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ORIGINAL ARTICLE
Arrhythmia/Electrophysiology

Prognosis of Japanese Patients With Coronary Artery Disease Who Underwent Implantable Cardioverter Defibrillator Implantation

— The JID-CAD Study —

Tomoyuki Kabutoya, MD, PhD; Takeshi Mitsuhashi, MD, PhD; Akihiko Shimizu, MD, PhD; Takashi Nitta, MD, PhD; Hideo Mitamura, MD, PhD; Takashi Kurita, MD, PhD; Haruhiko Abe, MD, PhD; Yuji Nakazato, MD, PhD; Naokata Sumitomo, MD, PhD; Kazushige Kadota, MD, PhD; Kazuo Kimura, MD, PhD; Ken Okumura, MD, PhD

Background: There has been no large multicenter clinical trial on the prognosis of implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy with a defibrillator (CRT-D) in Japanese patients with coronary artery disease (CAD). The aim of the present study was to compare differences in the prognoses of Japanese patients with CAD between primary and secondary prevention, and to identify potential predictors of prognosis.

Methods and Results: We investigated 392 CAD patients (median age 69 years, 90% male) treated with ICD/CRT-D enrolled in the Japan Implantable Devices in CAD (JID-CAD) Registry. The primary endpoint was all-cause death, and the secondary endpoint was appropriate ICD therapies. Endpoints were assessed by dividing patients into primary prevention (n=165) and secondary prevention (n=227) groups. The mean (±SD) follow-up period was 2.1±0.9 years. The primary endpoint was similar in the 2 groups (P=0.350).

Conclusions: The mortality rate in Japanese patients with CAD who underwent ICD/CRT-D implantation as primary prevention was not lower than that of patients who underwent ICD/CRT-D implantation as secondary prevention, despite the lower cardiac function in the patients undergoing ICD/CRT-D implantation as primary prevention.

Key Words: Coronary artery disease; Implantable cardioverter defibrillator; Primary prevention

The risk of sudden cardiac death in patients with coronary artery disease (CAD) is a serious problem. An implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy with a defibrillator (CRT-D) is useful not only as secondary prevention, but also for the primary prevention of sudden cardiac death in patients with CAD.[1–3] Thus, ICD and CRT-D have been widely implanted as primary prevention in patients with CAD. The rate of appropriate therapy was similar in Japanese patients undergoing CRT-D implantation as primary or secondary prevention.[4]

In previous reports, the prognosis of Japanese patients with CAD was relatively good.[5,6] In the Heart Institute of Japan Acute Myocardial Infarction-II (HIJAMI-II) study, the rate of sudden death in patients with myocardial infarction was 1.2% during an average follow-up period of 4.1 years.[5] In the Chronic Heart Failure Analysis and Registry in the Tohoku District 2 (CHART-2) study, the rate of sudden death in patients with a left ventricular ejection fraction (LVEF) <30% (including patients with ischemic and non-ischemic heart disease) was 4.9% during an average follow-up period of 2.7 years.[6] Nonetheless,

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Department of Medicine, Division of Cardiovascular Medicine, Jichi Medical University, Shimotsuke (T. Kabutoya); Cardiology and Vascular Medicine, Hoshi General Hospital, Koriyama (T.M.); Ube-Kohsan Central Hospital, Ube (A.S.); Cardiovascular Surgery, Nippon Medical School, Tokyo (T.N.); Cardiology, Tachikawa Hospital, Tachikawa (H.M.); Cardiology, Kindai University School of Medicine, Osaka-Sayama (T. Kurita); Department of Heart Rhythm Management, University of Occupational and Environmental Health, Kitakyushu (H.A.); Cardiology, Juntendo University Urayasu Hospital, Urayasu (Y.N.); Pediatric Cardiology, Saitama Medical University International Medical Center, Hidaka (N.S.); Cardiology, Kurashiki Central Hospital, Kurashiki (K. Kadota); Division of Cardiology, Yokohama City University Medical Center, Yokohama (K. Kimura); and Division of Cardiology, Saiseikai Kumamoto Hospital, Kumamoto (K.O.), Japan

Mailing address: Tomoyuki Kabutoya, MD, PhD, Division of Cardiovascular Medicine, Department of Medicine, Jichi Medical University School of Medicine, 3311-1 Yakushiji, Shimotsuke 329-0498, Japan. E-mail: kabu@jichi.ac.jp

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Table 1. Patient Characteristics

	Primary prevention (n=165)	Secondary prevention (n=227)	P value
Age (years)	70 [63–76]	68 [63–74]	0.189
Male sex (%)	90.9	89.4	0.629
NYHA-FC I/II/III/IV (n)	20/71/68/6	104/79/38/6	<0.001
CRT (%)	49.7	15.0	<0.001
Atrial fibrillation (%)	11.5	6.6	0.089
Myocardial infarction (%)	87.3	92.1	0.118
Lesion of myocardial infarction (%)			
Left main trunk	4.8	3.5	0.514
Left anterior descending	60.0	56.4	0.476
Left circumflex artery	12.1	19.4	0.055
Right coronary artery	32.7	35.2	0.605
Coronary artery lesions 0VD/1VD/2VD/3VD (n)	62/51/20/20	73/66/31/36	0.576
Prior revascularization (%)	92.1	81.9	0.026
Diabetes (%)	53.3	41.4	0.019
Hypertension (%)	60.0	69.2	0.060
Dyslipidemia (%)	72.1	60.8	0.020
Hyperuricemia (%)	40.6	20.7	<0.001
Stroke (%)	13.9	14.5	0.868
Peripheral artery disease (%)	13.9	7.0	0.024
Chronic kidney disease (%)	44.2	34.4	0.047
COPD (%)	4.8	2.6	0.246
Medication (%)			
Antiarrhythmic agent	89.1	96.5	0.004
β-blocker	84.8	84.6	0.942
ACEI	41.8	48.9	0.166
ARB	35.2	23.3	0.010
LVEF (%)	28 [25–34]	37 [28–47]	<0.001
eGFR (mL/min/1.73 m^2)	47.5±19.8	52.0±22.9	0.040
QRS duration (ms)	127 [109–161]	116 [100–142]	0.002
BNP (pg/dL)	349 [155–718]	218 [95–450]	0.391

Unless indicated otherwise, data are shown as the mean±SD or median [interquartile range]. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers; BNP, B-type natriuretic peptide; COPD, chronic obstructive pulmonary disease; CRT, cardiac resynchronization therapy; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; NYHA-FC, New York Heart Association Functional Class; VD, vessel disease.

there has been no large multicenter clinical trial on the prognosis of ICD/CRT-D as an intervention for lethal arrhythmic events in Japanese patients with CAD. In addition, it is not yet known how often ICD therapy has been provided as primary prevention, and the prognosis of Japanese CAD patients who underwent ICD/CRTD as primary prevention is unclear.

Therefore we conducted a prospective multicenter observational study in patients with CAD treated with an ICD/CRT-D, the Japan Implantable Devices in Coronary Artery Disease (JID-CAD) study.[7] The aim of this study was to investigate differences in the prognosis of Japanese patients with CAD focusing on the effects of ICD/CRT-D used for primary and secondary prevention; in addition, we investigated predictors of prognosis, including interventions for ischemic events.

Methods

Patients

The details of the JID-CAD study have been reported elsewhere.[7] Patients were enrolled from October 2014 to October 2016. To be eligible for enrolment, patients had to meet the following criteria: (1) newly implanted ICD/CRT-D in accord with the guidelines on non-pharmacological therapy for cardiac arrhythmias published by the Japanese Circulation Society (JCS) in 2011;[8] (2) CAD, including myocardial infarction, effort angina, and vasospastic angina; and (3) age ≥20 years, regardless of sex. The exclusion criteria were age <20 years, no interest in participating in the study, and an inability to participate as judged by patients' physicians. The JID-CAD study was approved by the ethics committee at each participating institution, and written informed consent was obtained from all patients.

Definitions of Primary and Secondary Prevention

Secondary prevention was defined as a case in which a cardiac implantable device was implanted to prevent sudden cardiac death from spontaneous sustained ventricular tachycardia (VT) or ventricular fibrillation (VF), not including VT/VF induced during electrophysiological testing.[7] Primary prevention was defined as: (1) patients with chronic heart failure due to CAD who had New York

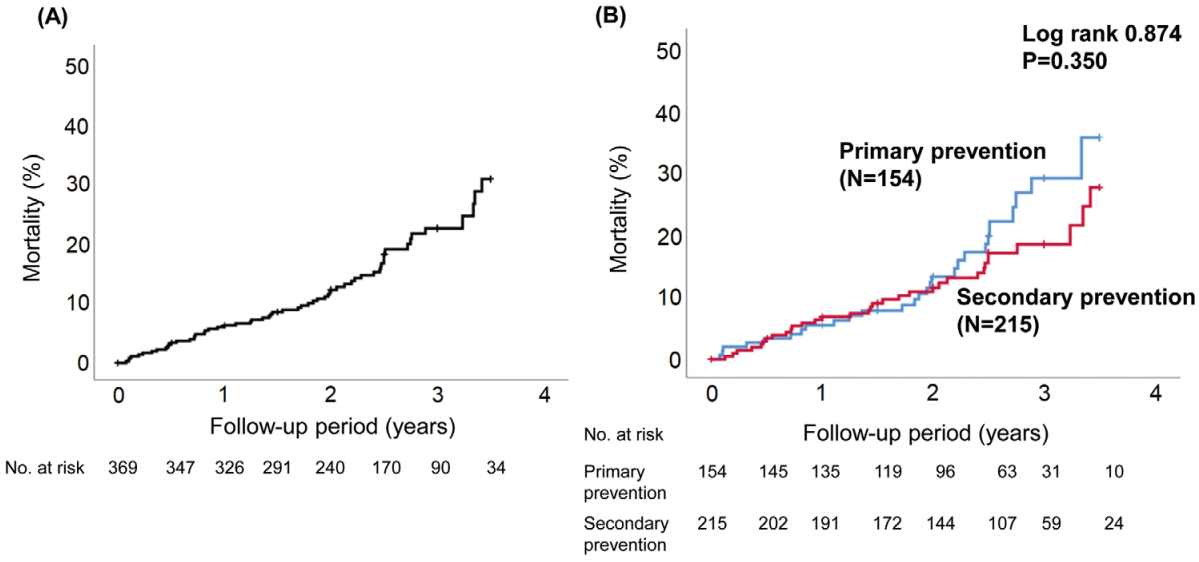

Figure 1. Mortality for (**A**) all patients and (**B**) the primary and secondary prevention groups separately.

Heart Association functional class (NYHA-FC) II or III symptoms of heart failure, an LVEF ≤35%, and non-sustained VT; (2) patients with NYHA-FC I symptoms of heart failure who had left ventricular dysfunction (LVEF ≤35%) associated with CAD and non-sustained VT in whom sustained VT or VF was induced during an electrophysiological study; and (3) patients with chronic heart failure associated with CAD who had NYHA-FC II or III symptoms of heart failure despite appropriate pharmacotherapy and an LVEF ≤35%.[8]

Data Collection and Follow-up

Creatinine and B-type natriuretic peptide brain natriuretic peptide (BNP) concentrations were measured and QRS duration was evaluated by electrocardiography in all patients. The estimated glomerular filtration rate (eGFR; mL/min/1.73 m^2) was calculated using the following equation:[9]

$$eGFR = 194 \times Cr^{-1.094} \times Age^{-0.287} \times 0.739 \text{ (if female)}$$

where Cr is the creatinine concentration. Follow-up data were collected by each participating center every 6 months for 4 years after implantation. In outpatient clinics, follow-up data were retrieved from the cardiac devices. The medical staff at the participating institutions input information for their own patients into the JID-CAD website. To protect patient confidentiality, patients' names were not included in the reports. The above method facilitates data sharing with an independent committee for data management.

Two endpoints were evaluated: (1) the primary endpoint, which was all-cause death (i.e., cardiovascular death [heart failure, arrhythmic, sudden death, extracardiac vascular death, and cardiovascular death of unknown origin] and non-cardiovascular death [malignant tumor, accident, infection, and other]); and (2) the secondary endpoint, which was appropriate ICD therapies (i.e., shock therapy and/or antitachycardia pacing for VT/VF). We also assessed coronary revascularization (percutaneous coronary intervention [PCI], coronary artery bypass graft [CABG]) for ischemic events and catheter ablation for VT/VF during the follow-up period.

Statistical Analyses

Data are presented as the mean±SD, median and interquartile range (IQR), number, or percentage. Comparisons between groups were performed using the Chi-squared test of independence for categorical variables and an unpaired t-test or Mann-Whitney U-test for continuous variables. The cumulative incidence of endpoints was plotted as a Kaplan-Meier curve, and differences were assessed by the log-rank test. Hazard ratios (HR) and 95% confidence intervals (CIs) for the incidence of the primary endpoint were calculated using Cox regression analyses after adjustment for age, sex, and covariates for which the P value was <0.10 by univariate analysis. Analyses were performed using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). Two-sided P<0.05 was considered significant.

Results

The median age of patients was 69 years, and 90% were male. In all, 392 patients were enrolled in the study: 353 myocardial infarction patients (including 5 patients with myocardial infarction due to vasospasm), 33 patients with angina pectoris, 5 patients with vasospastic angina, and 1 patient with both angina pectoris and vasospastic angina. Implantation was performed as primary intervention in 165 patients and as secondary prevention in 227 patients. The clinical features of the primary and secondary prevention groups are given in **Table 1**.

The rates of cardiac resynchronization therapy (CRT), diabetes, dyslipidemia, hyperuricemia, peripheral artery disease, and chronic kidney disease were lower in the secondary than primary prevention group. LVEF was higher in the secondary than primary prevention group (38.2±12.9% vs. 29.2±9.4%, respectively; P<0.001).

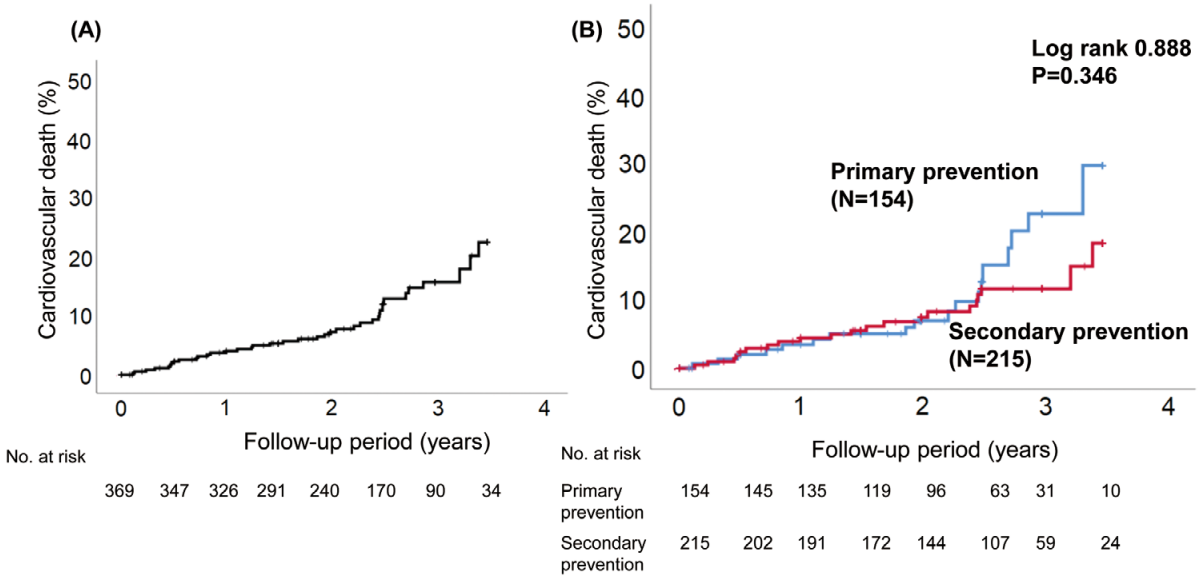

Figure 2. Cardiovascular death for (**A**) all patients and (**B**) the primary and secondary prevention groups separately.

Table 2. Cox Proportional Hazard Model for the Primary Endpoint

	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Age >70 years	0.96 (0.64–1.42)	0.824	0.81 (0.53–1.26)	0.356
Male sex	1.84 (0.81–4.19)	0.148	1.35 (0.58–3.16)	0.492
NYHA-FC >II	0.84 (0.53–1.33)	0.844		
Secondary prevention	1.09 (0.73–1.61)	0.682		
CRT	1.11 (0.71–1.71)	0.649		
Atrial fibrillation	1.87 (1.06–3.28)	0.030	1.68 (0.91–3.11)	0.099
Myocardial infarction	3.08 (1.13–8.37)	0.027	2.67 (0.97–7.32)	0.056
Diabetes	1.12 (0.76–1.65)	0.555		
Hypertension	1.39 (0.91–2.14)	0.130		
Dyslipidemia	0.95 (0.63–1.42)	0.802		
Hyperuricemia	1.15 (0.76–1.74)	0.514		
Stroke	1.45 (0.88–2.39)	0.143		
Peripheral artery disease	1.82 (1.05–3.14)	0.033	1.76 (0.99–3.11)	0.052
Chronic kidney disease	1.74 (1.18–2.56)	0.005	1.20 (0.69–2.08)	0.516
COPD	1.75 (0.71–4.31)	0.221		
Antiarrhythmic agent	0.68 (0.33–1.41)	0.299		
β-blocker	1.07 (0.62–1.86)	0.797		
ACEI	0.87 (0.59–1.28)	0.473		
ARB	1.07 (0.70–1.65)	0.744		
LVEF <35%	1.01 (0.69–1.49)	0.951		
eGFR (per 10 mL/min/1.73 m^2)	0.88 (0.80–0.97)	0.008	0.92 (0.81–1.06)	0.245
QRS duration >120 ms	1.35 (0.91–1.98)	0.132		
Log[BNP]	1.35 (1.11–1.63)	<0.001	1.29 (1.04–1.59)	0.020

CI, confidence interval; HR, hazard ratio. Other abbreviations as in Table 1.

Follow-up data were obtained for 369 patients (94.1%): 154 patients in the primary prevention group and 215 patients in the secondary prevention. The mean follow-up period was 2.1±0.9 years. Sixty patients died during the follow-up period: cardiovascular death was recorded for 39 patients (65%; heart failure in 17 patients, arrhythmic death in 2, sudden death in 7, extracardiac vascular death in 2, and cardiovascular death of unknown origin in 11) and non-cardiovascular death was recorded for 21 patients (35%; malignant tumor in 6 patients, infection in 4, and

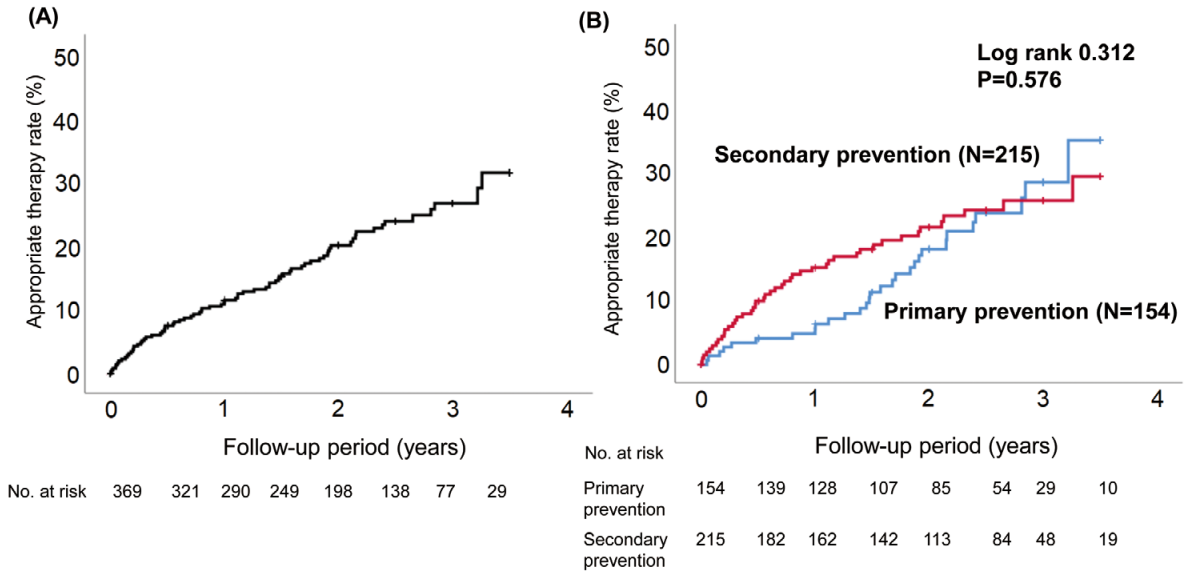

Figure 3. Appropriate implantable cardioverter defibrillator therapies for (**A**) all patients and (**B**) the primary and secondary prevention groups separately.

other causes in 11).

The overall mortality and the difference in mortality between the primary and secondary groups are shown in **Figure 1**. The mortality rates were similar in the 2 groups (log rank statistic=0.874, P=0.350). Kaplan-Meier curves were used to analyze cardiovascular death data and the difference in cardiovascular deaths between the primary and secondary prevention groups (**Figure 2**). There was no significant difference in the rate of cardiovascular death between the 2 groups (log rank statistic=0.888, P=0.346).

Cox regression analyses, after adjustment for age, sex, and covariates for which P<0.10 by univariate analysis, revealed that an increase in BNP concentrations was an independent predictor of the primary endpoint (**Table 2**).

The rate of appropriate ICD therapy was approximately 10% after 1 year and 20% after 2 years (**Figure 3A**). The rates of appropriate ICD therapy in the primary and secondary prevention groups are shown in **Figure 3B**. Although the rates of appropriate ICD therapy tended to be higher in the secondary prevention group at 1 year, the rates in the primary and secondary groups were similar at 2 years (log rank statistic=0.312, P=0.576; **Figure 3B**). Total appropriate ICD therapy was observed in 74 patients and included antitachycardia pacing (n=41; 55%), shock (n=13; 18%), and antitachycardia pacing with shock (n=20; 27%).

Mortality and appropriate ICD therapy were compared between patients who underwent coronary revascularization at baseline and those who did not (**Table 3**). Patients who underwent revascularization at baseline had a significantly higher prevalence of myocardial infarction (91.4% vs. 81.5%; P=0.023) and significantly lower LVEF values (31% vs. 35%; P=0.016), which resulted in a significantly higher mortality rate (18.2% vs. 4.0%; P=0.011). During the follow-up period, interventions for cardiac ischemia were performed in 34 patients (PCI in 28 patients, CABG in 5 patients, and both PCI and CABG in 1 patient). All patients who underwent intervention for cardiac ischemia were alive at the end of the follow-up period, and the mortality rate in this group was significantly lower than that in patients who did not undergo intervention for cardiac ischemia (0.0% vs. 17.9%; P=0.007; **Table 3**).

The percentage of angiotensin-converting enzyme inhibitor use and eGFR tended to higher in patients who underwent revascularization during the follow-up period (**Table 3**). Sixteen patients underwent ablation for VT during the follow-up period. The survival rate of patients who underwent ablation was not significantly different from that of the patients who did not (94% vs. 83%, respectively; P=0.268).

We also evaluated the prognosis of 11 patients with vasospastic angina (5 patients with and 6 patients without myocardial infarction; **Table 4**). Among patients with both vasospastic angina and myocardial infarction, a non-cardiovascular death was recorded for 1 patient and another patient underwent a session of appropriate antitachycardia therapy during the follow-up period. Among patients with vasospastic angina but without myocardial infarction, no adequate therapy was observed during the follow-up period, but 1 patient in this group died due to respiratory failure.

Inappropriate ICD therapies were observed in 19 patients, including T wave oversensing (n=1), sinus tachycardia (n=1), and supraventricular tachyarrhythmias (n=17). Complications were observed in 11 patients at baseline (pneumothorax, n=1; hemorrhage, n=5; shock due to local anesthesia, n=1; dislodgement, n=3; necrosis, n=1) and in 9 patients during the follow-up period (pocket infection, n=2; lead infection, n=2; lead failure, n=5).

Discussion

The main finding of this study was that the rates of mortality and appropriate ICD therapy were similar between the primary and secondary prevention groups.

Table 3. Prognosis of Patients Who Underwent Coronary Revascularization or Not

	Coronary revascularization at baseline			Coronary revascularization during follow-up		
	No (n=54)	Yes (n=338)	P value	No (n=335)	Yes (n=34)	P value
Baseline data						
Age (years)	68 [60–74]	69 [63–75]	0.423	69 [62–75]	68 [63–76]	0.861
Male sex (%)	88.9	90.2	0.759	90.4	88.2	0.680
CRT (%)	20.4	31.1	0.110	28.7	20.6	0.319
Secondary prevention (%)	75.9	55.0	0.004	58.2	58.8	0.945
Myocardial infarction (%)	81.5	91.4	0.023	90.2	88.2	0.724
Antiarrhythmic agent (%)	90.7	93.8	0.405	93.7	91.2	0.566
β-blocker (%)	72.2	86.7	0.006	84.5	85.3	0.900
ACEI (%)	46.3	45.9	0.952	45.1	61.8	0.063
ARB (%)	27.8	28.4	0.925	27.8	26.5	0.873
LVEF (%)	35 [27–50]	31 [26–40]	0.016	32 [26–40]	34 [28–40]	0.792
eGFR (mL/min/1.73 m^2)	54.7±23.1	49.4±21.5	0.096	49.6±21.5	56.5±25.4	0.085
QRS duration (ms)	104 [119–134]	122 [104–151]	0.048	120 [104–150]	120 [102–145]	0.670
BNP (pg/dL)	68 [145–348]	265 [134–628]	0.011	255 [113–585]	269 [164–857]	0.280
Follow-up data (n=369)						
Mortality	4.0	18.2	0.011	17.9	0.0	0.007
Appropriate ICD therapy	24.0	19.4	0.455	20.3	17.6	0.714

Unless indicated otherwise, data are shown as the mean±SD or median [interquartile range]. Abbreviations as in Table 1.

Table 4. Prognosis of Patients With Vasospastic Angina

	Mortality events	Appropriate ICD therapy events
With myocardial infarction (n=5)	1 (non-cardiovascular death)	1 (antitachycardia therapy)
Without myocardial infarction (n=6)	1 (respiratory failure)	0

ICD, implantable cardioverter defibrillator.

In this study, the mortality and the rate of appropriate ICD therapy in the primary prevention group were similar to those in the secondary prevention group. The rate of appropriate ICD therapy in the primary prevention group was lower than in the secondary prevention group at 1 year, but the rate in the primary prevention group increased after 1 year. This finding differs from that of an earlier Japanese study.[4] The prognosis of patients with CAD is thought to worsen in accordance with the degree of decreased systolic function, and European and American guidelines therefore recommend ICD implantation for symptomatic patients with CAD with decreased systolic function.[10,11] The rate of primary prevention patients in the present study (~40%) was relatively small, and the mean age of the patients in this study was higher than that in a previously reported large clinical trial.[12]

In prior studies of patients with CAD in the US and Europe, the rate of primary prevention was approximately 70%,[13,14] whereas in the present study the rate of primary prevention was 40%. The lower number of patients in the primary prevention group in the present study may be a reflection of an underuse of implantation for Japanese CAD. In Japan, the underuse of ICD is a problem. Satake et al indicated that only 1.6% of patients eligible for ICD prophylactic implantation had undergone ICD implantation before enrolment in the CHART-2 Study.[6] How to determine whether to perform ICD implantation for secondary prevention is relatively easily understood, but is sometimes complex for primary prevention.

We also observed that the mortality rate in Japanese patients with CAD who underwent ICD/CRT-D implantation as a primary prevention and in whom an ICD had been implanted based on the appropriate guideline was not lower than that of patients who underwent ICD/CRT-D implantation as secondary prevention, despite the lower cardiac function among patients in the primary prevention group. The primary prevention of ICD implantation in CAD patients may improve the mortality rate by reducing sudden deaths and/or heart failure caused by untreated VT/VF. In CAD patients with reduced cardiac function and without prior VT/VF, physicians should consider the indications for an ICD according to the guidelines for primary prevention. The percentage of CRT was greater in the primary prevention group in the present study; the optimal use of CRT may contribute to improvements in the mortality rate of patients treated for primary prevention.

All the patients who underwent an intervention for cardiac ischemia during the present study were alive at the end of the study follow-up period. The role of interventions for cardiac ischemia is important in ICD cases, because the activity of the ischemic myocardium modifies the arrhythmogenic substrate and results in a higher rate of ventricular arrhythmia.[15] Thus, the optimal intervention for cardiac ischemia was useful in improving the prognosis of Japanese patients with CAD who underwent ICD implantation in the present study. Both the percentage of those using angiotensin-converting enzyme inhibitors and eGFR tended to be higher in patients who underwent coronary

revascularization during their follow-up. Patients who undergo coronary revascularization can be expected to be in good condition, and this may have contributed to their good prognoses.

The success rate of catheter ablation for VT of CAD was not high because most of the arrhythmogenic substrate existed on the epicardial side of the myocardium.[16] In the Ventricular Tachycardia Ablation versus Escalated Antiarrhythmic Drug Therapy in Ischemic Heart Disease (VANISH) trial, the prognosis of ICD patients with ischemic cardiomyopathy was better in the ablation group than in the antiarrhythmic drug therapy group.[17] The beneficial effect consisted mainly of a reduction in the VT storm and the use of appropriate ICD therapies, with the mortality similar between the ablation and antiarrhythmic drug therapy groups.[17]

In the present study, a patient with myocardial infarction due to vasospastic angina underwent appropriate antitachycardia therapy during follow-up. In high-risk patients with vasospastic angina, ICD implantation for the secondary prevention of vasospastic angina is useful,[18–20] and thus ICD implantation is considered appropriate for high-risk patients with vasospastic angina in the revised JCS/Japanese Heart Rhythm Society (JHRS) guidelines.[21] Takagi et al indicated that a previous myocardial infarction was an independent predictor of major adverse cardiovascular events in vasospastic angina patients.[22] In the present study, appropriate ICD therapy was administered to a patient with vasospastic angina and a history of myocardial infarction; thus, ICD implantation in vasospastic angina patients with a history of myocardial infarction due to vasospastic angina is adequate.

The percentage of inappropriate ICD therapies in the present study was lower than that in a previous report.[23] In the Multicenter Automatic Defibrillator Implantation Trial-Reduce Inappropriate Therapy (MADIT-RIT) study, the programming of ICD therapies for tachyarrhythmias with a prolonged delay was associated with reductions in inappropriate ICD therapy and all-cause mortality compared with conventional programming.[24] In addition to improvements to the algorithm for identifying supraventricular tachycardia, the programming of the ICD may have contributed to the lower rate of inappropriate ICD therapies in the present study.

Several study limitations should be considered. First, this study lacked control patients for whom ICD was recommended but not implanted. Thus, we could not assess the merits of ICD implantation compared with patients without ICD implantation. Second, patients were enrolled based on the JCS 2011 guidelines,[8] in which the indications for primary prevention differ from those in the JCS/JHRS 2018 guidelines. Finally, the prognosis of the patients who underwent coronary revascularization may have been affected by selection bias, and we did not obtain the reasons why patients were chosen for coronary revascularization at baseline and during follow-up. We obtained data of prior revascularization, but we did not assess myocardial viability at baseline in the present study. Patients who did not undergo revascularization may have included patients who were advised to undergo revascularization but did not undergo the procedure due to some medical and/or social reasons. Further studies are needed to assess the details of the prognoses and the effects of coronary revascularization and ablation for VT/VF in patients with CAD and an implanted ICD/CRT. We performed a cohort study (the Japan Cardiac Device Treatment Registry: JCDTR database),[25] and are now conducting another cohort study (the new JCDTR). In the future, the details of the long-term prognoses of CAD patients will be clarified using the new JCDTR database.

Conclusions

The mortality rate in Japanese patients with CAD who underwent ICD/CRT-D implantation as primary prevention was not lower than that of patients who underwent ICD/CRT-D implantation as secondary prevention, despite the lower cardiac function in the primary prevention patients.

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IRB Information

This study was approved by the Ethics Committee of Yamaguchi University Graduate School of Medicine (Reference no. H25-132).

Data Availability

The de-identified participant data will not be shared.

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Appendix

Individual members of the Implantable Cardioverter–Defibrillator Committee of the Japanese Heart Rhythm Society (JHRS) and members of the JHRS who registered data in the JID-CAD study and their associated facilities are listed below:

Members of the Implantable Cardioverter-Defibrillator Committee of the JHRS

Kohei Ishibashi, National Cerebral and Cardiovascular Center; Yasuhiro Yoshiga, Yamaguchi University Graduate School of Medicine; Ritsuko Kohno, University of Occupational & Environmental Health, Japan; Hisashi Yokoshiki, Sapporo City General Hospital

Members of the JHRS Who Registered Data in the JID-CAD Study

Masaya Watanabe, Hokkaido University; Shingo Sasaki, Hirosaki University; Makoto Nakano, Tohoku University; Yukio Sekiguchi, University of Tsukuba; Takeshi Mitsuhashi, Saitama Medical Center, Jichi Medical University; Ritsushi Kato, Saitama Medical University International Medical Center; Morio Shoda, Tokyo Women's Medical University; Jun Umemura, Sakakibara Heart Institute; Wataru Shimizu, Nippon Medical School; Yoshiyasu Aizawa, Keio University; Seiji Fukamizu, Tokyo Metropolitan Hiroo Hospital; Teiichi Yamane, Jikei University School of Medicine; Toshiaki Sato, Kyorin University School of Medicine; Yoshinori Kobayashi, Tokai University Hachioji Hospital; Kazuhiro Satomi, Tokyo Medical University; Shinichi Niwano, Kitasato University; Makoto Suzuki, Yokohama Minami Kyosai Hospital; Akinori Sato, Niigata University; Wataru Shoin, Shinshu University; Yasuya Inden, Nagoya University; Yuichiro Sakamoto, Tohyohashi Heart Center; Yukihiko Yoshida, Nagoya Second Red Cross Hospital; Eiichi Watanabe, Fujita Health University School of Medicine; Tomoya Ozawa, Shiga University of Medical Science; Takeshi Shirayama, Kyoto Prefectural University of Medicine; Takashi Noda, National Cerebral and Cardiovascular Center; Takashi Kurita, Kindai University School of Medicine; Atsushi Doi, Osaka City University Graduate School of Medicine; Yoshio Furukawa, Osaka General Medical Center; Hiroya Mizuno, Osaka University; Koichi Inoue, Sakurabashiwatanabe Hospital; Akira Shimane, Himeji Cardiovascular Center; Koji Fukuzawa, Kobe University Graduate School of Medicine; Nobuhiro Nishii, Okayama University Graduate School of Medicine; Yasuhiro Yoshiga, Yamaguchi University Graduate School of Medicine; Takayuki Nagai, Ehime University Graduate School of Medicine; Kenji Ando, Kokura Memorial Hospital; Masahiro Ogawa, Fukuoka University; Haruhiko Abe, University of Occupational & Environmental Health; Junjiro Koyama, Saiseikai Kumamoto Hospital; Tomoyuki Kabutoya, Jichi Medical University; Naohiko Takahashi, Naohiko Takahashi, Oita University; Hiroshi Tada, University of Fukui; Yukio Hosaka, Niigata City General Hospital; Yoshiaki Kaneko, Gunma University; Toshihiro Nakamura, National Hospital Organization Kyushu Medical Center; Kazuoki Dai, Hiroshima City Hospital; Umetani Ken, Yamanashi Prefectural Central Hospital; Itsuro Morishima, Ogaki Municipal Hospital; Takanao Mine, Hyogo College of Medicine; Keiichi Ashikaga, Miyazaki Medical Association Hospital; Toshiko Nakai, Nihon University; Shiro Ono, Saiseikai Yamaguchi General Hospital; Michiro Maruyama, Toyama Prefectural Central Hospital; Toshihiko Goto, Nagoya City University Graduate School of Medical Sciences; Mikio Kakishita, Higashi Takarazuka Satoh Hospital; Kazumasa Adachi, Akashi Medical Center; Fumiharu Miura, Hiroshima City Hospital