Original Article

Disparity Between Indications for and Utilization of Implantable Cardioverter Defibrillators in Asian Patients With Heart Failure

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Background—Implantable cardioverter defibrillators (ICDs) are lifesaving devices for patients with heart failure (HF) and reduced ejection fraction. However, utilization and determinants of ICD insertion in Asia are poorly defined. We determined the utilization, associations of ICD uptake, patient-perceived barriers to device therapy and, impact of ICDs on mortality in Asian patients with HF.

Methods and Results—Using the prospective ASIAN-HF (Asian Sudden Cardiac Death in Heart Failure) registry, 5276 patients with symptomatic HF and reduced ejection fraction (HFrEF) from 11 Asian regions and across 3 income regions (high: Hong Kong, Japan, Korea, Singapore, and Taiwan; middle: China, Malaysia, and Thailand; and low: India, Indonesia, and Philippines) were studied. ICD utilization, clinical characteristics, as well as device perception and knowledge, were assessed at baseline among ICD-eligible patients (EF ≤35% and New York Heart Association Class II-III). Patients were followed for the primary outcome of all-cause mortality. Among 3240 ICD-eligible patients (mean age 58.9±12.9 years, 79.1% men), 389 (12%) were ICD recipients. Utilization varied across Asia (from 1.5% in Indonesia to 52.5% in Japan) with a trend toward greater uptake in regions with government reimbursement for ICDs and lower out-of-pocket healthcare expenditure. ICD (versus non-ICD) recipients were more likely to be older (63±11 versus 58±13 year; $P<0.001$), have tertiary (versus ≤primary) education (34.9% versus 18.1%; $P<0.001$) and be residing in a high (versus low) income region (64.5% versus 36.5%; $P<0.001$). Among 2000 ICD nonrecipients surveyed, 55% were either unaware of the benefits of, or needed more information on, device therapy. ICD implantation reduced risks of all-cause mortality (hazard ratio, 0.71; 95% confidence interval, 0.52–0.97) and sudden cardiac deaths (hazard ratio, 0.33; 95% confidence interval, 0.14–0.79) over a median follow-up of 417 days.

Conclusions—ICDs reduce mortality risk, yet utilization in Asia is low; with disparity across geographic regions and socioeconomic status. Better patient education and targeted healthcare reforms in extending ICD reimbursement may improve access.

Clinical Trial Registration—URL: https://clinicaltrials.gov/ct2/show/NCT01633398. Unique identifier: NCT01633398.

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WHAT IS KNOWN

- Implantable cardioverter defibrillators (ICDs) are an established therapy for prevention of sudden cardiac deaths.

WHAT THE STUDY ADDS

- Our study is the first pan-Asian study across 11 regions which describes the utilization, associations of ICD uptake, patient-perceived barriers to device therapy and, impact of ICDs on mortality in Asian patients with heart failure and reduced ejection fraction.
- It shows that ICD utilization within Asia is low (12%) with marked disparity across geographic regions and socioeconomic status.
- The financial burden of ICD therapy is a key deterrent to uptake and extending reimbursement coverage for the devices could improve its acceptance.
- Lack of patient and physician education on primary prevention ICD therapy is another barrier to its uptake that should be addressed with educational strategies targeting both physicians and patients.

Heart failure (HF) is a chronic debilitating syndrome associated with significant morbidity and mortality.[1] Five-year survival rates are ≈50%[2] with at least half of all deaths attributed to sudden cardiac deaths (SCDs).[3] Prophylactic insertion of implantable cardioverter defibrillators (ICDs) in patients with HF and reduced ejection fraction (HFrEF) are associated with a 23% to 31% reduced risk of all-cause mortality.[4–6] However, in Asia, there has been controversy about benefits of ICD. When criteria from the MADIT-II (Second Multicenter Automatic Defibrillator Implantation Trial)[4] were applied to a Japanese cohort,[7] eligible patients who did not undergo ICD implantation had better survival than the historical Western MADIT-II population; whereas patients from a Chinese cohort[8] were at similarly high risk of SCD. In a subgroup analysis of Western data on SCD,[9] Asian Americans were at lower risk of SCD compared with White Americans. These studies have contributed to the perception that Asians may be at lower risk of SCD and thus less likely to benefit from ICD therapy. Indeed, limited published crude implantation rates suggest a low and heterogeneous uptake within Asia, with ICD implantation rates per million inhabitants ranging from 0.5 in Philippines to 45.9 in Japan.[10]

At a macro level, regional differences in healthcare systems and the availability of government reimbursement for primary prevention ICD implantation could influence uptake rates.[11] Other factors may also contribute to the disparity in ICD utilization in Asia. Socioeconomic barriers or cultural differences in device knowledge or perception may limit the application of device therapy in Asia, even in the face of proven outcome benefits. However, prospective, multinational data among patients with HFrEF from Asia have thus far been lacking.

We examined prospectively a large cohort of patients with HFrEF from a vast geography in Asia, with the primary aim of determining the ICD utilization, associations of ICD uptake, and patient-perceived barriers to device therapy. We hypothesized that among Asian patients eligible for primary prevention ICD implantation, there would be underutilization of ICDs and utilization would vary across Asia; with both socio and national economic factors and patients' perception toward device therapy influencing ICD implantation. We further examined the impact of ICDs on mortality outcomes.

Methods

Study Population

ICD-eligible patients were identified from the ASIAN-HF (Asian Sudden Cardiac Death in Heart Failure) registry,[12,13] a prospective observational registry comprising 5276 symptomatic patients with HFrEF recruited from 11 Asian regions from 2010 to 2015. Medical centers were carefully selected based on HF patient volume, availability of HF specialty units and care; and expertise in both echocardiography and ICD implantation skills.[12]

ICD eligibility criteria for primary prevention are the Class I recommendations from the American College of Cardiology/American Heart Association/Heart Rhythm Society guidelines[14] and include the following: (1) left ventricular EF ≤35% and New York Heart Association (NYHA) Class II-III with ischemic heart disease or nonischemic dilated cardiomyopathy; or (2) left ventricular EF ≤30% because of prior myocardial infarction and NYHA Class I.

ICD recipients were eligible patients with an ICD or cardiac resynchronization therapy with defibrillator implanted at baseline. Patients who had an implantable device without a defibrillator component or qualifying for secondary prevention ICD implantation in view of a history of ventricular fibrillation or ventricular tachycardia were excluded.

Data Collection

Patients' sociodemographics and clinical characteristics including clinical symptoms, comorbidities, and medication use were collected at baseline. Patients were prospectively followed over a 3-year period for the primary outcome of all-cause mortality and the secondary outcome of SCD.

Patients were categorized as recruited from regions of high (Hong Kong, Japan, Korea, Singapore, and Taiwan), middle (China, Malaysia, and Thailand), or low (India, Indonesia, and Philippines) stage of economic development based on the World Bank income grouping.[15] A modified Charlson Comorbidity Index,[16] which excluded connective tissue disease and renal disease; and replaced acute myocardial infarction with ischemic heart disease, was calculated.

To understand patients' perception toward utilization of device therapy, a semiqualitative questionnaire, was developed based on findings from previous pilot studies performed in Asian populations.[17,18] The following questions were administered in the patients' local languages by trained interviewers:

1. Do you believe device therapy would benefit you?
2. Are you willing to receive device therapy?
   a. If no or uncertain, what is the main reason?
   b. If yes, how do you think health professionals can help patients make informed treatment choices?

A grounded theory approach to thematic analysis was used to analyze the open-ended responses.

Event Adjudication

All deaths were classified as cardiac (sudden or nonsudden) or noncardiac. Events were adjudicated independently based on prespecified criteria by a central event adjudication committee. Details on death data collection and the adjudication process have been reported previously.[12] In brief, SCD was defined as an unexpected death and,

where sufficient information was available, death that occurred within 1 hour of onset of cardiac symptoms.[12]

Statistical Analysis

Continuous variables were expressed as mean±SD, whereas categorical variables were expressed as number (percentage). ICD utilization was calculated as the proportion of ICD recipients among the total ICD-eligible cohort at baseline. To compare baseline characteristics of ICD recipients to eligible nonrecipients, the χ^2 test and independent *t* test were used for categorical and continuous variables respectively. Logistic regression was used to determine the associations of ICD implantation. Variables with $P \leq 0.20$ on univariable analysis or variables found previously to be associated with ICD utilization, such as NYHA class, were included in the multivariable regression model.

Multivariable Cox proportional hazards model was used to compare risk of all-cause mortality and checked for proportionality assumption. A competing risk approach based on the Fine and Gray model,[19] which accounts for SCDs and other competing causes of death separately, was used to derive the cumulative incidence of SCD. Outcome models were adjusted for clinically relevant variables including age, sex, ischemic cause, body mass index, left ventricular EF, NYHA, systolic blood pressure, Charlson Comorbidity Index, medications, and patient type (inpatient versus outpatient). Patients with missing data on variables for adjustment were excluded from the multivariable regression analyses. A total of 2656 patients were analyzed in the multivariable logistic regression model and among these patients, 2431 and 2118 patients were included in the fully-adjusted all-cause mortality and SCD models respectively.

A *P* value of ≤0.05 was considered statistically significant. All statistical analysis was performed using SPSS version 23 (IBM Corporation, NY). Ethics approval was obtained from the local institutional review committee of each participating center and all participating subjects gave informed consent.

Results

Study Cohort

Patients were recruited across Asia, which is a region of immense social, cultural, and economic diversity, contributing to the disparate healthcare systems at various stages of evolution. Although some countries have universal health insurance policies and reimbursement for ICD implantation, others are more reliant on private payment; leading to large variation (7.9%–62.4%) in out-of-pocket (OOP) healthcare expenses (Table 1; Figure 1).[10,15,20,21] Among the 5276 patients recruited, 3240 (61.4%) were ICD eligible (Figure 2). Of the 3240 patients, 1292 (39.9%) resided in a high-, 666 (20.5%) in a middle-, and 1282 (39.6%) in a low-income region. Approximately two-thirds (65.4%) of patients were in NYHA class I-II and majority were men (79.1%; Table 2).

ICD Utilization Within Asia

Among 3240 ICD-eligible patients, 389 (12%) patients were ICD recipients. ICD utilization varied across Asia with the highest in Japan (52.5%) and the lowest in Indonesia (1.5%; Figure 3). ICD utilization was correlated positively to a higher stage of economic development with average rates of 4.2% for low-, 12.6% for middle-, and 19.4% for high-income regions. There was a general trend of higher ICD utilization in regions with greater healthcare expenditure and lower OOP healthcare expenses. This was accentuated by the disproportionately high utilization in Japan, which had the highest government healthcare expenditure and was among the regions with the lowest OOP healthcare expenses (Figure 1). Patients residing in a high- (versus low-) income region were 6.5× more likely to have an ICD implanted (Table 3).

Patient Characteristics Associated With ICD Uptake

Compared with nonrecipients, ICD recipients were more likely to be older (62.9±11.3 versus 58.3±13.0 years; $P<0.001$), male (versus female, 83.5% versus 78.5%; $P=0.021$), had a higher comorbidity burden (modified Charlson Comorbidity

Table 1. Variations in Socioeconomic Development, Healthcare Systems, and ICD Reimbursement Across Asia

	China	Hong Kong	India	Indonesia	Japan	Korea	Malaysia	Philippines	Singapore	Taiwan	Thailand
No. of patients recruited	477	50	1436	290	540	317	541	91	1066	274	194
No. of ICD-eligible patients	229	19	1029	196	305	160	319	57	704	104	118
Total health expenditure (% of GDP)[15,20,21]	5.5	5.2	4.7	2.8	10.2	7.4	4.2	4.7	4.9	6.9	6.5
Out-of-pocket health expenditure (% of total health expenditure)[15,20,21]	32.0	34.9	62.4	46.9	13.9	36.1	35.3	53.7	54.8	25.8	7.9
ICD implanting physicians[10]	3 000		475	23			24	15	22	71	115
ICD implanting centers[10]	368		350	7	394	96	18	23	5	40	55
Reimbursement for primary prevention*	N	N		N	Y	Y	Partial†	N	Partial‡		N
Reimbursement for secondary prevention*	N	Y	Y	Y	Y	Y	Partial†	Y	Partial‡		Y
Government reimbursement for ICD, %[10]			20		100	95	90–100	10	60–80		
Population aged 55–59 y with secondary/tertiary education in 2010 (% of country's population)[15]	42.6	56.0	31.9	24.3	83.7	77.9	41.6	46.9	67.6	61.8	19.5
ICD-eligible patients with secondary/tertiary schooling (% of ICD-eligible patients)	71.8	52.6	69.4	76.4	94.8	57.8	71.7	89.5	47.5	58.7	60.2

Empty cells represent unavailable information. GDP indicates gross domestic product; and ICD, implantable cardioverter defibrillator.
*N indicates no; and Y, yes.
†Reimbursement is mainly for civil servants and the needy population.
‡Reimbursement is only for Class B and C paying populations.

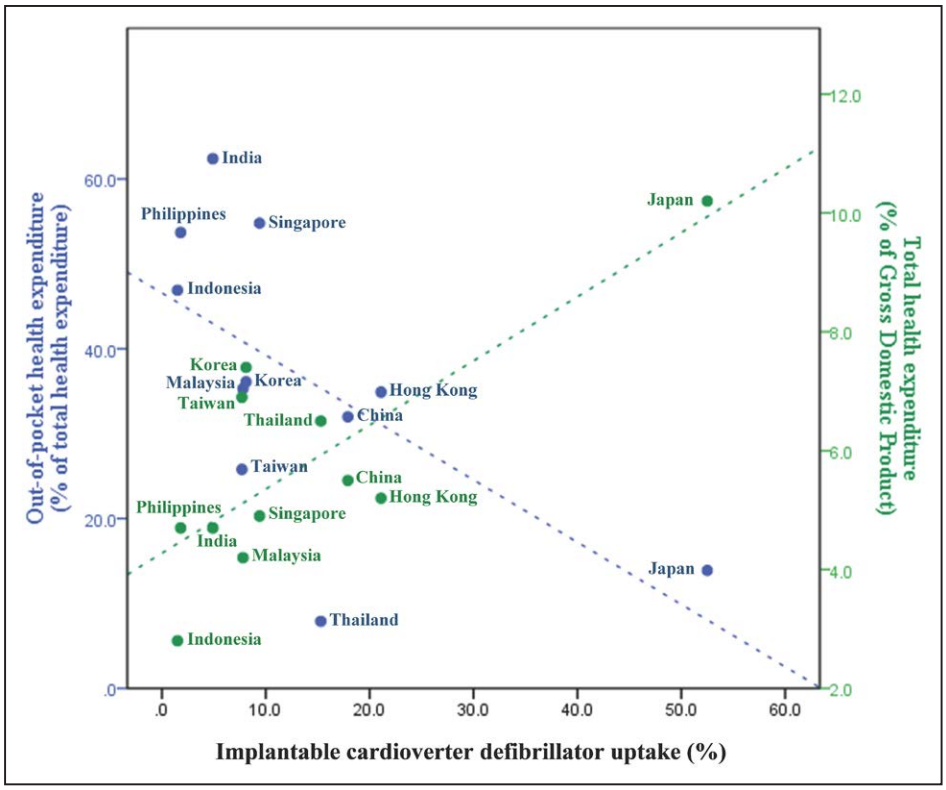

Figure 1. Association of out-of-pocket health expenditure and total government health expenditure with implantable cardioverter defibrillator utilization (%).

Index ≥3 versus <3; 21.3% versus 15.3%; *P*=0.002) and a higher prevalence of individual comorbidities such as atrial fibrillation, cerebrovascular diseases, and pulmonary diseases (all *P*≤0.01; Tables 2 and 3). Tertiary (versus primary and lower) educated patients were 5.5 more likely to have an ICD implanted (Table 3). Notably, patients' household income was not found to be associated with ICD implantation.

In subgroup analysis comparing ICD (n=176, 45.2%) to cardiac resynchronization therapy with defibrillator (n=213, 54.8%) recipients, there were no differences in most baseline characteristics such as age, sex, and comorbidity burden. However, as expected, cardiac resynchronization therapy with defibrillator patients were more likely to have prolonged QRS interval (≥120 ms; 85.3% versus 45.1%; *P*<0.001), NYHA class III (versus Class I-II, 44.1% versus 26.1%; *P*<0.001), and ischemic cause of HF (54.9% versus 34.1%; *P*<0.001).

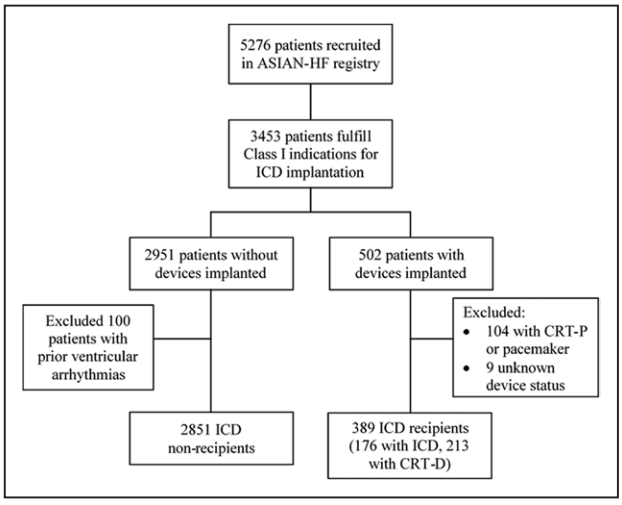

Figure 2. Flowchart indicating the process of patient selection. ASIAN-HF indicates Asian Sudden Cardiac Death in Heart Failure; CRT-D, cardiac resynchronization therapy with defibrillator; CRT-P, cardiac resynchronization therapy with pacemaker; and ICD, implantable cardioverter defibrillator.

Barriers to ICD Uptake

Among the 2000 (70.2%), ICD nonrecipients who responded to the questionnaire on device therapy, nearly half (44.7%) thought that a device could improve their quality of life and survival; whereas a third (32.6%) were uncertain (Table 4). A third (33.0%) of patients were willing to receive a device and a fifth (22.1%) wanted more information to make a decision on device therapy.

The top 3 reasons to decline device therapy included financial issues (28.8%), a belief that they could manage their symptoms without devices (24.3%), and that the device would be ineffective in helping them (14.0%). Among the 659 patients willing to receive device therapy, 15.3% suggested that further education by a healthcare provider could aid them in making informed treatment choices (Table 4).

All-Cause Mortality and SCD

Over a median follow-up period of 417 days, 459 (14.2%) patients died with 109 (23.7%) of all deaths attributed to SCDs. SCDs comprised of 30.1% of all deaths among ICD nonrecipients and 16.7% of all deaths among ICD recipients. After multivariable adjustment, ICD (versus non-ICD) implantation was

Table 2. Baseline Patient Characteristics for ICD Recipients and Nonrecipients

Characteristics	Total (n=3240)	ICD Nonrecipients (n=2851)	ICD Recipients (n=389)
Age, y	58.9±12.9	58.3±13.0	62.9±11.3
Men	2562 (79.1)	2237 (78.5)	325 (83.5)
Race/ethnicity			
Chinese	821 (25.4)	727 (25.5)	94 (24.2)
Indian	1165 (36.0)	1091 (38.3)	74 (19.0)
Japanese	305 (9.4)	146 (5.1)	159 (40.9)
Korean	159 (4.9)	145 (5.1)	14 (3.6)
Malay	564 (17.4)	540 (19.0)	24 (6.2)
Thai	117 (3.6)	99 (3.5)	18 (4.6)
Others (eg, Filipino, indigenous Southeast Asians)	106 (3.3)	100 (3.5)	6 (1.5)
Highest educational level*			
Primary and below	858 (30.9)	801 (32.7)	57 (17.2)
Secondary	1004 (36.1)	895 (36.6)	109 (32.8)
Preuniversity	360 (12.9)	310 (12.7)	50 (15.1)
Tertiary	558 (20.1)	442 (18.1)	116 (34.9)
Current or former smoker	1459 (45.1)	1264 (44.4)	195 (50.1)
Current or former alcohol user	926 (28.6)	768 (27.0)	158 (40.6)
Body mass index, kg/m^2	24.9±5.2	25.0±5.2	24.2±4.9
Ischemic heart disease	1926 (59.5)	1714 (60.1)	212 (54.5)
Baseline NYHA functional class			
I or II	2119 (65.4)	1870 (65.6)	249 (64.0)
III	1121 (34.6)	981 (34.4)	140 (36.0)
Baseline LVEF, %	25.5±6.2	25.6±6.1	25.0±6.6
Baseline heart rate, bpm	79.6±15.3	80.4±15.4	73.6±13.2
Systolic blood pressure, mm Hg	117.1±19.1	118.0±19.2	110.2±17.2
Comorbidities			
Atrial fibrillation	493 (15.2)	377 (13.2)	116 (29.8)
Cerebrovascular disease	204 (6.3)	168 (5.9)	36 (9.3)
Chronic kidney disease†‡	1090 (43.2)	921 (42.3)	169 (49.0)
Diabetes mellitus	1312 (40.5)	1162 (40.8)	150 (38.6)
Hypertension	1618 (50.0)	1442 (50.6)	176 (45.2)
Liver disease	102 (3.1)	87 (3.1)	15 (3.9)
Peripheral vascular disease	103 (3.2)	91 (3.2)	12 (3.1)
Pulmonary disease	239 (7.4)	197 (6.9)	42 (10.8)
Modified CCI Score			
<3	2713 (84.0)	2407 (84.7)	306 (78.7)
≥3	517 (16.0)	434 (15.3)	83 (21.3)
Household income grouping§			
<1000 USD/mo	1594 (64.7)	1500 (68.1)	94 (36.2)
2000–3000 USD/mo	556 (22.6)	466 (21.2)	90 (34.6)
>3000 USD/mo	313 (12.7)	237 (10.8)	76 (29.2)

CCI indicates Charlson Comorbidity Index; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; and NYHA, New York Heart Association.

*Four hundred sixty patients (14.2%) did not have educational level recorded.

†Seven hundred eighteen patients (22.2%) did not have baseline creatinine values recorded.

‡Chronic kidney disease was defined as an estimated glomerular filtration rate of 60 mL·kg·1.73 m^2 and below, calculated using the Modification of Diet in Renal Disease formula.

§Seven hundred seventy-seven patients (24.0%) did not have household income recorded.

associated with lower hazard ratio for all-cause mortality of 0.71 (95% confidence interval, 0.52–0.97) and lower subhazard ratio for SCDs of 0.34 (95% confidence interval, 0.14–0.82).

Discussion

These first prospective multinational data on ICD utilization among patients with HFrEF across Asia revealed 4 key findings: First, overall primary prevention ICD utilization in Asia was low with significant heterogeneity across Asian regions. Second, higher ICD utilization was directly related to higher socio and national economic status, presumably reflecting in part, the cost burden of ICD devices. Third, lack of knowledge about device therapy was a barrier to patients' acceptance of ICD implantation, underscoring the need for better patient education. Finally, ICD implantation was found to be associated with reduced risks of both all-cause mortality and SCDs.

Our Asian ICD recipients had a 29% reduced risk of death from any cause. Although the confidence interval was wide, the effect size was comparable to prior landmark trials which saw a 23% to 31% reduction in mortality.[4,5] Improving the accessibility of ICDs; as a lifesaving device, is therefore of

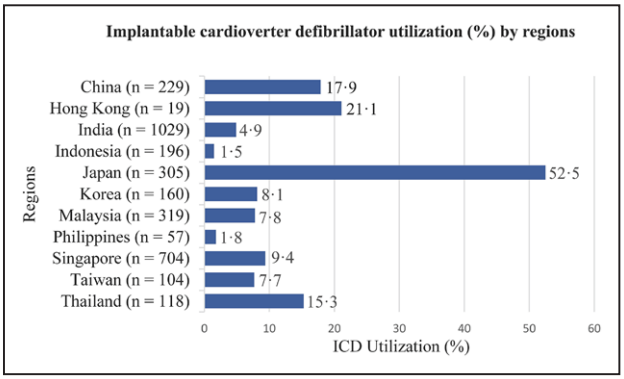

Figure 3. Implantable cardioverter defibrillator (ICD) utilization (%) by regions, grouped according to the region's stage of economic development.

Table 3. Factors Associated With ICD Utilization Among Eligible Patients With Heart Failure

Characteristics	Unadjusted Odds Ratio (95% Confidence Interval)	*P* Value	Adjusted* Odds Ratio† (95% Confidence Interval)	*P* Value
Age, per 10-y increase	1.29 (1.19–1.41)	<0.001	1.37 (1.22–1.55)	<0.001
Gender, male vs female	1.39 (1.05–1.85)	0.021	1.12 (0.76–1.65)	0.584
Highest educational level				
Primary and below	1.0 (ref)		1.0 (ref)	
Secondary	1.71 (1.23–2.39)	<0.001	2.08 (1.42–3.04)	<0.001
Preuniversity	2.27 (1.52–3.39)		2.53 (1.59–4.01)	
Tertiary	3.69 (2.63–5.17)		5.46 (3.64–8.18)	
Current or former smoker	1.26 (1.02–1.56)	0.033	0.95 (0.69–1.32)	0.768
Current or former alcohol user	1.85 (1.49–2.31)	<0.001	1.67 (1.21–2.29)	0.002
Body mass index, kg/m^2	0.97 (0.95–0.99)	0.007	1.01 (0.98–1.04)	0.431
NYHA class, III vs I or II	1.07 (0.86–1.34)	0.539	1.28 (0.96–1.70)	0.089
Baseline LVEF, %	0.99 (0.97–1.00)	0.081	1.00 (0.98–1.02)	0.881
Baseline heart rate, bpm	0.97 (0.96–0.97)	<0.001	0.96 (0.95–0.97)	<0.001
Baseline SBP, mm Hg	0.98 (0.97–0.98)	<0.001	0.98 (0.97–0.99)	<0.001
Atrial fibrillation	2.79 (2.19–3.55)	<0.001	1.54 (1.11–2.12)	0.009
Diabetes mellitus	0.91 (0.73–1.13)	0.405		
Hypertension	0.81 (0.65–1.00)	0.046	0.62 (0.46–0.84)	0.002
Ischemic heart disease	0.79 (0.64–0.98)	0.034	0.66 (0.49–0.89)	0.007
Modified CCI, ≥3 vs <3	1.50 (1.16–1.96)	0.002	1.56 (1.08–2.26)	0.017
Stage of economic development				
Low	1.0 (ref)		1.0 (ref)	
Middle	3.28 (2.30–4.69)	<0.001	3.70 (2.43–5.61)	<0.001
High	5.48 (4.04–7.44)		6.52 (4.43–9.60)	

CCI indicates Charlson Comorbidity Index; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; and SBP, systolic blood pressure.

*Adjusted for age, sex, education, smoking or alcohol status, body mass index, NYHA class, LVEF, heart rate, systolic blood pressure, atrial fibrillation, hypertension, ischemic heart disease, modified CCI, and stage of economic development.

†Two thousand six hundred fifty-six patients (82.0%) were included in the final analysis.

paramount importance in HFrEF patients especially because the syndrome is more deadly than cancer.[22]

Underutilization of ICD Within Asia

ICD utilization varies from 24% in Europe[23] to 30% to 50% in USA,[24–27] with the majority of patients at risk of SCD not receiving this device. The recent PARADIGM-HF Trial (Prospective Comparison of ARNI [Angiotensin Receptor-Neprilysin Inhibitor] with ACEI [Angiotensin-Converting-Enzyme Inhibitor] to Determine Impact on Global Mortality and Morbidity in Heart Failure) too affirmed the low utilization with fewer than 15% of their study cohort having an ICD implanted.[28] Our study showed that average ICD utilization is lowest in Asia with only 12% of eligible patients receiving the device. Furthermore, utilization across Asia ranged greatly from 1.5% in Indonesia to 52.5% in Japan. To improve the uptake of this lifesaving device among Asian patients with HF, there is a need to understand the barriers to ICD utilization that can exist at 3 key levels—the government/economy, the healthcare provider, and the patient.

Barriers at the Government Level and Differences in Healthcare Systems in Asia

Reimbursement for Device Therapy

Primary prevention ICD therapy has borderline cost-effectiveness in Western countries[29] and unknown cost-effectiveness in Asian countries. This leads to less motivation from healthcare policymakers, particularly those from developing countries, to provide reimbursements. Against the backdrop of rapid socioeconomic and epidemiological transitions in Asia, policymakers have to grapple with public health challenges, in the areas of control of emerging infectious diseases and the rise of chronic diseases.[30] Within Asia, patients in low to middle income countries thus receive minimal to no reimbursement for ICD therapy and reimbursement, where available, is restricted to secondary prevention implantations.[10,11,31]

Healthcare Financing System

In Asia, the healthcare topography in terms of government health expenditure, availability of universal health insurance coverage and reliance on private payment varies greatly, contributing to the disparity in ICD utilization across geographical regions. OOP expenses tend to be higher in low-income regions such as Indonesia (46.9%), Philippines (53.7%), and India (62.4%);[32,33] where we found the lowest ICD uptake rates. Greater reliance on private payment perpetuates an inequitable access to healthcare and the use of expensive therapy could lead to a catastrophic expenditure, pushing families into poverty.[34] In contrast, the low OOP healthcare expenses, high government health expenditure and implementation of universal health coverage insurance are likely to be important contributors to the disproportionately high utilization in Japan.

Barriers at the Healthcare Provider Level

Physicians' Awareness on ICD Indications and Referral Rates

A significant proportion of our patients were unaware of the benefits (32.6%) and lacked information to make a decision (22.1%) on device therapy. Although we did not examine whether an ICD discussion occurred between patients and their healthcare provider, however, previous studies have suggested that physicians' awareness on the indications for ICD therapy is low.[35,36] This leads to low referral rates for ICD implantation which has been noted to be an important barrier to ICD utilization.[23,36,37]

Uncertainty About ICD Benefit for Asian Patients With HF

The low ICD utilization in Asia could also be attributed to less enthusiastic recommendations by physicians. Asians tend to rely on their physicians for health information and are more accepting of ICD therapy if their physician strongly recommends it.[38] However, as mentioned earlier, there has been controversy about SCD risks and benefits of ICD insertion for Asian patients with HFrEF.[7,8,39] Given the high cost of device therapy and suggested lower crude incidence of SCD in Asia as compared with the West,[40] physicians might be more reserved in applying Western-derived guidelines to an Asian cohort of patients with HFrEF.

Barriers at the Patient Level

Clinical Factors

Advanced age and greater comorbidity burden were not barriers to ICD implantation. In fact, ICD recipients were older and had a greater comorbidity burden compared with nonrecipients. Of note, the mean age of our older Asian ICD recipients (63 years) was comparable to the younger Western ICD recipients (61 to 67 years) reported,[41,42] emphasizing the growing concern that HF afflicts Asians at a younger age than their Western counterparts.[13,43] A high proportion (79.1%) of ICD-eligible patients were male, and among ICD recipients, an even higher proportion (83.5%) were male. There are 2 explanations for the male preponderance (1) a higher proportion of men (78.2%) were recruited in the ASIAN-HF registry[13] and (2) sex disparities in ICD eligibility and utilization may exist. Indeed, male sex was a univariable predictor of ICD utilization among eligible patients, although this was not seen after multivariable adjustment.

Socioeconomic Status and Health Literacy

Our patients with tertiary education were 5.5× more likely to receive an ICD as compared with patients with primary or lower level education, reflecting the importance of health literacy as a determinant of ICD implantation. More educated patients were likely to have a better understanding of the risks versus benefits of an ICD, whereas lack of such understanding may have been a barrier to device uptake among less educated patients.[44] Educational status may also be a surrogate measure for individual socioeconomic status, and the financial burden of ICDs is further emphasized by the fact that 28.8% of our patients cited cost as the main reason for their lack of willingness to receive device therapy.

Lack of Knowledge

A lack of knowledge about the preventive role of ICD was a recurrent theme present among patients' responses to the questionnaire. Among patients not willing to receive device therapy, more than a third either believed the device would be ineffective or stated that they could cope symptomatically without a device. These responses suggest that our patients might not understand the preventive role of defibrillator devices in reducing SCDs[38] or might think their SCD risk is low because of a lack of overt HF symptoms.[44]

Strengths and Limitations

Our study provides novel insight into the ICD utilization and associations of uptake among eligible Asian patients with HF. As a multinational study, it allowed for comparisons across Asia and exploratory analyses of how healthcare systems may influence ICD implantations. By introducing a semiqualitative dimension to our study design, we could appreciate the barriers to device therapy from the patient's perspective. However, this study has a few limitations. First, we assumed all ICDs were implanted for primary prevention. Second, selection bias is present because utilization was based on registry data. However, a comparison of the educational status of our patients (mean age, 58.9 years) with the national average for population aged 55 to 59 years shows that a higher proportion of our patients received secondary or tertiary education. Hence, we think our study participants, compared with the general population, had better health literacy with greater access to specialized cardiology care and ICD implantation; overestimating the utilization within each region. Third, we acknowledge that the effect of ICD on mortality is likely to be influenced by selection bias that may not be completely addressed by statistical adjustment.

Implications and Future Research

Our study highlights the low ICD utilization in Asia and emphasizes the fact that cost and lack of patient/physician education on ICD therapy are key barriers to its uptake. Given that HF afflicts Asians more than a decade earlier than their Western counterparts,[13] ICD implantation for primary prevention of SCD is an urgent unmet need to improve survival among these young Asian patients with HF. Multicenter randomized trials in Asia are thus necessary to determine

Table 4. Patient's Perception Toward Device Therapy for Heart Failure

Question	Responses	No. of Patients (%)
Do you believe this therapy would be beneficial to you by helping to improve your quality of life and survival? (n=2000)	Yes	894 (44.7)
	No	454 (22.7)
	I don't know	652 (32.6)
Are you willing to receive device therapy? (n=2000)	Yes	659 (33.0)
	No	897 (44.9)
	I want to know more	442 (22.1)
	Others	2 (0.1)
If you are unwilling or would want to know more about device therapy, what is the main reason that you are not willing or uncertain about receiving device therapy? (n=1339)	Cost	385 (28.8)
	Can cope with symptoms	325 (24.3)
	Do not believe the device would be effective	187 (14.0)
	Uncertain about benefits of device	62 (4.6)
	Personally experienced or heard negative reviews about device therapy	56 (4.2)
	Fear for complications	19 (1.4)
	Prefer not to use devices	7 (0.5)
	Told not suitable for device	4 (0.3)
	Others	6 (0.4)
	Declined to respond	288 (21.5)
If you are willing to receive device therapy, what do you think health professionals could do to help patients better in making informed treatment choices? (n=659)	Would like more information about devices from a physician	51 (7.7)
	Would like more information about devices from any healthcare professional	50 (7.6)
	Satisfied with current care	23 (3.5)
	Already planning for a device	8 (1.2)
	Financial assistance	4 (0.6)
	Not sure	12 (1.8)
	Others	52 (7.9)
	Declined to respond	459 (69.7)

the efficacy and cost-effectiveness of primary prevention ICD implantations, which would then provide the necessary framework for decision-making on reimbursement by health policy makers. Further research into qualitative factors influencing device therapy acceptance among both Asian patients and physicians is also warranted to increase the utilization of ICDs.

Conclusions

This first prospective multinational data on ICD utilization among patients with HFrEF across Asia suggests that ICD reduces mortality and there is a myriad of complex factors influencing the low and heterogeneous utilization within Asia. The financial burden of ICD therapy is an important deterrent to uptake which could potentially be addressed with reforms in healthcare policy, to extend reimbursement coverage for the devices as well as the adoption of more innovative medical insurance policies. Importantly, targeted educational efforts are also warranted to improve both physicians' and patients' understanding of the preventive role of ICDs as lifesaving devices, particularly in enabling patients to make an informed decision about its usage.

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Disparity Between Indications for and Utilization of Implantable Cardioverter Defibrillators in Asian Patients With Heart Failure

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