease by age group: <65 years, 65–74 years, and ≥75 years. (**A**) All-cause death. (**B**) Composite of adverse cardiovascular events: cardiac death, appropriate ICD therapy, and HF hospitalization. (**C**) Cardiac death, (**D**) appropriate ICD therapy, and (**E**) HF hospitalization. HF, heart failure; ICD, implantable cardioverter-defibrillator.

between the IHD and NIHD without inherited cardiac arrhythmias (Supplementary Figure 4A,B). In addition, no significant differences between IHD and NIHD without inherited cardiac arrhythmias were observed in any age group (Supplementary Figure 4C–H).

Complications occurred in 24 (5.8%) patients. Of them, 12 patients had lead-related complications: perforation in 3 patients, right ventricular lead dislodgement in 2 patients, left ventricular lead dislodgement in 4 patients, lead fracture in 1 patient, left ventricular lead replacement because of frequent phrenic nerve stimulation in 1 patient, and intrathoracic placement of a subcutaneous implantable defibrillator lead in 1 patient. Two patients had accessrelated complications, and 2 patients had hematomas. A total of 10 patients developed infectious complications.

Discussion

This study used real-world data to evaluate the effect of age on long-term clinical outcomes in patients with ICD. The data supporting the clinical efficacy of ICD in elderly patients are ambiguous and sometimes contradictory. Yung et al. observed that although elderly patients showed higher mortality rates after ICD implantation, the rates of appropriate shocks were similar across age groups.³¹ Our study results indicated that ICD implantation may be beneficial for elderly patients. However, Krahn et al. reported a diminishing proportional risk of sudden cardiac death with advancing age.³² Prior landmark studies have suggested that the survival benefit for elderly patients receiving ICDs may be limited,^{4,5} but the recommendations for

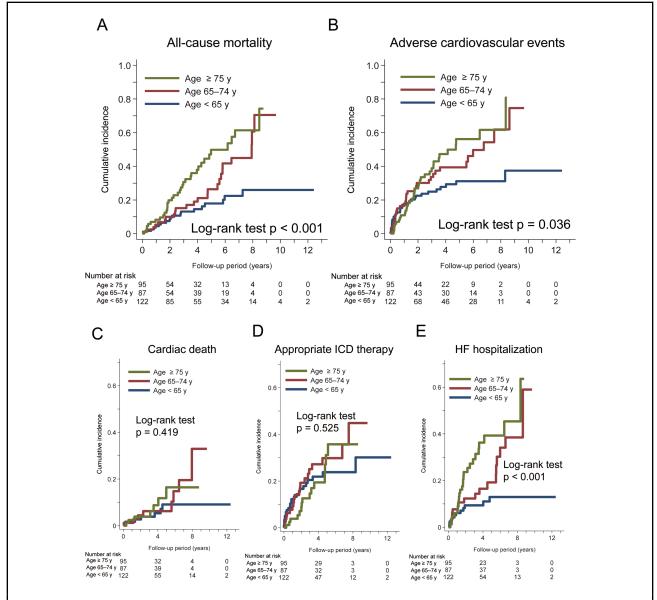
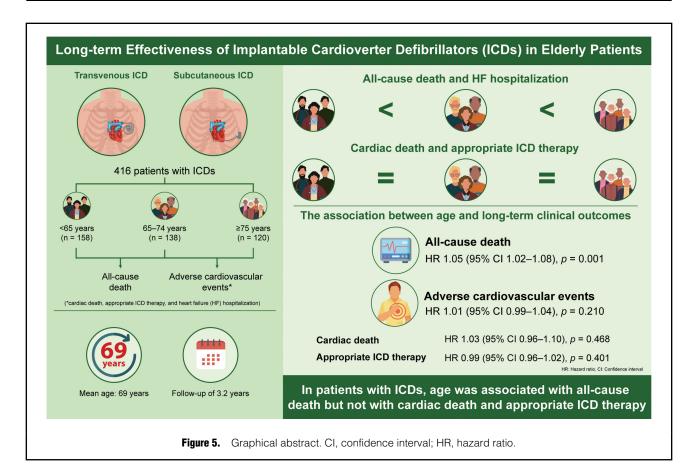


Figure 4. Survival analyses for the long-term clinical outcomes of non-ischemic heart disease by age group: <65 years, 65–74 years, and ≥75 years. (**A**) All-cause death. (**B**) Composite of adverse cardiovascular events: cardiac death, appropriate ICD therapy, and HF hospitalization. (**C**) Cardiac death, (**D**) appropriate ICD therapy, and (**E**) HF hospitalization. HF, heart failure; ICD, implantable cardioverter-defibrillator.

ICD implantation in European and American guidelines are not clear regarding age recommendations.^{33,34} The discussed benefits of ICD implantation in elderly patients are controversial. Age was not an exclusion criterion in previous clinical trials that evaluated the effectiveness of ICDs, but in contrast to real-world clinical practice, clinical trials usually limit the enrollment of patients aged over 75 years.³⁵ However, because of aging populations and the increasing total number of patients living with HF worldwide, the number of elderly patients requiring ICD implantation is increasing.

We retrospectively analyzed the data of consecutive cases from 2011 to 2022. In our study, the median age of patients at the time of ICD implantation or upgrade was 69 years, with the largest proportion of patients aged 70–74

years. The major finding of this study was that age was significantly associated with all-cause death but not with adverse cardiovascular events, particularly cardiac death, and appropriate ICD therapy (Figure 5). Non-cardiac health issues become more prevalent with advancing age, but ICDs may prevent arrhythmogenic death and prolong survival at any age. Our findings suggest a benefit of ICD implantation in elderly patients, which is contrary to the results of previous studies, ^{4,5} possibly because we included patients who were older than those in the previous reports. According to current ICD guidelines, ICD therapy is recommended for patients with a reasonable expectation of meaningful survival of ≥1 year. ³⁶ There was no difference in mortality rate at 1 year after ICD implantation among our 3 study groups, and we consider there was no over-



indication for elderly patients in this study.

The Seattle Proportional Risk Model score, which is calculated from 10 variables, including age, indicates that the risk of sudden cardiac death is greater in younger patients with HF.³⁷ That study excluded patients with previous ICD implantation, and the discrepancy with the results of the present study may be related to the prevention of cardiac death by appropriate ICD therapy. In Japan, markedly lower ICD use has been reported: approximately 7% of patients with HF receive primary prevention ICD. If ICD implantation increases in the future, cardiac death rates may become similar across all generations, as observed in the present study.

In this study, we evaluated non-arrhythmic death, defined as death without experiencing appropriate ICD therapy at any time during follow-up. We also evaluated the VT/VF and non-arrhythmic mortality scores without the non-sustained VT score or NYHA category, because those data could not be retrieved for all patients. The MADIT-ICD benefit score is a risk prediction score of prophylactic ICD therapy developed by weighing the patient's specific risk of VT/VF against the competing risk of non-arrhythmic death. The results suggested that ICD implantation in patients aged ≥75 years may offer little benefit compared with implantation in other age groups, as the risk reduction for sudden cardiac death was smaller and more non-arrhythmia-related deaths occurred. However, in this study, the cumulative incidence of appropriate ICD therapy was comparable among the groups, probably because this score has been proposed to predict the likelihood of prophylactic ICD benefit. In this study, 64% of patients underwent secondary prevention ICD implantation. Although age was not an exclusion criterion for the study patients, the usual limit to enrolling patients ≥75 years old may explain the differences between the present study results and those of previous reports. Interestingly, among the VT/VF score variables, significant differences were observed for atrial arrhythmia, myocardial infarction, and age. Patients aged ≥75 years had the highest incidence of atrial arrhythmia, but similar incidence of myocardial infarction as in patients aged <65 years. Among patients aged <75 years, 2 points were added to the VT/VF score, which seems to offer an advantage to this population.

Several randomized trials have demonstrated the efficacy of ICD therapy for IHD.38,39 Recently, the Danish Study to Assess the Efficacy of ICDs in Patients with Non-Ischemic Systolic Heart Failure on Mortality reported that prophylactic ICD implantation in patients with NIHD and reduced LVEF was not associated with all-cause death.3 Therefore, many past studies have distinguished between IHD and NIHD, and guidelines do the same.³⁴ Therefore, in this study we evaluated the prognosis by age for IHD and NIHD. Among patients with IHD, patients aged <65 years had lower all-cause death, and appropriate ICD therapy tended to be more frequent in younger patients. The benefits may be stronger in younger patients with IHD. In contrast, older patients with NIHD had higher all-cause death, although there were no differences in cardiac death or appropriate ICD therapy among the 3 age

groups. Among patients with NIHD, the benefits may be equal across all age groups. Moreover, in all age groups, we compared the prognoses between the IHD and NIHD groups. In patients <65 years of age and 65–74 years of age, patients with IHD tended to be at a higher risk of all-cause death and adverse cardiovascular events than patients with NIHD. However, in patients ≥75 years of age, the risk was similar for both IHD and NIHD. In elderly patients, distinguishing between IHD and NIHD may be unnecessary.

Study Limitations

First, comparing elderly ICD recipients with non-implanted controls is the most convincing way to examine the effectiveness of ICDs in elderly patients, but we could not identify all patients who refused ICD implantation despite having an indication it. Therefore, it was not possible to compare elderly ICD recipients with non-implanted controls. Our study showed that although there was a difference in all-cause deathg, age was not associated with cardiac death or appropriate ICD therapy, suggesting the effectiveness of ICD in elderly patients. Second, this was a retrospective study. Therefore, device detection or therapy settings were individually determined for each patient. We were unable to collect data on history of NSVT, frailty, and dementia in all patients. We may have missed ventricular tachyarrhythmia outside the device detection zone. However, we were able to include elderly patients who are unlikely to be registered in a prospective study.

In conclusion, age had a significant effect on all-cause death but not on adverse cardiovascular events in patients with ICDs. These results provide evidence that age should not be the only indication considered for ICD implantation, and such decisions should be made carefully and individually.

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Disclosures

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IRB Information

This retrospective observational study was approved by the ethics committees of Kushiro City General Hospital (2022-10), Hakodate Municipal Hospital (2023-103), Sunagawa City Medical Center (2023-5), and the National Hospital Organization Hokkaido Medical Center. Participants were informed of the study through information posted at each institution using the opt-out method.

Data Availability

The deidentified participant data will not be shared.

Author Contributions

H.H.: Writing – review & editing, Supervision, Project administration. N.N.: Data curation. K.O.: Data curation. S.S.: Data curation. H.A.: Data curation. Y.C.: Data curation. H.K.: Data curation. Y.K.: Validation; Visualization. M.T.: Data curation and Investigation. Y.T.: Project administration. T.S.: Project administration. M.S.: Writing - review & editing. T.N.: Methodology, Writing - review & editing. T.A.: Writing - review & editing.

References

- Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med 2002; 346: 877–883, doi:10.1056/NEJMoa013474.
- Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 2005; 352: 225–237, doi:10.1056/NEJMoa043399.
- 3. Kober L, Thune JJ, Nielsen JC, Haarbo J, Videbaek L, Korup E, et al. Defibrillator implantation in patients with nonischemic systolic heart failure. *N Engl J Med* 2016; **375:** 1221–1230, doi:10.1056/NEJMoa1608029.
- Santangeli P, Di Biase L, Dello Russo A, Casella M, Bartoletti S, Santarelli P, et al. Meta-analysis: Age and effectiveness of prophylactic implantable cardioverter-defibrillators. *Ann Intern Med* 2010; 153: 592–599, doi:10.7326/0003-4819-153-9-201011020-00009.
- Aktas MK, Goldenberg I, Moss AJ, Huang DT, Kutyifa V, Wang PJ, et al. Comparison of age (<75 years versus ≥75 years) to risk of ventricular tachyarrhythmias and implantable cardioverter defibrillator shocks (from the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy). Am J Cardiol 2014; 114: 1855–1860, doi:10.1016/j. amjcard.2014.09.026.
- Healey JS, Hallstrom AP, Kuck KH, Nair G, Schron EP, Roberts RS, et al. Role of the implantable defibrillator among elderly patients with a history of life-threatening ventricular arrhythmias. Eur Heart J 2007; 28: 1746–1749, doi:10.1093/eurheartj/ehl438.
- Ermis C, Zhu AX, Vanheel L, Sakaguchi RN, Lurie KG, Lu F, et al. Comparison of ventricular arrhythmia burden, therapeutic interventions, and survival, in patients < 75 and patients ≥ 75 years of age treated with implantable cardioverter defibrillators. Europace 2007; 9: 270–274, doi:10.1093/europace/eum015.
- 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: 503–514, doi:10.5603/cj.2011.0005.
- Éarley A, Persson R, Garlitski AC, Balk EM, Uhlig K. Effectiveness of implantable cardioverter defibrillators for primary prevention of sudden cardiac death in subgroups: A systematic review. *Ann Intern Med* 2014; 160: 111–121, doi:10.7326/M13-1787.
- Amini M, Zayeri F, Salehi M. Trend analysis of cardiovascular disease mortality, incidence, and mortality-to-incidence ratio: Results from global burden of disease study 2017. BMC Public Health 2021; 21: 401, doi:10.1186/s12889-021-10429-0.
- Nogami A, Kurita T, Abe H, Ando K, Ishikawa T, Imai K, et al. JCS/JHRS 2019 guideline on non-pharmacotherapy of cardiac arrhythmias. *Circ J* 2021; 85: 1104–1244, doi:10.1253/circj. CJ-20-0637.
- JCS Joint Working Group. Guidelines for non-pharmacotherapy of cardiac arrhythmias (JCS 2011). Circ J 2013; 77: 249–274, doi:10.1253/circj.CJ-66-0054.
- Chinushi M, Aizawa Y. Non-pharmacological management of ventricular tachycardia. Circ J 2007; 71(Suppl A): A97–A105, doi:10.1253/circj.71.a97.
- Younis A, Goldberger JJ, Kutyifa V, Zareba W, Polonsky B, Klein H, et al. Predicted benefit of an implantable cardioverterdefibrillator: The MADIT-ICD benefit score. *Eur Heart J* 2021; 42: 1676–1684, doi:10.1093/eurheartj/ehaa1057.
- Taylor CJ, Ordonez-Mena JM, Jones NR, Roalfe AK, Lay-Flurrie S, Marshall T, et al. National trends in heart failure mortality in men and women, United Kingdom, 2000–2017. Eur J Heart Fail 2021; 23: 3–12, doi:10.1002/ejhf.1996.
- Cao X, Zhang L, Wang X, Chen Z, Zheng C, Chen L, et al. Cardiovascular disease and all-cause mortality associated with individual and combined cardiometabolic risk factors. BMC Public Health 2023; 23: 1725, doi:10.1186/s12889-023-16659-8.
- Lee G, Choi S, Kim K, Yun JM, Son JS, Jeong SM, et al. Association of hemoglobin concentration and its change with cardiovascular and all-cause mortality. *J Am Heart Assoc* 2018; 7: e007723, doi:10.1161/JAHA.117.007723.
- Yamaguchi J, Kasanuki H, Ishii Y, Yagi M, Nagashima M, Fujii S, et al. Serum creatinine on admission predicts long-term mortality in acute myocardial infarction patients undergoing successful primary angioplasty: Data from the Heart Institute of Japan Acute Myocardial Infarction (HIJAMI) Registry. Circ J 2007; 71: 1354–1359, doi:10.1253/circj.71.1354.
- 19. Ford I, Robertson M, Komajda M, Bohm M, Borer JS, Tavazzi

L, et al. Top ten risk factors for morbidity and mortality in patients with chronic systolic heart failure and elevated heart rate: The SHIFT Risk Model. *Int J Cardiol* 2015; **184:** 163–169, doi:10.1016/j.ijcard.2015.02.001.

- Bouzas-Mosquera A, Broullon FJ, Alvarez-Garcia N, Mendez E, Peteiro J, Gandara-Sambade T, et al. Left atrial size and risk for all-cause mortality and ischemic stroke. CMAJ 2011; 183: E657–E664, doi:10.1503/cmaj.091688.
- 21. York MK, Gupta DK, Reynolds CF, Farber-Eger E, Wells QS, Bachmann KN, et al. B-type natriuretic peptide levels and mortality in patients with and without heart failure. *J Am Coll Cardiol* 2018; **71:** 2079–2088, doi:10.1016/j.jacc.2018.02.071.
- 22. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Bohm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2021; **42:** 3599–3726, doi:10.1093/eurhearti/ehab368.
- Amiodarone Trials Meta-Analysis Investigators. Effect of prophylactic amiodarone on mortality after acute myocardial infarction and in congestive heart failure: Meta-analysis of individual data from 6500 patients in randomised trials. *Lancet* 1997; 350: 1417–1424, https://www.ncbi.nlm.nih.gov/pubmed/9371164.
- Moss AJ, Hall ŴJ, Cannom DS, Klein H, Brown MW, Daubert JP, et al. Cardiac-resynchronization therapy for the prevention of heart-failure events. N Engl J Med 2009; 361: 1329–1338, doi:10.1056/NEJMoa0906431.
- Zhang S, Ching CK, Huang D, Liu YB, Rodriguez-Guerrero DA, Hussin A, et al. Utilization of implantable cardioverter-defibrillators for the prevention of sudden cardiac death in emerging countries: Improve SCA clinical trial. *Heart Rhythm* 2020; 17: 468–475, doi:10.1016/j.hrthm.2019.09.023.
- Maron BJ, Towbin JA, Thiene G, Antzelevitch C, Corrado D, Arnett D, et al. Contemporary definitions and classification of the cardiomyopathies: An American Heart Association Scientific Statement from the Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functional Genomics and Translational Biology Interdisciplinary Working Groups; and Council on Epidemiology and Prevention. Circulation 2006; 113: 1807–1816, doi:10.1161/CIRCULATIONAHA.106.174287.
- Chung FP, Lin CY, Lin YJ, Chang SL, Lo LW, Hu YF, et al. Ventricular arrhythmias in nonischemic cardiomyopathy. *J Arrhythm* 2018; 34: 336–346, doi:10.1002/joa3.12028.
- Wang Y, Jia H, Song J. Accurate classification of non-ischemic cardiomyopathy. *Curr Cardiol Rep* 2023; 25: 1299–1317, doi:10. 1007/s11886-023-01944-0.
- Priori SG, Wilde AA, Horie M, Cho Y, Behr ER, Berul C, et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes: Document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013. *Heart Rhythm* 2013; 10: 1932–1963, doi:10.1016/j. hrthm.2013.05.014.
- 30. Schwartz PJ, Ackerman MJ, Antzelevitch C, Bezzina CR, Borggrefe

- M, Cuneo BF, et al. Inherited cardiac arrhythmias. *Nat Rev Dis Primers* 2020; **6:** 58, doi:10.1038/s41572-020-0188-7.
- Yung D, Birnie D, Dorian P, Healey JS, Simpson CS, Crystal E, et al. Survival after implantable cardioverter-defibrillator implantation in the elderly. *Circulation* 2013; 127: 2383–2392, doi:10.1161/CIRCULATIONAHA.113.001442.
- Krahn AD, Connolly SJ, Roberts RS, Gent M, Investigators A. Diminishing proportional risk of sudden death with advancing age: Implications for prevention of sudden death. *Am Heart J* 2004; 147: 837–840, doi:10.1016/j.ahj.2003.12.017.
- Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure: Executive summary: A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* 2013; 128: 1810–1852, doi:10.1161/CIR.0b013e31829e8807.
- Zeppenfeld K, Tfelt-Hansen J, de Riva M, Winkel BG, Behr ER, Blom NA, et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Eur Heart J 2022; 43: 3997–4126, doi:10.1093/ eurhearti/ehac262.
- 35. Aktas MK, Younis A, Saxena S, Diamond A, Ojo A, Kutyifa V, et al. Age and the risk of ventricular tachyarrhythmia in patients with an implantable cardioverter-defibrillator. *JACC Clin Electrophysiol* 2023; **9:** 979–988, doi:10.1016/j.jacep.2022.11.020.
- Correction to: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2023; 147: e674, doi:10.1161/CIR.0000000000001142.
- Shadman R, Poole JE, Dardas TF, Mozaffarian D, Cleland JG, Swedberg K, et al. A novel method to predict the proportional risk of sudden cardiac death in heart failure: Derivation of the Seattle Proportional Risk Model. *Heart Rhythm* 2015; 12: 2069–2077, doi:10.1016/j.hrthm.2015.06.039.
- McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail 2012; 14: 803–869, doi:10.1093/eurjhf/hfs105
- Priori SG, Blomstrom-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. *Rev Esp Cardiol (Engl Ed)* 2016; 69: 176, doi:10.1016/j.rec.2016.01.001.

Supplementary Files

Please find supplementary file(s); https://doi.org/10.1253/circrep.CR-24-0131