



Clinical and Hospital Factors Affecting Treatment with Primary Prevention Implantable Cardioverter-Defibrillators in Ischemic Cardiomyopathy Patients

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Purpose: Implantable cardioverter defibrillators (ICD) are the standard of care for primary prevention (PP) in patients with ischemic cardiomyopathy (ICM). However, PP ICD implantation is underused in Asian countries. This study investigated ICD implantation rates and factors associated with appropriate PP ICD implants for ICM.

Materials and Methods: In this prospective multicenter observational registry (ADVANCE-ICM registry), ICM patients who were eligible for PP ICD were screened and enrolled. Factors associated with appropriate ICD implantation, including hospital and clinical factors, were investigated.

Results: Of the 1453 ICM patients eligible for PP ICD [1111 male; median age, 71.0 (61.0–78.0) years], only 76 (5.2%) patients underwent ICD implantation. Among hospital factors, a non-monetary incentive for referral (72.4% vs. 52.9%, $p=0.001$) and total hospital system score (6.0 vs. 5.0, $p=0.013$) were higher in the ICD than in the no-ICD group. In multivariate analysis, total hospital system score [odds ratio (OR), 1.28; 95% confidence interval (CI), 1.10–1.50] was an independent factor for predicting ICD implantation, along with clinical factors, including high New York Heart Association class (\geq III: OR, 7.29; 95% CI, 2.97–17.87) and younger age (<70 years: OR, 2.14; 95% CI, 1.30–3.53).

Conclusion: PP ICD implantation for ICM patients is underused in Korea. Hospital factors were important for improving PP ICD implantation rate, suggesting that new screening and referral systems for ICM patients would improve the PP ICD implantation rate (Clinical trial registration No. NCT03590925).

Key Words: Defibrillators, implantable; myocardial ischemia; primary prevention

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INTRODUCTION

Heart failure (HF) patients with a reduced left ventricular ejection fraction (LVEF) are at increased risks for arrhythmic events and sudden cardiac death,¹ and its prevention has been a clinical subject of interest for more than 25 years.² Implantable cardioverter defibrillator (ICD) device therapy has been shown to reduce the risk of sudden cardiac death and all-cause mortality in primary³⁻⁵ and secondary prevention.⁶⁻⁹ The guidelines of the European Society of Cardiology^{10,11} and the American College of Cardiology Foundation/American Heart Association^{12,13} give class 1 recommendations for implantation of ICD devices for primary prevention (PP) in symptomatic [New York Heart Association (NYHA) functional class II, III] HF patients with a LVEF \leq 35% despite optimal medical therapy for more than 3 months.

Randomized clinical trials have shown a mortality benefit from PP ICD in patients at high risk of sudden cardiac death.^{3,4,14-16} Indications for PP ICD implantation in Korea were published in 2008 and revised in 2016. The Korean indication guidelines for PP ICD implantation in ischemic cardiomyopathy (ICM) are as follows: 1) LVEF \leq 30% [at least 40 days post-myocardial infarction (MI)]; 2) LVEF 31-35%, NYHA class II, III (at least 40 days post-MI); and 3) LVEF \leq 40%, non-sustained ventricular tachycardia, and inducible ventricular fibrillation or sustained ventricular tachycardia on an electrophysiological study (at least 40 days post-MI). Despite these well-publicized guidelines, implant rates are lower than national targets, and PP ICD accounts for only a minority of implants in Korea.

Despite extensive clinical trial evidence and recommendations in national guidelines, treatment guidelines are adopted slowly in Asian countries and applied inconsistently.¹⁷ Poor guideline adherence often fails to lead to improvements in patient care quality and outcomes.¹⁸⁻²⁴ The reasons for low PP implant rates are likely to be multifactorial and include a lack of physician knowledge (particularly non-implanting cardiologists); failure to implement guidelines; failure to screen patients and collect relevant data, such as LVEF; a lack of financial resources or available implanting cardiologists; age, sex, or race bias; or even patient refusal to accept therapy. For hospitalized HF patients and outpatients, gaps, variations, and disparities between evidence-based guideline recommendations and actual treatments provided have been documented.¹⁸⁻²⁴ The underuse of ICD and cardiac resynchronization therapy with a defibrillator is an issue in Asian countries.²⁵⁻²⁹ Collaboration between interventionists and electrophysiologists may facilitate ICD implantation in eligible patients. This study investigated ICD implantation rates and factors associated with appropriate PP ICD implants for ICM using data from a prospective multicenter registry.

MATERIALS AND METHODS

Study design

The Evaluation of the Improvement of Primary Prevention in Ischemic Cardiomyopathy patients using new screening and referral systems (ADVANCE-ICM) is a prospective multicenter observational study of patients aged $>$ 18 years and $<$ 90 years with ICM and an LVEF \leq 40% who were attending any of the 12 tertiary centers encompassing all geographical regions of Korea. The study enrollment period started in July 2018 and will end in June 2021.

The aim of the ADVANCE-ICM study is to evaluate the effect of the new screening and referral systems to improve PP in ICM patients through a prospective, non-randomized, non-blinded, observational, multicenter design. Patients were enrolled in this study if they were eligible for ICD implantation for PP with ICM and offered adequate treatment regardless of actual ICD implantation. Patients who underwent ICD implantation for PP of sudden cardiac death with severe LV dysfunction due to ICM during follow-up period were evaluated. Indications for ICD implantation for PP were according to the 2016 revised Korean indication guidelines. The data collection was usually conducted by personnel with no clinical activity assigned to the project. The data were entered into a common electronic database that limits inconsistencies and errors and provides online help for key variables. The study staff at each center could see their own center's data and the data from all other participating centers.

The study was approved by the ethics committees of each center, and all patients provided informed consent for their inclusion (IRB number: 4-2018-0075). The study complied with the ethical rules of the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects by the World Medical Association. We followed all ethical, scientific, and medical standards that protect the rights of participants and required informed consent from all study participants and review and approval of study protocols, including patient information forms, from respective ethics committees: Severance Hospital, Seoul National University Hospital, Korea University Medical Center, Daegu Catholic University Medical Center, Ewha Womans University Medical Center, Kyung Hee University Hospital, Inha University Hospital, Gangnam Severance Hospital, CHA Bundang Medical Center, Seoul St. Mary's Hospital, Seoul National University Bundang Hospital, and Wonju Severance Hospital. This study was registered at ClinicalTrials.gov (NCT03590925).

Among the 12 hospitals, three started enrollment late because of delayed IRB approval or late participation in this study. For accurate results, we analyzed the data of patients from nine hospitals. A total of 1453 ICM patients with PP ICD indications were enrolled in the ADVANCE-ICM registry from July 2018 to February 2020. Among them, ICD was implanted in 76 patients (ICD group), but not in 1377 patients (no-ICD group).

Patient factors

Age; sex; body mass index; medical histories of hypertension, diabetes mellitus, valvular heart disease, congestive HF, peripheral arterial occlusive disease (PAOD), stroke or transient ischemic attack, dyslipidemia, chronic kidney disease, malignancy, and bleeding; NYHA class; prescribed medication; and echocardiographic parameters, such as LVEF, left atrial (LA) anteroposterior diameter, LA volume index, and E/Em, were obtained from medical records at the time of enrollment.

Hospital factors

Hospital factors of each center associated with ICD implantation were evaluated by a questionnaire. Total hospital system score was defined as the sum of the number of applied systems, including multidisciplinary conference, non-monetary incentive for referral, automated notice system, patient education system, patient brochure, HF clinic, and ICD check-up clinic. Non-monetary incentive for referral was defined as a reward system for encouraging physicians to refer patients to electrophysiology doctors. The term 'non-monetary incentive' in this paper does not mean economic rewards or compensation, but a recognition of medical performance or clinical achievement. The automated notice system was a computerized system that automatically shows a pop-up memo to physicians when patients who are eligible for ICD implantation visit the outpatient clinic.

Statistical analysis

Continuous variables are presented as medians [interquartile range (IQR)] for non-normally distributed value, and categorical variables are shown as numbers and percentages in each group. Continuous and categorical variables were compared using the Wilcoxon rank-sum test and Fisher's exact test, respectively. To investigate factors associated with appropriate ICD implantation, univariate and multivariate logistic regression were employed, and odds ratio (OR), 95% confidence intervals (CI), and *p* values were determined. Since system factors have multicollinearity, total hospital system score was used as the system factor in the multivariate logistic regression analysis. Additional analyses to elucidate characteristics among centers were performed based on a questionnaire and information of each center using Kruskal-Wallis test and Fisher's exact tests. Two-sided *p* values <0.05 were considered statistically significant. The Statistical Package for the Social Sciences version 25.0 for Windows (IBM Corporation, Armonk, NY, USA) and R software version 3.6.2 (The R foundation for Statistical Computing, Vienna, Austria) were employed in the data analysis.

RESULTS

Baseline clinical characteristics

A total of 1453 ICM patients [1111 male, median age 71.0 (61.0-

78.0) years] eligible for PP ICD were enrolled in the ADVANCE-ICM registry from July 2018 to February 2020. Among them, ICD was implanted in 76 patients during 11 (IQR, 7-12) months of follow-up. The patients in the ICD group were significantly younger (67.0 years vs. 71.0 years, *p*=0.002), had a higher (\geq III) NYHA functional class (10.5% vs. 2.8%, *p*<0.001), had a lower LVEF (29.0% vs. 31.0%, *p*<0.001), and were taking more angiotensin converting enzyme inhibitor (ACEi)/angiotensin receptor antagonist (ARB) and antiarrhythmic agents than patients in the no-ICD group (Table 1).

Hospital factors

The detailed applied systems for advancing ICD implantation in each center and the characteristics of the nine tertiary centers, including hospital bed supply, number of electrophysiologists, absolute ICD implantation number, ICD implantation rate, and referral rate for ICD implantation from other parts, are shown in Supplementary Table 1 (only online).

To elucidate the effect of hospital size on ICD implantation, the centers were divided into three groups according to the number of hospital beds as a marker of hospital size (group 1, \geq 1200 beds; group 2, \geq 850 but <1200 beds; and group 3, <850 beds). Groups 1 and 2 had significantly higher total hospital system scores than group 3 (group 1 vs. group 3, *p*=0.046; group 2 vs. group 3, *p*=0.043) (Fig. 1A). The absolute number of ICD implantations was higher in group 1 than groups 2 and 3 (group 1 vs. group 2, *p*=0.043; group 1 vs. group 3, *p*=0.046) (Fig. 1B). However, ICD implantation rate did not differ significantly among the three groups (Fig. 1C). To investigate factors affecting the ICD implantation rate in the larger (group 1) and smaller (group 3) centers, the centers' characteristics were reviewed. A higher referral rate was noted in centers with higher ICD implantation rates (Supplementary Table 1, only online). To evaluate the effects of the referral rate, centers were divided into two groups according to their referral rates (group A, \geq 30%; group B, <30%). Group A had significantly higher total hospital system scores than group B (group A vs. group B; *p*=0.032) (Fig. 2A). Group A also had a significantly higher number of absolute ICD implantations than group B (group A vs. group B; *p*=0.032) (Fig. 2B). However, ICD implantation rate did not differ between the two groups (group A vs. group B; *p*>0.999) (Fig. 2C). Instead, additional analysis of the association between individual hospital factors with ICD implantation rate revealed that ICD implantation rates were higher in hospitals that applied non-monetary incentives for referral systems than hospitals that did not (*p*=0.016) (Fig. 3).

Table 2 shows a comparison hospital system factors between the ICD and no-ICD groups. Among hospital factors, a non-monetary incentive for referral (72.4% vs. 52.9%; *p*=0.001) and total hospital system score (6.0 vs. 5.0; *p*=0.013) were higher in the ICD group than in the no-ICD group (Table 2).

Table 1. Baseline Clinical and Echocardiographic Parameters in the ICD and No-ICD Groups

	All subjects (n=1453)	ICD group (n=76)	No-ICD group (n=1377)	p value
Age (yr)	71.0 (61.0–78.0)	67.0 (59.0–72.5)	71.0 (61.0–78.0)	0.002
Male	1111 (76.5)	60 (78.9)	1051 (76.3)	0.700
BMI (kg/m ²)	23.5 (21.3–25.7)	24.4 (21.6–26.0)	23.5 (21.3–25.7)	0.076
Hypertension	942 (64.8)	50 (65.8)	892 (64.8)	0.955
Diabetes mellitus	720 (49.6)	37 (48.7)	683 (49.6)	0.970
Valvular heart disease	275 (18.9)	11 (14.5)	264 (19.2)	0.386
Congestive heart failure	1305 (89.8)	68 (89.5)	1237 (89.8)	>0.999
PAOD	847 (58.3)	36 (47.4)	811 (58.9)	0.062
Stroke/TIA	195 (13.4)	8 (10.5)	187 (13.6)	0.557
Dyslipidemia	881 (60.6)	39 (51.3)	842 (61.1)	0.112
Chronic kidney disease	351 (24.2)	19 (25.0)	332 (24.1)	0.969
Malignancy	83 (5.7)	3 (3.9)	80 (5.8)	0.669
Bleeding history	47 (3.2)	3 (3.9)	44 (3.2)	0.978
NYHA functional class				
Class I, II	1407 (96.8)	68 (89.5)	1339 (97.3)	<0.001
Class III, IV	46 (3.2)	8 (10.5)	38 (2.8)	<0.001
LVEF (%)	31.0 (26.0–35.0)	29.0 (25.0–32.0)	31.0 (26.0–35.0)	<0.001
LA AP diameter (mm)	44.0 (39.0–49.0)	43.9 (36.3–57.6)	43.7 (32.5–56.8)	0.266
LA volume index (mL/m ²)	43.8 (32.8–56.8)	45.0 (40.0–49.0)	44.0 (39.0–49.0)	0.644
E/Em	15.5 (11.4–22.5)	14.0 (10.5–21.7)	15.5 (11.5–22.5)	0.301
Medication				
ACEi/ARB	1119 (81.3)	68 (91.9)	1051 (80.7)	0.025
Beta blocker	1096 (79.7)	66 (89.2)	1030 (79.1)	0.052
Aldosterone antagonist	684 (49.7)	44 (59.5)	640 (49.2)	0.108
Anticoagulant	301 (21.9)	19 (25.7)	283 (21.7)	0.514
Diuretics	753 (54.7)	48 (64.9)	705 (54.1)	0.093
Statin	1095 (79.6)	63 (85.1)	1032 (79.3)	0.284
Antiplatelet	1130 (82.1)	56 (75.7)	1074 (82.5)	0.183
Antiarrhythmic agent	65 (4.7)	8 (10.8)	57 (4.4)	0.024
CCB	152 (11.0)	8 (10.8)	144 (11.1)	>0.999

ACEi, angiotensin converting enzyme inhibitor; AP, anteroposterior; ARB, aldosterone receptor blocker; BMI, body mass index; CCB, calcium channel blocker; E/Em, ratio of mitral valve inflow and tissue doppler; ICD, implantable cardioverter defibrillator; LA, left atrial; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PAOD, peripheral arterial occlusive disease; TIA, transient ischemic attack.

Values are presented as a median [Q1–Q3 quartiles (25th and 75th percentiles)] or number (%).

Factors associated with appropriate ICD implantation

In univariate analysis, age <70 years, absence of a history of PAOD; taking ACEi/ARB, beta blocker, or antiarrhythmic agents; severe NYHA functional class (III and IV) were significantly associated with appropriate ICD implantation [Table 3 and Supplementary Table 2 (only online)]. Due to multicollinearity among the applied systems, total hospital system score was used to represent hospital systems, and the score was significantly high in the ICD group. The univariate analysis results of all variables are shown in Supplementary Table 2 (only online).

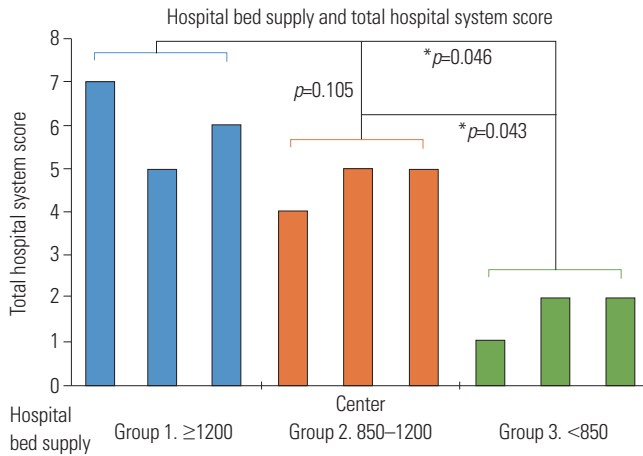
Multivariate analysis was performed with adjustment for age <70 years; presence of PAOD; NYHA functional class (III and IV); taking ACEi/ARB, beta blocker, and antiarrhythmic agents; and total hospital system score. Total hospital system score

(OR, 1.28; 95% CI, 1.10–1.50) was an independent factor predictive of ICD implantation with clinical factors, including high NYHA class (≥III: OR, 7.29; 95% CI, 2.97–17.87) and younger age (<70 years: OR, 2.14; 95% CI, 1.30–3.53) (Table 3).

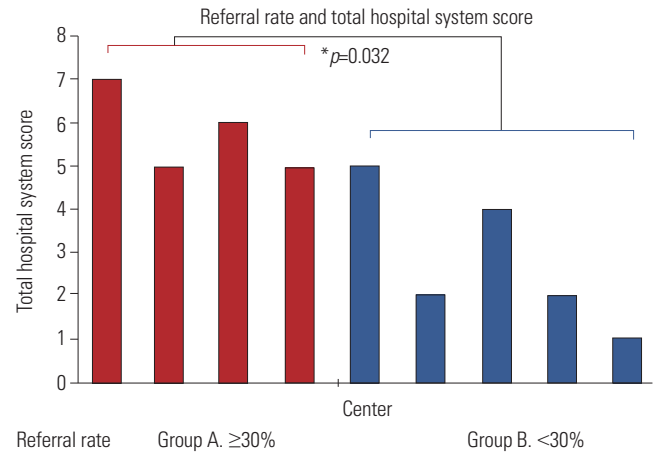
DISCUSSION

Main findings

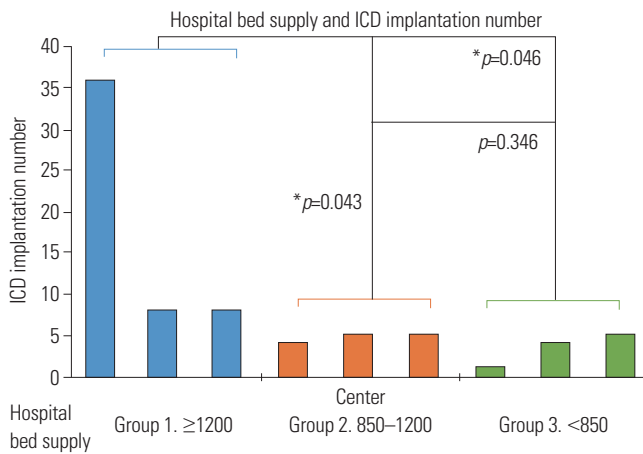
The main findings of the present study are as follows: 1) the ICD implantation rate for PP for ICM in nine tertiary centers in Korea was only 5.23%; 2) age <70 years, absence of history of PAOD, taking antiarrhythmic agents, NYHA functional class III and IV, and high total hospital system scores were associated with appropriate ICD implantation; and 3) larger centers



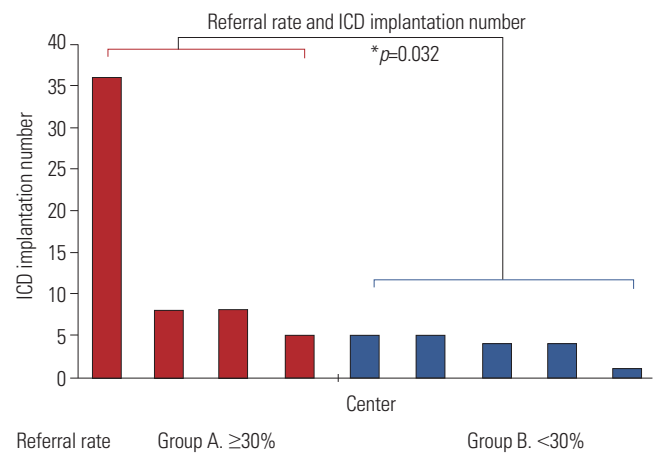
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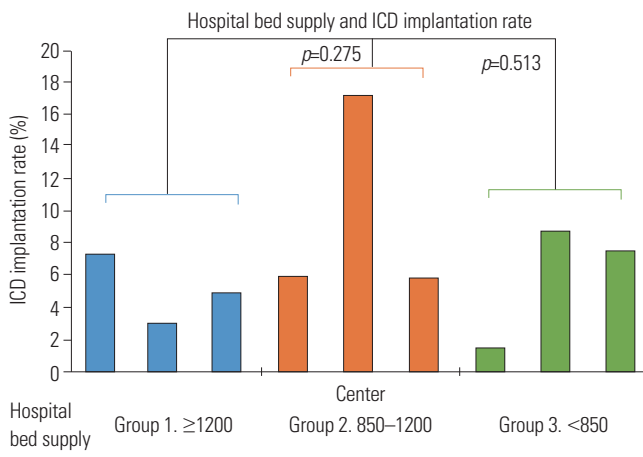
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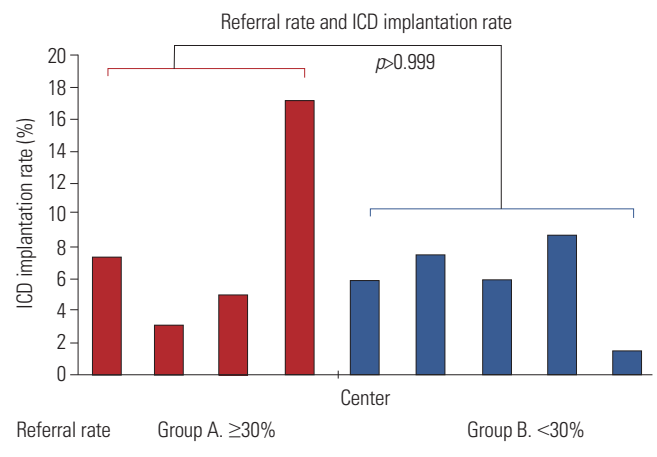
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C



C

Fig. 1. Associations between center size and total hospital system score, ICD implantation number, and ICD implantation rate. (A) Large centers (groups 1 and 2) applied more systems for improving ICD implantation than relatively small centers (group 3). (B) Large centers (group 1) also implanted higher numbers of ICDs than smaller centers (group 2 and 3). (C) However, ICD implantation rate did not differ according to center size. ICD, implantable cardioverter defibrillator.

Fig. 2. Associations between referral rate and total hospital system score, ICD implantation number, and ICD implantation rate. (A) Centers with a high referral rate from other departments (group A) applied more systems than centers with a low referral rate (group B). (B) Furthermore, centers with a high referral rate (group A) implanted more ICD implantations than centers with a low referral rate (group B). (C) However, ICD implantation rate did not differ according to referral rate. ICD, implantable cardioverter defibrillator.

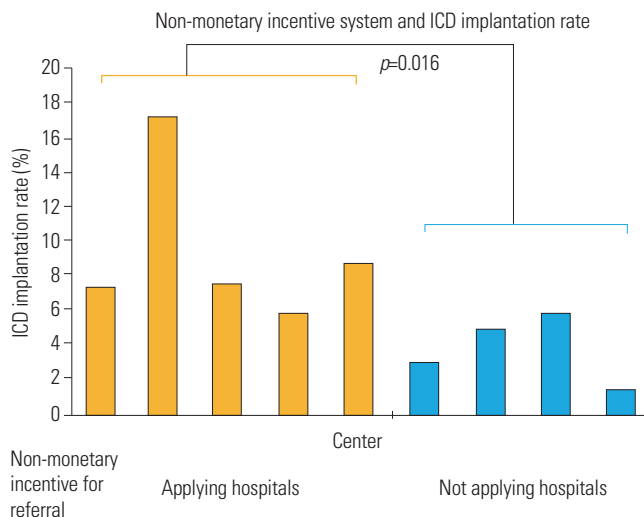


Fig. 3. Association between non-monetary incentive systems and ICD implantation rate. ICD implantation rates were higher in centers that applied non-monetary incentive systems than in those that did not. ICD, implantable cardioverter defibrillator.

and centers with higher referral rates applied more hospital systems for improving ICD implantation and implanted more absolute numbers of PP ICDs. However, implantation rate did not differ significantly according to the sizes or referral rates for each hospital. Instead, implantation rates differed significantly according to the application of a non-monetary incentive for referral systems.

Discordant practice in PP ICD

Despite the existence of evidence-based and well-established national guidelines, PP ICD implant rates vary among countries and are low in Asian countries.^{17,29} Previous studies reported that PP ICD implantation rates for eligible patients were 10%, 60%, and 5% in Sweden, US, and an Asian country, respectively.^{25,26,29} The present study showed that only 5.23% of patients who were eligible for PP ICD were treated with ICDs. We could not evaluate whether electrophysiology study was performed in patients whose LVEF was over 35% according to guidelines because of the multicenter study design. Instead,

Table 2. Baseline Hospital Factors Related to ICD Implantation in the ICD and No-ICD Groups

	All subjects (n=1453)	ICD group (n=76)	No-ICD group (n=1377)	p value
Multidisciplinary conference	1012 (69.6)	57 (75.0)	955 (69.4)	0.361
Non-monetary incentive for referral	784 (54.0)	55 (72.4)	729 (52.9)	0.001
Automated notice system	957 (65.9)	57 (75.0)	900 (65.4)	0.109
Patient education system	1316 (90.6)	70 (92.1)	1246 (90.5)	0.788
Patient brochure	981 (67.5)	58 (76.3)	923 (67.0)	0.119
Heart failure clinic	1158 (79.7)	62 (81.6)	1096 (79.6)	0.785
ICD check-up clinic	1315 (90.5)	66 (86.8)	1249 (90.7)	0.359
Total hospital system score*	5.0 (4.0–7.0)	6.0 (5.0–7.0)	5.0 (4.0–7.0)	0.013

ICD, implantable cardioverter defibrillator.

Values are presented as a median [Q1–Q3 quartiles (25th and 75th percentiles)] or number (%).

*A sum of the number of applied systems, including multidisciplinary conference, non-monetary incentive for referral, automated notice system, patient education system, patient brochure, heart failure clinic, and ICD check-up clinic.

Table 3. Univariate and Multivariate Logistic Regression Analyses of Patient and System Score Factors Affecting ICD Implantation

	Univariate		Multivariate*	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Age <70	1.92 (1.19–3.08)	0.007	2.14 (1.30–3.53)	0.003
PAOD	0.63 (0.40–1.00)	0.049	0.55 (0.34–0.91)	0.019
NYHA class ≥3	4.15 (1.86–9.23)	<0.001	7.29 (2.97–17.87)	<0.001
LVEF <25%	1.64 (0.95–2.85)	0.076		
Medication				
ACEi/ARB	2.71 (1.16–6.31)	0.021	1.95 (0.80–4.77)	0.141
Beta blocker	2.18 (1.03–4.59)	0.041	1.93 (0.89–4.22)	0.098
Diuretics	1.56 (0.96–2.55)	0.074		
Antiarrhythmic agent	2.65 (1.21–5.78)	0.014	3.77 (1.66–8.60)	0.002
Total hospital system score [†]	1.17 (1.01–1.35)	0.038	1.28 (1.10–1.50)	0.002

ACEi, angiotensin converting enzyme inhibitor; ARB, aldosterone receptor blocker; CI, confidence interval; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PAOD, peripheral arterial occlusive disease.

*Odds ratio was adjusted for age <70 years, presence of PAOD, NYHA functional class (III and IV), taking ACEi/ARB, beta blocker, and antiarrhythmic agent, and total hospital system score. [†]A sum of the number of applied systems, including multidisciplinary conference, non-monetary incentive for referral, automated notice system, patient education system, patient brochure, heart failure clinic, and ICD check-up clinic.

we additionally evaluated ICD implantation rates in patients whose LVEF was lower than 35%, and therein, the ICD implantation rate was 5.31%. These centers have better established electrophysiology laboratories than relatively small hospitals, indicating that the implantation rate of PP ICD in community settings could be much lower. Previous studies explained that the discordant practice in PP ICD was largely influenced by referral failure from general cardiologists to electrophysiology cardiologists in the UK.^{30,31} Since health care systems differ among countries, a direct comparison of the results of the present study with those of other studies is impossible. However, the present study revealed that the application of hospital systems for referral pathway, such as a non-monetary incentive system for referral, was associated with high ICD implantation rates, and this result could indicate the importance of referral pathways for appropriate PP ICD implantation in ICM patients, in line with previous studies.

Characteristics of patients with appropriate PP ICD

Previous trials have described an underutilization of ICD implantation in women and ethnic minorities.³² However, the results of the present study showed no sex-based differences between the ICD and no-ICD groups. We did not evaluate ethnic factors because there is fundamentally no ethnic difference among people in Korea. Limited data are available about ICD implantation in older patients because several trials excluded patients 80 years or older.^{33,34} A previous questionnaire survey also revealed that physicians tended not to follow guidelines in patients who are older and have comorbidities.³⁰ In accordance with previous studies, the present study revealed that age <70 years and less PAOD were factors associated with appropriate PP ICD implantation. Physicians may hesitate to refer older patients for ICD implantation due to limited evidence. Furthermore, since older patients and those with PAOD might have other comorbidities, physicians may have difficulty choosing additional procedures with consideration of the risks and benefits. A previous study reported that, among HF patients with indications for ICD, there was a higher ICD implantation rate in patients who were treated with guideline-based optimal medical therapy.²¹ However, the present study demonstrated that taking HF medications was not associated with appropriate ICD implantation. The present study revealed that taking antiarrhythmic agents and having a higher NYHA functional class (III, IV) independently affected appropriate ICD implantation. Patients with more severe symptoms or deteriorated cardiac function should be considered at high risk for future arrhythmic events.

Systems for ICD implantation and characteristics of each center

Previous studies have reported that underutilization of PP ICD implantation could be the result of a lack of knowledge and complex guideline criteria. Therefore, an automated, com-

puterized screening system could help countries overcome those problems.³⁰ In the present study, a total hospital system score and a non-monetary incentive for referral were associated with improved appropriate ICD implantation. An automated notice system might help physicians decrease the risk of overlooking ICD-eligible patients during follow up in outpatient clinics. A non-monetary incentive for referral can motivate physicians and could be an effective way to improve the referral pathway. The results of this study showed that a high rate of system application, regardless of composition, was a significant independent factor for ICD implantation. This result indicates that both system type and harmony might be important for improving PP ICD.

The present study showed that, although larger hospital had more systems for improving ICD implantation and more ICDs were implanted in large volume centers, the implantation rate was not significantly associated with hospital size. Previous studies have reported that barriers to the referral pathway and non-referral were the most common factors contributing to eligible patients not being treated with ICD.^{28,31,35} However, the present study revealed that the ICD implantation rates of each hospital did not differ according to referral rates. Referral rates in this study were assessed via questionnaires with multiple choice questions. Therefore, the cutoff for a referral rate of 30% in the analysis was not an exact determinant for a high or low referral rate. This could be the reason for the non-statistical significance between referral rate and ICD implantation rate. Instead, the number of applied hospital systems and the non-monetary incentive for referral, which were designed for better screening and referral pathways, showed a beneficial influence on appropriate PP ICD treatment. This results could emphasize the need for better screening and referral pathways for appropriate PP ICD implantation. To our knowledge, this is the first study to investigate the usefulness of hospital systems for improving appropriate ICD implantation in multiple tertiary centers.

Study limitations

There are several limitations to this study. First, although it was prospective and enrolled a large population, the follow-up period (median 10 months) was relatively short. In Korea, patients usually visit the outpatient clinic every 6 months, so the follow-up period of this study could be inadequate for evaluating the benefit of new applied systems. Furthermore, ICD implantation rate could be underestimated with the short follow-up duration because there could be a delay in procedures for several reasons, even though physicians properly recommended PP-ICD according to set guidelines. Second, since some systems were usually applied together, analysis of the usefulness of each system was limited due to multicollinearity. We tried to correct for this limitation by using a new variable of total hospital system score. Third, the timing of the application of hospital factors varied, and the actual application

of the systems to each patient could not be traced. This could obscure the effect of hospital systems. However, since most hospital factors were applied through established hospital systems and performed by physicians, we believed that a substantial portion of hospital factors would be applied to each patient.

Conclusion

PP ICD implantation for ICM is underused in Korea. Hospital factors appear to contribute to improving PP ICD implantation rates, suggesting that new screening and referral systems for ICM patients would help improve PP ICD implantation rates.

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AUTHOR CONTRIBUTIONS

Conceptualization: all authors. **Data curation:** all authors. **Formal analysis:** Jae-Hyuk Lee, Hee Tae Yu, Junbeom Park, and Boyoung Joung. **Funding acquisition:** Boyoung Joung. **Investigation:** all authors. **Methodology:** Jae-Hyuk Lee, Hee Tae Yu, Junbeom Park, and Boyoung Joung. **Project administration:** all authors. **Resources:** all authors. **Software:** Jae-Hyuk Lee, Hee Tae Yu, Junbeom Park, and Boyoung Joung. **Supervision:** all authors. **Validation:** Jae-Hyuk Lee, Hee Tae Yu, Junbeom Park, and Boyoung Joung. **Visualization:** Jae-Hyuk Lee, Hee Tae Yu, Junbeom Park, and Boyoung Joung. **Writing—original draft:** Jae-Hyuk Lee, Hee Tae Yu, and Boyoung Joung. **Writing—review & editing:** Jae-Hyuk Lee, Hee Tae Yu, Junbeom Park, and Boyoung Joung. **Approval of final manuscript:** all authors.

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