学位論文

Current clinical practice of subcutaneous implantable cardioverter-defibrillator: Analysis using the JROAD-DPC database
（我が国における皮下植え込み型除細動器の診療実態の解明）

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Current clinical practice of subcutaneous implantable cardioverter-defibrillator: Analysis using the JROAD-DPC database

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BACKGROUND Current evidence describing the characteristics of subcutaneous implantable cardioverter-defibrillator (S-ICD) therapy, its trend, and perioperative outcomes compared with transvenous implantable cardioverter-defibrillator (TV-ICD) based on a real-world, large-scale database is scarce.

OBJECTIVE The purpose of this study was to identify the characteristics of current S-ICD therapy using a nationwide database.

METHODS A retrospective analysis of ICD implantation was performed using a nationwide database obtained between 2016 and 2020. A total of 8690 patients implanted with ICD (median age 65 [52–72] year; 6902 men; 2021 S-ICD recipients) were analyzed.

RESULTS Younger patients were more prone to have S-ICD ($P < .001$). A history of ventricular fibrillation (VF) (odds ratio [OR] 2.45; 95% confidence interval [CI] 2.04–2.93), nonsustained ventricular tachycardia (VT) (OR 1.73; 95% CI 1.36–2.21), Brugada syndrome (BrS) (OR 3.14; 95% CI 2.48–4.00), and dialysis treatment (OR 2.02; 95% CI 1.44–2.82) were independent predictors of S-ICD selection on mixed-model logistic analysis. The proportion of S-ICD implantations has been increasing ($P < .001$), especially in patients with BrS ($P < .001$) and dialysis ($P = .04$). The proportion of combined complications after S-ICD implantation was low (1.3%) in the unmatched cohort and was comparable to TV-ICD in the 1:1 propensity-matched cohort of 3354 patients (1.5% vs 2.3%; OR 0.65; 95% CI 0.38–1.10).

CONCLUSION S-ICD was more likely to be implanted in younger patients and those with a history of VF, nonsustained VT, BrS, and dialysis treatment. The proportion of S-ICD implantation increased, especially in patients with BrS. The incidence of in-hospital complications was low in S-ICD recipients.

KEYWORDS Nationwide database; Perioperative outcomes; Propensity-matched analysis; S-ICD; Subcutaneous implantable cardioverter-defibrillator

(Heart Rhythm 2022;■:1–8)

Introduction

Implantable cardioverter-defibrillators (ICDs) have been proven efficacious in preventing sudden cardiac death.[1–4] Transvenous lead placement for cardiac sensing and defibrillation has been the standard for ICD design for several decades. However, significant limitations of the technique include complications related to lead insertion, such as pneumothorax, cardiac perforation, or lead endocarditis.[5,6] The subcutaneous implantable cardioverter-defibrillator (S-ICD) is a relatively recent device that was approved in 2013 in the United States (US) and in 2016 in Japan. The S-ICD is an entirely subcutaneous system that does not require vascular access or permanent intravascular indwelling defibrillator leads or coils. It was developed to overcome many of the limitations and complications (eg, cardiac perforation, lead fracture, lead endocarditis, and venous

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thrombosis) associated with the traditional transvenous implantable cardioverter-defibrillator (TV-ICD).[7] The safety and efficacy of S-ICD have been confirmed in several retrospective and prospective studies (single arm or in comparison with TV-ICD) and a randomized controlled trial comparison with TV-ICD.[8–14] However, data on the current practice pattern for ICD implantation, which would be important for understanding the current issues and unmet needs of optimal prevention of sudden cardiac death, are limited. In addition, the characteristics of ICD recipients was different in Japan (ie, less ischemic heart disease and more secondary prevention and Brugada syndrome [BrS]) compared with those of patients in western countries.[8,15] Also, length of hospital stay after ICD implantation is longer in Japan than in western countries, making it possible to observe in-hospital complications that become apparent a few days after implantation.

The Japanese Registry of All Cardiac and Vascular Diseases–Diagnosis Procedure Combination (JROAD-DPC) is a nationwide claims database that uses data from the Japanese DPC/Per Diem Payment System.[16]

In this study, by using the nationwide database just after approval of the S-ICD, we sought to (1) describe the adoption of the S-ICD in real-world clinical practice in Japan; and (2) clarify in-hospital outcomes of patients who underwent implantation of an S-ICD by comparing them with patients who received a traditional TV-ICD.

Methods

Data source

This retrospective cross-sectional study used the JROAD-DPC database, which has been previously described in detail.[16,17] The JROAD-DPC database includes the following information for each patient: age, sex, height, weight, Barthel index, primary diagnoses/comorbidities/conditions arising after admission based on the *International Statistical Classification of Diseases, Tenth Revision* (ICD-10) codes, drugs, diagnostic and therapeutic procedures, length of stay, medical cost, and discharge status. Regarding diagnosis, in addition to the ICD-10 codes, detailed names of diagnoses are listed so that detailed names of disease that cannot be identified using ICD-10 codes alone can be determined. Procedure code, ICD-10 codes, and other definitions used for baseline characteristics are listed in Supplemental Table S1. The hospital ICD implantation volume and number of years since the initiation of S-ICD implantation at each hospital were determined using unique hospital identification numbers.

This study was approved by the institutional review board of the National Cerebral and Cardiovascular Center (R19066; October 6, 2019). Informed consent was waived because information specific to individuals was not included in the database.

Study population

The flowchart of the study is shown in Figure 1. We initially identified 12,634 hospitalizations with S-ICD or TV-ICD implantation between April 2016 and March 2020. To facilitate the comparison of patients with S-ICD and TV-ICD implantation, the following patients were excluded: (1) patients who underwent both S-ICD and TV-ICD implantation within the same hospitalization period (n = 5); (2) age <18 years (n = 163) or age unknown (n = 28); (3) patients who underwent other procedures after S-ICD or TV-ICD implantation (percutaneous coronary intervention [n = 163]; catheter ablation [n = 96]; transaortic valve repair [n = 4]; percutaneous mitral valve repair [n = 2]; lead extraction [n = 152]); (4) patients with cardiac surgery before S-ICD or TV-ICD implantation (n = 3); (5) patients with pacing indication of complete/advanced atrioventricular block, trifascicular block with episode of syncope, or sick sinus syndrome (n = 918); (6) patients with cardiovascular implantable electronic device

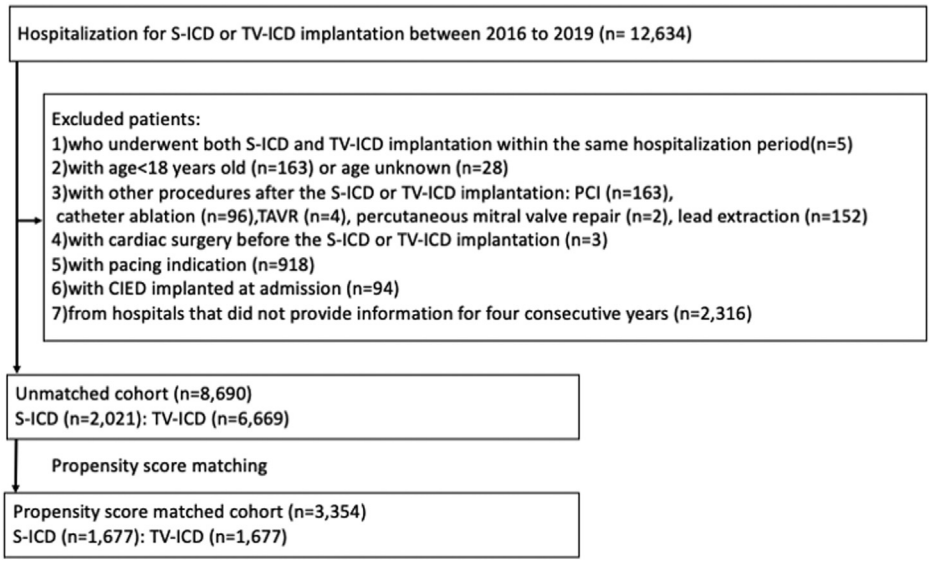

Figure 1 Flowchart of the study. CIED = cardiovascular implantable electronic device; PCI = percutaneous coronary intervention; S-ICD = subcutaneous implantable cardioverter-defibrillator; TAVR = transaortic valve repair; TV-ICD = transvenous implantable cardioverter-defibrillator .

Table 1 Baseline characteristics of the unmatched and propensity score-matched cohorts

	Unmatched cohort				Propensity score-matched cohort			
	S-ICD group (N = 2021)	TV-ICD group (N = 6669)	|Std diff |	*P* value	S-ICD group (N = 1677)	TV-ICD group (N = 1677)	|Std diff |	*P* value
Age (y)	52 (40–64)	67 (57–74)	0.893	<.001	55 (45–66)	56 (44–66)	0.023	.84
Emergency hospitalization	865 (43)	3532 (53)	0.206	<.001	775 (46)	765 (46)	0.014	.73
Barthel score <100 at admission	206 (10)	1004 (15)	0.15	<.001	182 (11)	179 (11)	0.01	.87
Arrhythmia								
Ventricular fibrillation	1090 (54)	1993 (30)	0.502	<.001	923 (55)	941 (56)	0.026	.53
Ventricular tachycardia	566 (28)	4150 (62)	0.728	<.001	553 (33)	516 (31)	0.055	.17
Nonsustained ventricular tachycardia	141 (7.0)	701 (11)	0.128	<.001	139 (8.3)	126 (7.5)	0.026	.41
Atrial fibrillation	299 (15)	1580 (24)	0.229	<.001	279 (17)	275 (16)	0.004	.85
Cardiovascular comorbidity								
Heart failure	88 (4.4)	721 (11)	0.242	<.001	88 (5.2)	83 (4.9)	0.028	.69
Ischemic cardiomyopathy	202 (10)	1447 (22)	0.322	<.001	198 (12)	181 (11)	0.034	.35
Nonischemic cardiomyopathy	272 (14)	1647 (25)	0.287	<.001	269 (16)	272 (16)	0.004	.89
Brugada syndrome	444 (22)	263 (3.9)	0.563	<.001	222 (13)	226 (14)	0.007	.84
Long QT, short QT, or early repolarization syndrome	78 (3.9)	136 (2.0)	0.114	<.001	61 (3.6)	61 (3.6)	0.006	1
Noncardiovascular comorbidity								
Chronic kidney disease	111 (5.5)	493 (7.4)	0.076	.003	107 (6.4)	109 (6.5)	0.003	.89
Dialysis	101 (5.0)	264 (4.0)	0.052	.041	96 (5.7)	91 (5.4)	0.01	.71
Diabetes	422 (21)	1936 (29)	0.188	<.001	414 (25)	409 (24)	0.017	.84
Anticoagulant								
Warfarin	210 (10)	1340 (20)	0.272	<.001	205 (12)	217 (13)	0.025	.53
Direct oral anticoagulant	255 (13)	1641(25)	0.312	<.001	251 (15)	240 (14)	0.023	.59

S-ICD = subcutaneous cardioverter-defibrillator; TV-ICD = transvenous cardioverter-defibrillator.

implanted at admission (n = 94); and (7) patients from hospitals that did not provide information for 4 consecutive years (n = 2316). As a result, 8690 patients (age 65 [52–72] years; 6902 men; 2021 S-ICD and 6669 TV-ICD recipients) were included in the study.

Outcomes

We identified the in-hospital complications attributed to S-ICD/TV-ICD implantation using ICD-10 diagnosis and DPC procedure codes (Supplemental Table S1). In-hospital complications were extracted from diagnoses coded for "conditions arising after admission" or procedure/device codes for those used after ICD implantation. The combined complication was a composite of all complications (cardiac tamponade, pneumothorax, hematoma, local infection, and blood transfusion) and in-hospital death. We also analyzed the length of hospital stay after ICD implantation, total medical cost, and proportion of patients with transvenous antibiotics administration for >4 consecutive days. Based on the average exchange rate in 2019, 109 Japanese Yen was converted to 1 US dollar.

Statistical analysis

Descriptive and trend analysis

Categorical data are given as frequency (percentage). Continuous data are given as median (interquartile range). The Wilcoxon rank-sum test was used to compare continuous data. The χ^2 or Fisher exact test was used to compare categorical data. Mixed-effects multivariable logistic regression analysis using institute as random intercept, adjusted for 17 baseline characteristics that were P <.05 in univariate analysis, was performed to estimate the odds ratio (OR) and 95% confidence interval (CI) for S-ICD selection. Collinear variables identified with variance inflation factor >10 (sex, body mass index, and hypertension) were excluded from multivariable analysis. Moreover, mixed-effects univariate logistic regression analysis using institute as a random intercept was performed to estimate OR and 95% CI with hospital characteristics for combined outcomes in S-ICD recipients.

To characterize year trend of S-ICD use in Japan, we calculated the annual volume and proportion of admissions with S-ICD implantation among patients with ischemic/nonischemic cardiomyopathies, BrS, and dialysis treatment, as well as in the entire cohort. The Cochran-Armitage trend test was performed to test for trends.

Comparative analysis of in-hospital outcomes

We performed propensity score (PS) matching analysis to compare the in-hospital outcomes of S-ICD and TV-ICD recipients. PS was calculated using multivariable logistic regression models for S-ICD implantation. The same 17 baseline characteristics (Table 1) that were P <.05 in the univariate logistic regression analysis to estimate S-ICD selection were used as independent variables. Matching was performed with a nearest neighbor matching algorithm (ratio

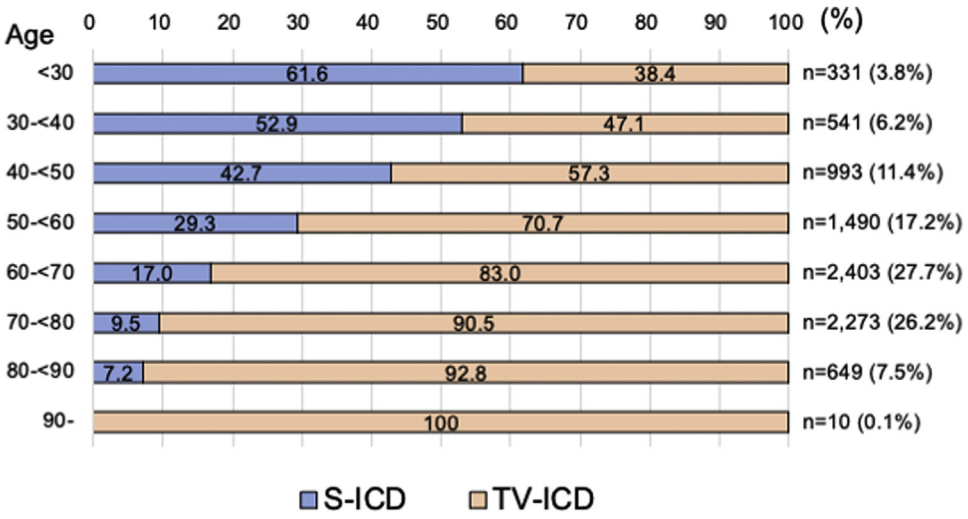

Figure 2 Distribution of S-ICD and TV-ICD in each age group. The proportion of S-ICD recipients was higher in younger patients ($P < .001$). S-ICD = subcutaneous implantable cardioverter defibrillator; TV-ICD = transvenous implantable cardioverter defibrillator.

1:1 without replacement), with a caliper of width 0.2 SD of the logit of the estimated PS. After matching, 1677 patients in each of the S-ICD and TV-ICD groups were included in the comparative analysis. The balance of each covariate before and after matching between the 2 groups was evaluated using standardized differences. The absolute value of standardized differences <10% was considered a relatively small imbalance. Mixed-effects logistic regression analysis using institute as random intercept was performed to estimate OR and 95% CI with S-ICD implantation for combined complications, in-hospital mortality, as well as each complication. All statistical comparisons were 2-sided, and $P < .05$ was considered significant. All analyses were performed using STATA16.0 (StataCorp, College Station, TX).

Results

Description of S-ICD use in Japan

A total of 8690 patients (median age 65 [52–72] years; 6902 men) were included in the study. S-ICD implantation accounted for 23% of all implants. Recipients of S-ICDs were different from those of TV-ICD recipients (Table 1 and Supplemental Table S2). In the age-specific analysis, the percentage of patients who were selected for S-ICD was higher in younger patients ($P < .001$) (Figure 2). Moreover, compared with TV-ICD recipients, S-ICD recipients were more likely to have a history of ventricular fibrillation (VF) (S-ICD vs TV-ICD: 54% vs 30%; $P < .001$) or BrS (22% vs 3.9%; $P < .001$). The proportion of patients who underwent ICD implantation for primary prevention was higher in S-ICD recipients compared to TV-ICD recipients (25% vs 21%; $P = .001$).

In contrast, TV-ICD recipients compared to S-ICD recipients were more likely to have a history of ischemic cardiomyopathy (10% vs 22%; $P < .001$); ventricular tachycardia (VT) (28% vs 62%; $P < .001$); and lower Barthel index (10% vs 15%; $P < .001$). The proportion of patients with S-ICDs inserted under general anesthesia was much higher than that of TV-ICD patients (55% vs 7.4%; $P < .001$). There were 2 hospitals in which only S-ICD implantations were performed and 66 hospitals in which only TV-ICD implantation were performed. S-ICDs were more likely to be implanted in hospitals with a higher ICD implantation volume during the study period (52 [34–80] vs 44 [26–66] cases per hospital; $P < .001$).

On mixed-effects multivariable analysis, younger age (OR 0.95; 95% CI 0.95–0.96); history of VF (OR 2.45; 95% CI 2.04–2.93); nonsustained VT (OR 1.73; 95% CI 1.36–2.21); BrS (OR 3.14; 95% CI 2.48–4.00); and dialysis treatment (OR 2.02; 95% CI 1.44–2.82) were associated with S-ICD selection (Table 2). However, emergency hospitalization (OR 0.61; 95% CI 0.53–0.70); VT (OR 0.50; 95% CI 0.42–0.60); ischemic cardiomyopathy (OR 0.62; 95% CI 0.51–0.75); nonischemic cardiomyopathy (OR 0.56; 95% CI 0.47–0.67); use of warfarin (OR 0.74; 95% CI 0.62–0.90); and direct oral anticoagulants (DOACs) (OR 0.74; OR 0.60–0.91) were associated with TV-ICD selection.

Annual trend of S-ICD/TV-ICD recipients

Since S-ICD was approved in Japan in April 2016, the proportion of S-ICD implantations generally increased from 18% in 2016 to 27% in 2019 ($P < .001$) (Figure 3A). There was no significant upward trend for S-ICDs in patients with ischemic ($P = .20$) (Figure 3B) or nonischemic cardiomyopathy ($P = .10$) (Figure 3C). In patients with ischemic cardiomyopathy, TV-ICDs were still the treatment of choice in 84% of patients in 2019. In patients with BrS, the percentage of S-ICDs selected rose sharply from 46% in 2016 to 77% in 2019 ($P < .001$) (Figure 3D). In dialysis patients, S-ICD showed a gradually increasing trend, with 35% of patients opting for S-ICD in 2019 ($P = .04$) (Figure 3E). The incidence of combined complications and proportion of patients with ICDs inserted under general anesthesia did not change over time in

Table 2 Mixed-effects univariable and multivariable logistic analysis of predictors of S-ICD selection

	Univariable logistic analysis			Multivariable logistic analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Age	0.94	0.93–0.94	<.001	0.95	0.95–0.96	<.001
Male*	1.43	1.25–1.65	<.001			
Body mass index*	0.99	0.97–0.999	.04			
Emergency hospitalization	0.68	0.61–0.77	<.001	0.61	0.53–0.70	<.001
Barthel score <100 at admission	0.61	0.51–0.73	<.001	0.87	0.70–1.07	.17
Ventricular fibrillation	3.58	3.18–4.03	<.001	2.45	2.04–2.93	<.001
Ventricular tachycardia	0.19	0.17–0.22	<.001	0.50	0.42–0.60	<.001
Nonsustained ventricular tachycardia	0.57	0.46–0.69	<.001	1.73	1.36–2.21	<.001
Atrial fibrillation	0.54	0.47–0.62	<.001	1.18	0.97–1.43	.11
Heart failure	0.40	0.31–0.50	<.001	0.84	0.64–1.10	.21
Ischemic cardiomyopathy	0.37	0.31–0.44	<.001	0.62	0.51–0.75	<.001
Nonischemic cardiomyopathy	0.44	0.38–0.51	<.001	0.56	0.47–0.67	<.001
Brugada syndrome	8.86	7.33–10.70	<.001	3.14	2.48–4.00	<.001
Long QT, short QT, or early repolarization syndrome	2.00	1.47–2.72	<.001	0.88	0.62–1.27	.50
Chronic kidney disease	0.77	0.61–0.96	.02	1.10	0.81–1.49	.54
Dialysis	1.38	1.07–1.79	.01	2.02	1.44–2.82	<.001
Diabetes	0.64	0.57–0.73	<.001	1.06	0.91–1.23	.48
Hypertension*	0.21	0.18–0.25	<.001			
Warfarin	0.42	0.35–0.49	<.001	0.74	0.62–0.90	.002
Direct oral anticoagulant	0.42	0.36–0.50	<.001	0.74	0.60–0.91	.004

CI = confidence interval; OR = odds ratio; S-ICD = subcutaneous implantable cardioverter-defibrillator.

*Sex, body mass index, and hypertension showed collinearity with S-ICD selection; therefore, these variables were not included in the multivariable logistic analysis.

both the S-ICD and TV-ICD groups (Supplemental Figures S1 and S2).

S-ICD implantation in patients with BrS

Most of the BrS patients were male (685/707 BrS patients [97%]). Furthermore, compared with other patients, they were younger (44 [36–56] years vs 66 [54–73] years; *P* <.001), were less likely to have VT (9.1% vs 58%; *P* <0.001), and were more likely to have ICD implantation for primary prevention (53% vs 19%; *P* <.001) (Supplemental Table S3). Among BrS patients, only 4 local infection events were observed (2 events each in the S-ICD and TV-ICD groups), and no patient died after ICD implantation.

Outcomes of ICD implantations

In S-ICD recipients, the proportion of combined complications was 1.3%, and in-hospital mortality was low 0.3% (Table 3). There were no reported cases of cardiac tamponade or pneumothorax after S-ICD implantation. A small number of S-ICD recipients experienced hematoma (0.1%) or local infection (0.6%), and received blood transfusions (0.4%). The proportion of patients who experienced the combined complication (9.3% vs 2.0%; *P* <.001) or death (4.1% vs 0.4%; *P* <.001) was higher among those with dialysis treatment compared to other patients (Supplemental Table S4). The proportion of patients who experienced the combined complication was higher among those with warfarin or DOAC treatment compared to other patients (warfarin: 3.9% vs 2.0%, *P* <.001; DOAC: 0.5% vs 0.2%; *P* = .01) (Supplemental Table S5). In S-ICD recipients, S-ICD implantation in hospitals with a lower S-ICD implantation volume (Supplemental Figure S3) or shorter period of time since initiation of S-ICD implantation was not associated with combined complications (Supplemental Figure S4).

In the mixed-effects univariate logistic regression analysis in the PS-matched cohort, there were no significant differences in combined complication rates between S-ICD and TV-ICD recipients (1.5% vs 2.3%; OR 0.65; 95% CI 0.38–1.10) (Table 4). In-hospital mortality did not differ by device type (0.4% vs 0.3%; OR 1.24; 95% CI 0.37–4.14). In the PS-matched cohort, median length of stay after ICD implantation did not differ by device type. Medical costs were lower for S-ICD compared TV-ICD ($46,620 vs $48,007 USD; *P* = .004).

Discussion

Median postoperative hospital stay was 8 days, which was longer than that in western countries[8] because in Japan, it is common practice to stay in the hospital until surgical wound healing is confirmed.

Device selection in patients with ICD indication

In this study, lower age, history of VF, nonsustained VT, BrS, and dialysis treatment were associated with S-ICD selection. S-ICDs were more often chosen by younger patients, who may avoid TV-ICDs due to concerns about lead-related problems in the future. Also, we hypothesized that TV-ICDs

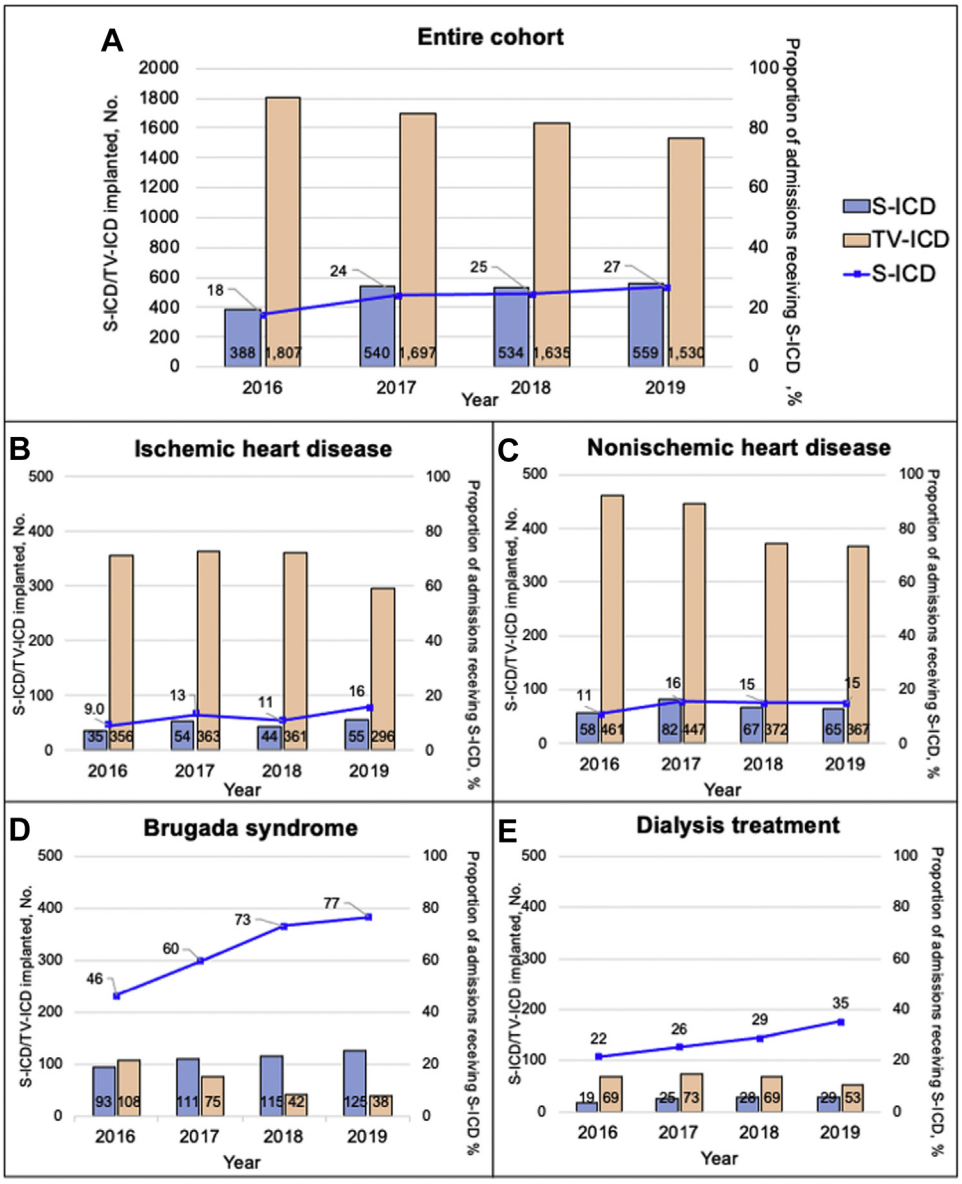

Figure 3 Absolute number and the proportion of S-ICDs and TV-ICDs implanted per year in entire cohort **(A),** ischemic cardiomyopathy **(B)**, nonischemic cardiomyopathy **(C)**, Brugada syndrome **(D)**, and dialysis treatment **(E)**. S-ICDs were approved for insurance coverage in Japan in April 2016. S-ICD = subcutaneous implantable cardioverter defibrillator; TV-ICD = transvenous implantable cardioverter defibrillator.

are more likely to be chosen by elderly patients in anticipation of the need for pacing function for bradycardia in the future.

As a reflection of the high prevalence of BrS in Japan,[18] the incidence of BrS accounted for 8% of our entire cohort and 22% of S-ICD recipients, and was higher than that in previous reports from western countries (0.3%–2.3%).[8,14] Moreover, in patients with BrS, the percentage of S-ICDs selected has dramatically increased over the years; as of 2019, 77% of patients had S-ICD implantation. This can be explained by the high risk of sudden-onset of VF but infrequent VT, and the acceptable rate of inappropriate S-ICD shocks rates in BrS patients.[19] It also could be due to high lead-related complication rates and inappropriate shocks of TV-ICD in patients with BrS.[20] The primary prevention rate was higher in BrS patients than in other patients. The diagnosis of BrS at a young age may have led to more aggressive implantation for primary prevention purposes. Further study is needed to determine whether the current status of ICD selection is heading in the right direction for BrS patients.

Dialysis patients also increasingly opted for S-ICDs; however, the proportion of S-ICD was not as high as that reported in a large-scale study using a nationally representative ICD registry from the United States, in which 68% of patients on dialysis underwent S-ICD implantation.[21] Dialysis patients are prone to develop VT due to advanced myocardial fibrotic change and often require antitachypacing, and TV-ICDs still might be selected often in Japan.

Patients who were receiving anticoagulant medication were likely to have TV-ICDs. Compared with the TV-ICD, the generator of the S-ICD is larger and must be inserted into a deeper area of the body, which gives the impression

Table 3 In-hospital clinical outcomes after ICD implantation

	Unmatched cohort			Propensity score-matched cohort		
	S-ICD group (N = 2021)	TV-ICD group (N = 6669)	*P* value	S-ICD group (N = 1677)	TV-ICD group (N = 1677)	*P* value
Clinical outcome						
Combined complications	27 (1.3)	177 (2.7)	<.001	25 (1.5)	39 (2.3)	.08
In-hospital mortality						
Death	6 (0.3)	38 (0.6)	.13	6 (0.4)	5 (0.3)	.76
Complication						
Cardiac tamponade	0 (0.0)	23 (0.3)	.01	0 (0.0)	5 (0.3)	.06
Pneumothorax	0 (0.0)	4 (0.1)	.58	0 (0.0)	1 (0.1)	>.99
Hematoma	2 (0.1)	13 (0.2)	.54	2 (0.1)	2 (0.1)	>.99
Local infection	12 (0.6)	36 (0.5)	.77	10 (0.6)	13 (0.8)	.53
Blood transfusion	9 (0.4)	86 (1.3)	.001	9 (0.5)	18 (1.1)	.08
Other outcome						
Length of stay after ICD implantation (days)	8 (7–10)	8 (7–11)	<.001	8 (7–10)	8 (7–10)	.53
Medical cost ($US)	45,829 (43,051–56,709)	49,143 (44,635–59,596)	<.001	46,620 (43,204–58,391)	48,007 (44,026–59,273)	.004
Intravenous antibiotics used >4 consecutive days	401 (20)	1,493 (22)	.02	313 (19)	349 (21)	.12

ICD = implantable cardioverter-defibrillator; S-ICD = subcutaneous implantable cardioverter-defibrillator; TV-ICD = transvenous implantable cardioverter-defibrillator

of a higher risk of bleeding; therefore, the S-ICD might be avoided in patients receiving anticoagulant therapy who are at high risk for bleeding. Because this study showed that the risk of bleeding was comparable between TV-ICD and S-ICD in PS-matched cohorts, S-ICD may be actively chosen by patients taking anticoagulant medication in the future.

Periprocedural complications of S-ICD/TV-ICD implantation

The overall complication rate of S-ICD implantation was 1.3%, which is comparable to previous reports (1.2%–3.4%).[8,14] A small number of patients in both groups had hematomas or required blood transfusions, but other serious complications, including death, were rare, especially in patients without dialysis treatment. Compared with the findings of a previous large study that analyzed the use of ICD in patients on dialysis,[21] the combined complication rate and in-hospital mortality in dialysis patients was higher in this study. In our cohort, the length of hospital stay after ICD implantation was longer than that in western countries, making it possible to observe complications (even death) that become apparent a few days after implantation. The safety of ICD implantation in hemodialysis patients will need to be carefully monitored.

In PS-matched analysis, although there were no significant differences in overall complication rates between S-ICD and TV-ICD recipients, cardiac tamponade or pneumothorax was observed only in TV-ICD recipients. In contrast to TV-ICD, which requires lead placement in the right ventricle, all systems in the S-ICD are subcutaneous, so it is likely that tamponade or pneumothorax would not occur, making this a significant advantage of S-ICD. Medical costs were lower for the S-ICD compared to TV-ICD; therefore, it would be more economical to choose the S-ICD if either device is acceptable. Understanding the benefits and risks associated with S-ICD compared with TV-ICD can help clinicians and patients make informed treatment decisions.

Study limitations

The design was observational and retrospective, and the treatment was not randomized. Because the DPC data are based on medical claims, data that do not directly relate to the cost are not completely validated. However, previous studies have proven the validity of the diagnoses of JROAD-DPC in comparison with other nationwide databases or the in-hospital registry.[22–24] In addition, although we used robust statistical methods to account for differences between groups, we cannot rule out the possibility of residual confounding factors. Information regarding defibrillation threshold testing at the time of device implantation was not available; however, it could affect the in-hospital complication rate, particularly in critically ill patients with hemodynamic instability. Moreover, characteristics of operators, appropriate or inappropriate device therapy, device setting, and precise clinical information, such as laboratory or echocardiology data, were not available. We were only able to identify complications during hospitalization. However, the postoperative hospitalization period is longer than in western countries, and we believe that we were able to evaluate complications that may have been overlooked in in-patient reports from countries with shorter hospitalization periods. Finally, although there are concerns of lead fractures or premature battery depletions in S-ICDs, which led to two Class I Food and Drug Administration recalls,[25] long-term follow-up data were not available in the database. Ongoing surveillance is needed to determine the long-term outcomes of S-ICD use.

Table 4 Mixed-effects univariate logistic regression analysis of the complications

	Unmatched cohort		Propensity-score matched cohort	
	OR (95% CI)		OR (95% CI)	
	S-ICD vs TV-ICD	*P* value	S-ICD vs TV-ICD	*P* value
Combined complication	0.51 (0.33–0.78)	.002	0.65 (0.38–1.10)	.11
In-hospital mortality				
Death	0.56 (0.23–1.34)	.19	1.24 (0.37–4.14)	.73
Complication				
Local infection	0.96 (0.47–1.97)	.91	0.72 (0.28–1.80)	.48
Blood transfusion	0.35 (0.17–0.69)	.003	0.50 (0.22–1.13)	.10
Other outcome				
Intravenous antibiotics used >4 consecutive days	0.70 (0.60–0.82)	<.001	0.74 (0.59–0.93)	.01

CI = confidence interval; OR = odds ratio; S-ICD = subcutaneous cardioverter-defibrillator; TV-ICD = transvenous cardioverter-defibrillator.

Conclusion

S-ICD was more likely to be implanted in younger patients and those with a history of VF, nonsustained VT, BrS, and dialysis treatment, and the proportion of S-ICD implantation gradually increased, especially in patients with BrS. The incidence of overall in-hospital complications was low in S-ICD recipients, and in PS-matched analysis, it was not significantly different from that of TV-ICD recipients. ICD implantation procedures were performed safely, regardless of device type.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2022.02.006.

References

1. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 2005;352:225–237.
2. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. N Engl J Med 1996;335:1933–1940.
3. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med 2002;346:877–883.
4. Nogami A, Kurita T, Abe H, et al. JCS/JHRS 2019 guideline on non-pharmacotherapy of cardiac arrhythmias. J Arrhythm 2021;37:709–870.
5. Kirkfeldt RE, Johansen JB, Nohr EA, et al. Complications after cardiac implantable electronic device implantations: an analysis of a complete, nationwide cohort in Denmark. Eur Heart J 2014;35:1186–1194.
6. Koneru JN, Jones PW, Hammill EF, et al. Risk factors and temporal trends of complications associated with transvenous implantable cardiac defibrillator leads. J Am Heart Assoc 2018;7:e007691.
7. Bardy GH, Smith WM, Hood MA, et al. An entirely subcutaneous implantable cardioverter-defibrillator. N Engl J Med 2010;363:36–44.
8. Friedman DJ, Parzynski CS, Varosy PD, et al. Trends and in-hospital outcomes associated with adoption of the subcutaneous implantable cardioverter defibrillator in the United States. JAMA Cardiol 2016;1:900.
9. Knops RE, Nordkamp LRAO, Delnoy P-PHM, et al. Subcutaneous or transvenous defibrillator therapy. N Engl J Med 2020;383:526–536.
10. Brouwer TF, Knops RE, Kutyifa V, et al. Propensity score matched comparison of subcutaneous and transvenous implantable cardioverter-defibrillator therapy in the SIMPLE and EFFORTLESS studies. Europace 2018;20:f240–f248.
11. Brouwer TF, Yilmaz D, Lindeboom R, et al. Long-term clinical outcomes of subcutaneous versus transvenous implantable defibrillator therapy. J Am Coll Cardiol 2016;68:2047–2055.
12. Burke MC, Gold MR, Knight BP, et al. Safety and efficacy of the totally subcutaneous implantable defibrillator: 2-year results from a pooled analysis of the IDE Study and EFFORTLESS Registry. J Am Coll Cardiol 2015;65:1605–1615.
13. Weiss R, Knight BP, Gold MR, et al. Safety and efficacy of a totally subcutaneous implantable-cardioverter defibrillator. Circulation 2013;128:944–953.
14. Lenarczyk R, Boveda S, Haugaa KH, et al. Peri-procedural routines, implantation techniques, and procedure-related complications in patients undergoing implantation of subcutaneous or transvenous automatic cardioverter-defibrillators: results of the European Snapshot Survey on S-ICD Implantation (ESSS-SICDI). Europace 2018;20:1218–1224.
15. Shimizu A, Nitta T, Kurita T, et al. Actual conditions of implantable defibrillation therapy over 5 years in Japan. J Arrhythm 2012;28:263–272.
16. Yasuda S, Nakao K, Nishimura K, et al. The current status of cardiovascular medicine in Japan—analysis of a large number of health records from a nationwide claim-based database. JROAD-DPC. Circ J 2016;80:2327–2335.
17. Yasuda S, Miyamoto Y, Ogawa H. Current status of cardiovascular medicine in the aging society of Japan. Circulation 2018;138:965–967.
18. Vutthikraivit W, Rattanawong P, Putthapiban P, et al. Worldwide prevalence of Brugada syndrome: a systematic review and meta-analysis. Acta Cardiol Sin 2018;34:267–277.
19. Lambiase PD, Eckardt L, Theuns DA, et al. Evaluation of subcutaneous implantable cardioverter-defibrillator performance in patients with ion channelopathies from the EFFORTLESS cohort and comparison with a meta-analysis of transvenous ICD outcomes. Heart Rhythm O^2 2020;1:326–335.
20. Conte G, Sieira J, Ciconte G, et al. Implantable cardioverter-defibrillator therapy in Brugada syndrome: a 20-year single-center experience. J Am Coll Cardiol 2015;65:879–888.
21. Pun PH, Parzynski CS, Friedman DJ, et al. Trends in use and in-hospital outcomes of subcutaneous implantable cardioverter defibrillators in patients undergoing long-term dialysis. Clin J Am Soc Nephrol 2020;15:1622–1630.
22. Nakai M, Iwanaga Y, Sumita Y, et al. Validation of acute myocardial infarction and heart failure diagnoses in hospitalized patients with the nationwide claim-based JROAD-DPC database. Circ Rep 2021;3:131–136.
23. Okushi Y, Kusunose K, Okayama Y, et al. Acute hospital mortality of venous thromboembolism in patients with cancer from registry data. J Am Heart Assoc 2021;10:e019373.
24. Yokoyama Y, Miyamoto K, Nakai M, et al. Complications associated with catheter ablation in patients with atrial fibrillation: a report from the JROAD-DPC Study. J Am Heart Assoc 2021;10:e019701.
25. Mandrola J, Enache B, Weiss R, Daoud EG. Point/counterpoint on halting implantation of the subcutaneous ICD. JACC Clin Electrophysiol 2021;7:685–689.