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Shortened Title:

Clinical Factors Associated with Atrial Fibrillation and Subsequent Clinical Outcomes Following Implantable Cardioverter-Defibrillator Placement

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Conflicts of Interest

Dr. Ho has received fellowship support from Medtronic, Boston Scientific, Abbott, and Biotronik, owns equity in Vektor Medical Inc, and has received research grants from American Heart Association (AHA 19CDA34760021), National Institutes of Health (NIH 1KL2TR001444), and Abbott.

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All other authors have no relevant disclosures to report.

Abstract

Background:

Atrial fibrillation (AF) is frequently present in patients with heart failure (HF) and an implantable cardioverter-defibrillator (ICD). This study aims to identify clinical factors associated with a baseline history of AF in ICD recipients, and compare subsequent clinical outcomes in those with and without a baseline history of AF.

Methods:

We studied 566 consecutive first-time ICD recipients at an academic center between 2011-2018. Logistic regression multivariable analyses were used to identify clinical factors associated with a baseline history of AF at the time of ICD implant. Cox-proportional hazard regression models were constructed for multivariate analysis to examine associations between a baseline history of AF with subsequent clinical outcomes, including ICD therapies, HF readmission, and all-cause mortality.

Results:

Of all patients, 201 (36%) had a baseline history of AF at the time of ICD implant. In multivariate analyses, clinical factors associated with a baseline history of AF included hypertension, valvular heart disease, body weight, PR interval, and serum creatinine level. After multivariate adjustment for potential confounders, a baseline history of AF was associated with an increased risk of anti-tachycardia pacing (HR= 1.84,

95% CI= 1.19-2.85, p=0.006), appropriate ICD shocks (HR= 1.80, 95% CI= 1.05-3.09, p=0.032) and inappropriate ICD shocks (HR= 3.72, 95% CI= 1.7-7.77, p=0.0001), but not other adverse outcomes.

Conclusion:

Among first-time ICD recipients, specific clinical characteristics were associated with a baseline history of AF at the time of ICD implant. After adjustment for potential confounders, a baseline history of AF was associated with a higher risk of all ICD therapies in follow-up.

Keywords: Atrial fibrillation, Implantable cardioverter-defibrillator, Heart failure, Inappropriate shock

Abbreviations List:

AF = atrial fibrillation

CHA_2DS_2-VASc = acronym for congestive heart failure, hypertension, age, diabetes, stroke, vascular disease, sex

CI = confidence interval

CRT-D = cardiac resynchronization therapy defibrillator

DOAC = direct oral anticoagulant

ECG = electrocardiogram

HF = heart failure

HR= hazard ratio

ICD = implantable cardioverter defibrillator

NCDR= national cardiovascular data registry

NYHA= New York Heart Association

1. Introduction

Implantable cardioverter-defibrillators (ICDs) are guideline-recommended therapy for the prevention of sudden cardiac death in survivors of ventricular arrhythmias and in patients with symptomatic heart failure (HF) with reduced left ventricular ejection fraction (1). Atrial fibrillation (AF) is common in patients with HF and its prevalence increases with severity of NYHA functional class, with prevalence estimates ranging from 10-50% (2, 3). In a patient population implanted with ICDs, the prevalence of AF has been reported to be 35% in one large national registry (4). Previous studies have shown that the presence of AF in patients implanted with an ICD has been variably associated with increased risk of recurrent ventricular arrhythmias, appropriate and inappropriate shocks, heart failure hospitalizations, and mortality (5–8). Many of these studies involved incident AF after initial ICD implant, included patients enrolled in clinical trials, and were conducted around the time of expansion of ICD indications for primary prevention (9). More contemporary studies are lacking.

It is projected that the incidence of AF, HF, and ICD implantation are all expected to grow (10–12). While the characterization and prognostic implications of comorbid AF at the time of ICD implant may become increasingly important, they remain incompletely understood. The present study aims to add to the available evidence by

investigating patients outside of a clinical trial undergoing first-time ICD implantation. We sought to delineate the clinical factors associated with a baseline history of AF versus no history of AF in patients undergoing *de novo* ICD implantation, and compare long-term clinical outcomes among those with and without a baseline history of AF at the time of ICD implantation.

2. Methods

2.1 Patient Population:

Baseline characteristics, procedural data, in-hospital outcomes, and discharge medications were prospectively collected at our institution based upon data definitions from the American College of Cardiology's National Cardiovascular Data Registry (NCDR) ICD registry (13). Additional data not included in the ICD registry were collected retrospectively via review of the electronic medical record. Patient specific data between March 2011 and March 2018 were used for data collection and analysis. Outcomes were recorded by follow-up clinic visits, hospital readmissions, and both in-person and remote ICD interrogations in the medical record. Medical record data was reviewed by study authors SG and MN independently, and further reviewed by SG, MN, and JCH when unclear or discrepancies existed.

All patients undergoing ICD implantation for either primary or secondary prevention between March 1, 2011 through March 30, 2018 at the University of California, San Diego (UCSD) medical center were

evaluated (n=1347). All patients considered for primary prevention ICD were optimized on guideline-directed medical therapy prior to implant. Only patients undergoing first-time ICD implantations were selected (n=566). Those who had previous ICD implants and were undergoing a generator explant or change (n=622), or a lead revision or implant only (n=159) were excluded (n=781). ICD models from various manufacturers, including Biotronik (Berlin, Germany), Boston Scientific (Marlborough, Massachusetts), Medtronic (Minneapolis, Minnesota), and Abbott/St. Jude Medical (Saint Paul, Minnesota), were implanted. Multiple operators performed the ICD implants. Initial device settings were at the discretion of implanting physician.

Patients were considered to have a diagnosis of a baseline history of AF at the time of ICD implant if they had AF documented on any prior 12-lead ECG, or duration greater than 30 seconds on Holter monitor or event monitor. Patients without a baseline history of AF were considered to have a diagnosis of incident AF in follow up if they were found to have new AF on a 12-lead ECG, duration greater than 30 seconds on Holter monitor or event monitor, or AF based on device interrogation. AF subtypes (paroxysmal, persistent, permanent) were classified by consensus guideline definitions (14).

2.2 *Statistical Analyses*:

For the analyses of clinical factors associated with a baseline history of AF, the primary outcome of interest was a baseline history of

AF at any point versus no previous history of AF. In-hospital outcomes were prospectively collected based upon data definitions from the NCDR ICD registry, and included time from implant to discharge (i.e. length of hospital stay), any procedural complication (including cardiac arrest, MI, cardiac perforation, coronary venous dissection, cardiac tamponade, stroke, TIA, hematoma, infection requiring antibiotics, hemothorax, pneumothorax, urgent cardiac surgery, venous obstruction, conduction block, peripheral emboli, valve injury, set screw problem, and lead dislodgement), and in-hospital mortality.

For the analyses of the association between a baseline history of AF and subsequent clinical outcomes, long-term clinical outcomes of interest included anti-tachycardia pacing (ATP) therapy, appropriate and inappropriate shocks, HF readmission, and all-cause mortality. Outcomes were reviewed and adjudicated by study authors SG and MN independently. ATP was defined as presence of timed pacing stimulus delivered to interrupt monomorphic ventricular tachycardia (VT). Instances of inappropriate ATP, such as those delivered for atrial tachyarrhythmia, were excluded when possible to identify. Appropriate shocks were defined as those delivered for ventricular tachyarrhythmia with a rate in a programmed therapy zone, that successfully terminated the arrhythmia. Inappropriate shocks were defined as shocks delivered for anything other than true ventricular arrhythmias. Distinguishing between appropriate versus inappropriate ICD therapies

was at times limited in patients whom had received a single chamber or subcutaneous ICD. HF readmission was defined as hospital readmission any time following ICD implantation where the primary diagnosis was acute decompensated heart failure. All-cause mortality was defined as death due to any cause.

Categorical variables were compared by chi-squared tests and reported as simple proportions and percentages. Normally-distributed continuous variables were compared by unpaired t-tests and reported as the mean and one standard deviation. To identify clinical factors associated with a baseline history of AF in patients undergoing ICD implantation, multivariable logistic regression models were constructed using the backwards stepwise elimination method to identify statistically significant clinical factors (p value for entry = 0.20, p value for retention = 0.05). Due to their potential association with a baseline history of AF all covariates in **Table 1,** with the exception of medications at discharge, were considered in this model. Multivariable logistic regression models were also used to identify clinical factors associated with incident AF in follow up.

To evaluate the association between a baseline history of AF versus no history of AF with subsequent clinical outcomes, time-to-event analyses with Kaplan-Meier curves were constructed for univariate analysis and evaluated with log-rank p values. Cox-proportional hazard regression models were constructed for

multivariate analysis, adjusting for selected important covariates (age, sex, serum creatinine, left ventricle ejection fraction, QRS duration, CRT, NYHA functional class, and use of beta blocker) that could be possible confounders. To determine which covariates to include for adjustment in the final multivariate model, a group of possible confounders were specified a priori and included for face validity. Other possible confounders were generated using a directed acyclic graph, which was constructed from general clinical knowledge and data from prior studies (8).

To examine any effect of widespread device programming changes to extend detection time on the incidence of inappropriate therapies, a sub-analysis was done. Two groups were analyzed separately by univariate and multivariate analyses described previously, before and after January 1st, 2013.

Statistical tests were two-sided and considered significant for any p value <0.05. Analyses were performed using STATA statistical software release 11 (Stata Corp 2010, College Station, TX). The UCSD institutional review board approved analysis of this data for this study.

3. Results

3.1 Baseline characteristics:

A total of 566 consecutive first-time ICD recipients were analyzed, and 36% (n=201) had a baseline history of AF at the time of ICD implant. Of those with a baseline history of AF, 56% (n=112) had

paroxysmal AF, 27% (n=54) had persistent AF, and 17% (n=35) had permanent AF. The mean CHA_2DS_2-VASc score in the AF group was 3.9±1.8. Baseline characteristics, clinical, diagnostic and procedural data, and discharge medications, stratified by a baseline history of AF versus no baseline history of AF, are shown in **Table 1.** Of all patients, 81% (n=460) had heart failure, with an average LV ejection fraction of 34±16%. A primary prevention indication for ICD implantation was present in 74% (n=419) of patients, whereas a secondary prevention indication was present in 26% (n=147).

Table 1 shows clinical variables stratified by a baseline history of AF versus no AF. Patients with a baseline history of AF were more often male, of white or Hispanic ethnicity, of advanced age, and had valvular heart disease, hypertension, chronic kidney disease or concurrent indication for a pacemaker. Patients with a baseline history of AF were also more likely to be discharged on a calcium channel blocker, diuretic, vitamin K antagonist, DOAC, or amiodarone.

3.2 Clinical factors associated with baseline AF:

In multivariable adjusted logistic regression models constructed to evaluate clinical factors associated with a baseline history of AF (**Table 2**), statistically significant clinical factors included body weight (odds ratio [OR]=1.06 per 1 kg increase in body weight, 95% confidence interval [CI]=1.03-1.09, p=0.02), PR interval (OR=1.14 per 10 msec increase in PR interval, 95% CI=1.06-1.22, p=0.001),

hypertension (OR=2.09, 95% CI=1.01-4.31, p=0.046), valvular heart disease (OR=6.19, 95% CI=2.41-15.8, p=<0.001), and serum creatinine level (OR=1.44 per 1 mg/dL increase in serum creatinine, 95% CI=1.03-2.02, p=0.033).

3.3 In-hospital outcomes:

A total of 25 in-hospital complications were observed (**Supplementary Data Table 1**), 10 in the group with a baseline history of AF and 15 in the group without a baseline history of AF (5% versus 4%, p=0.632). There were no significant differences between the two groups in the length of hospital stay or in risks of specific complications (e.g. cardiac arrest, MI, cardiac perforation, coronary venous dissection, cardiac tamponade, stroke, TIA, hematoma, infection requiring antibiotics, hemothorax, pneumothorax, urgent cardiac surgery, venous obstruction, conduction block, peripheral emboli, valve injury, set screw problem, or lead dislodgment). Four patients died during hospitalization for ICD implant, 1 in the group with a baseline history of AF versus 3 in the group with no history of AF (<1% versus 1%, p=0.659). None of these deaths were associated with the ICD implant procedure.

3.4 *Incident AF:*

Of those without a baseline history of AF (n=365), 49 (13%) patients developed incident AF in follow up. Multivariable adjusted

logistic regression models found no statistically significant clinical factors associated with incident AF.

3.5 Long-term outcomes:

Long-term clinical outcomes included ICD therapies, HF readmission, and mortality. Median follow-up was 469 (interquartile range 47-1223) days. A total of 112 patients (20% of all patients) received ATP therapy during follow-up. Fifty of 201 (25%) patients with a baseline history of AF received ATP therapy compared to 62 of 365 (17%) patients without AF (p=0.035) (**Fig. 1a**). After multivariate adjustment for potential confounders, a baseline history of AF was associated with a higher risk of ATP therapy (adjusted HR=1.84, 95% CI= 1.19-2.85, p=0.006). Long-term outcomes are reported in **Table 3**.

A total of 71 patients (13% of all patients) received appropriate shocks during follow-up. Thirty-four of 201 patients (17%) with a baseline history of AF received appropriate shocks compared to 37 of 365 patients (10%) without AF (p=0.050) (**Fig. 1b**). After multivariate adjustment for potential confounders, a baseline history of AF was associated with a higher risk of an appropriate shock (adjusted HR=1.80, 95% CI= 1.05-3.09, p=0.032).

A total of 37 patients (7% of all patients) received inappropriate shocks during follow-up. Twenty of 201 patients (10%) with a baseline history of AF received inappropriate shocks compared to 17 of 365 patients (5%) without AF (p=0.023) (**Fig. 1c**). After multivariate

adjustment for potential confounders, a baseline history of AF was associated with a higher risk of inappropriate shock (adjusted HR= 3.72, 95% CI= 1.78-7.77, p=0.0001). Between 2011-2012, 10 of 54 patients (19%) with a baseline history of AF received inappropriate shocks compared to 5 of 94 patients (5%) without AF (p=0.015). After multivariate adjustment for potential confounders, a baseline history of AF was associated with a higher risk of inappropriate shock in this time period (adjusted HR= 6.47, 95% CI= 1.80-23.21, p=0.004). Between 2013-2018, 10 of 147 patients (7%) with a baseline history of AF received inappropriate shocks compared to 12 of 271 patients (4%) without AF (p=0.394). There were no significant differences in inappropriate shocks between the two groups after multivariate adjustment for potential confounders in this time period (adjusted HR=2.35, 95% CI=0.85-6.50, p=0.101) (**Supplementary Data Table 2)**.

A total of 152 patients (27% of all patients) had at least one hospital readmission with decompensated HF during follow up. Sixty-four of 201 patients (32%) with a baseline history of AF had a HF readmission compared to 88 of 365 patients (24%) without AF (p=0.140) (**Fig. 1d**). There were no significant differences in HF readmissions between the two groups after multivariate adjustment for potential confounders (adjusted HR=1.13, 95% CI=0.78-1.63, p=0.529).

A total of 60 patients (11% of all patients) died during follow-up. Twenty-seven of 201 patients (13%) with a baseline history of AF died compared to 33 of 365 patients (9%) without AF (p=0.325) (**Fig. 1e**). There were no significant differences in all-cause mortality between the two groups after multivariate adjustment for potential confounders (adjusted HR=1.10, 95% CI=0.61-2.00, p=0.738).

4. Discussion

The main findings of our study can be summarized as follows: 1) In our patient population, over one-third of patients had a baseline history of AF at the time of ICD implantation (with over half of these having paroxysmal AF and the remainder with either persistent or permanent AF); 2) Several patient characteristics were associated with a baseline history of AF at the time of ICD implantation, including hypertension, valvular disease, body weight, PR interval, and serum creatinine; and 3) After multivariate adjustment for potential confounders, a baseline history of AF was associated with an increased risk of anti-tachycardia pacing, and both appropriate and inappropriate ICD shocks.

Our study adds to the previous literature in reporting on prevalence of AF, clinical factors associated with a baseline history of AF, and the association of a baseline history of AF with increased risk of ICD therapies in a contemporary real-world ICD patient population outside of a clinical trial. Our Kaplan-Meier curves demonstrate a later

separation over time for anti-tachycardia pacing, appropriate shocks, and heart failure readmissions. This might suggest that the negative impact of AF increases over several years after device implant. Studies such as ours, with a long duration of follow up, are important for determining the true impact of AF on clinical outcomes in patients with ICDs.

The prevalence of AF in our cohort (36%) is comparable to that of other published studies of ICD populations and to that of the general heart failure population (4, 8). This is likely due at least in part to the fact that over 80% of patients in our study had heart failure. In light of this, we suggest that novel rhythm control therapies for AF in patients with HF, such as catheter ablation, atrioventricular node ablation with biventricular pacing, optimized CRT pacing (e.g. AdaptivCRT™, Medtronic, Inc., Minneapolis, MN), and atrial anti-tachycardia pacing algorithms (e.g. Reactive ATP™, Medtronic, Inc., Minneapolis, MN), may become increasingly important in the future to reduce AF burden and improve clinically meaningful outcomes (15–17).

Our findings are consistent with known risk factors for AF previously reported in the literature, including hypertension, valvular disease, and obesity (14). Previous studies have shown that predictors of incident AF in patients with HF include hypertension, renal impairment, and left atrial volume (18, 19). Our study is unique in that we analyzed clinical factors associated with a baseline history of AF

rather than incident AF in patients implanted with ICDs, which may capture a broader patient population from which to apply our findings. Predictors and risk factors of AF are important, as the presence AF has prognostic implications in this population. Zareba et al. showed that both a baseline history of AF and incident AF in patients with ICD were associated with an increased risk of combined endpoint of HF hospitalization or death and mortality, respectively (6). Our contemporary data show the importance of AF in modern day clinical practice.

Atrial fibrillation with rapid ventricular response is a known cause of inappropriate shocks, along with other supraventricular tachycardias. In comparison to previous studies, the proportions of patients receiving inappropriate shocks (7%) and any ICD shock (19%) were lower in our study overall (20). A possible explanation for this difference is the lack of structured follow-up in our study, perhaps leading to underestimation of true event rates.

Prior studies have reported on the association between AF and increased risk of both appropriate ICD therapies and inappropriate shocks in patients implanted with ICDs. Both Rienstra et al. and Borleffs et al. reported that permanent AF, but not paroxysmal or persistent AF, was associated with twice the risk of appropriate therapies compared to those without AF (7,8). Our study by comparison, in which half of all AF patients had paroxysmal subtype,

found that all-type AF was associated with appropriate therapies. In a secondary analysis of the Multicenter Automatic Defibrillator Implantation Trial (MADIT) II cohort, Daubert et al. found that 11.5% of ICD patients received inappropriate shocks, accounting for 31.2% of total shock episodes in a cohort of primary prevention patients receiving first-time ICDs (21). AF was the most common reason (44%) for inappropriate shocks and was found to be a predictor (HR 2.90, 95% CI 1.65-5.09, p=<0.01) in that study. Borleffs et al. found that 15% of all ICD patients received inappropriate shocks and 40% received any ICD shock (8). In subgroup analysis, patients with permanent (HR 2.7, 95% CI 1.7-4.4), persistent (HR 2.5, 95% CI 1.4-4.4), and paroxysmal AF (HR 2.9, 95% CI 1.7-4.8) were all associated with significantly increased risk of inappropriate shocks.

ICD shocks have been associated with decreased quality of life, anxiety, depression, and post-traumatic stress (21). Subgroup analyses from large randomized controlled trials, as well as large prospective studies, have shown that both appropriate and inappropriate shocks are independently associated with increased mortality (21–23). As AF can cause inappropriate shocks, use of rhythm control therapies may be of increased clinical importance in an ICD population. In the Multicenter Automatic Defibrillator Implantation Trial-Reduce Inappropriate Therapy (MADIT-RIT) study, Moss et al. showed that ICD programming with rate settings of 200 bpm or higher, or a prolonged

delay in therapy at rate setting of 170 bpm or higher, was associated with a reduction in inappropriate ICD therapies and all-cause mortality during long-term follow up (24). In our sub-analysis of patients before and after 2013 (following publication of the MADIT-RIT study) a baseline history of AF was associated with a higher risk of inappropriate shock in 2011-2012, but not 2013-2018. These results suggest that widespread adoption of device programming changes to increase detection time may have had an effect on the incidence of inappropriate therapies in our cohort. In patients with a baseline history of AF implanted with ICDs, these settings should be strongly considered.

Limitations:

This was a non-randomized observational study at a University Hospital. Given the observational design, only associations can be drawn, and we cannot exclude the possibility that residual confounding explains our results. Our University Hospital population may also not be representative of the general population of patients undergoing ICD implantation, and thus our results may not be fully generalizable to all populations of patients undergoing ICD implantation. Furthermore, this study was limited to a small sample size, which may have resulted in a lack of power to detect true associations. The decreased statistical power explains why logistic regression and Cox proportional hazard regression analysis showed wide confidence intervals. In the presence

of single chamber devices (n=118), adjudication of appropriate and inappropriate therapies was imperfect, given the absence of atrial electrocardiography. The lack of structured follow-up in our study may have led to underestimation of true event rates. Lastly, ICD settings in patients included in this study were non-standardized, and providers performed adjustments as clinically indicated during follow up.

5. Conclusions

Our study demonstrates that among first-time ICD recipients, specific clinical characteristics including hypertension, valvular heart disease, body weight, PR interval, and serum creatinine were associated with a baseline history of AF at the time of ICD implant. After adjustment for potential confounders, a baseline history of AF was associated with a higher risk of anti-tachycardia pacing, appropriate and inappropriate ICD shocks in follow-up. Clinicians should be aware of the increased risk of both appropriate therapies and inappropriate ICD shocks in patients with a baseline history of AF and the potential harm of such occurrences. The use of rhythm control therapies for AF may be of increased clinical importance in an ICD population and ICD device settings should be optimized when possible to prevent inappropriate shocks.

Tables:

Table 1. Baseline characteristics of all first-time ICD recipients stratified by a baseline history of atrial fibrillation versus no history of atrial fibrillation at the time of implant.

Table 2. Statistically significant clinical factors associated with a baseline history of atrial fibrillation in ICD patients at the time of implant after multivariate adjustment.

Table 3. Event rates for clinical outcomes in follow-up in patients with and without a baseline history of atrial fibrillation.

Supplementary Data Table 1. In-hospital outcomes after ICD implantation stratified by a baseline history of atrial fibrillation versus no baseline history of atrial fibrillation.

Supplementary Data Table 2. Sub-analysis of inappropriate shocks in follow up
in patients with and without a baseline history of atrial fibrillation.

Table 1. Baseline characteristics of all first-time ICD recipients stratified by a baseline history of atrial fibrillation versus no history of atrial fibrillation at the time of implant.

	Baseline AF n=201	**No AF n=365**	**P value**
Age (years)	67.7 ± 13.2	59.3 ± 15.1	<0.001*
Height (cm)	173.6 ± 11.8	169.7 ± 12.2	<0.001*
Weight (kg)	85.3 ± 23.2	82.1 ± 22.4	.113
Body mass index	28.1 ± 6.3	28.2 ± 6.5	0.827
Male Gender	159 (79%)	232 (64%)	<0.001*
Ethnicity			
White	120 (60%)	171 (47%)	0.013*
Black	16 (8%)	33 (9%)	0.842
Hispanic	47 (23%)	128 (35%)	0.012*
Asian	10 (5%)	17 (5%)	0.925
American Indian	1 (1%)	1 (<1%)	0.855
Native Hawaiian/PI	1 (1%)	1 (<1%)	0.855
Heart Failure	168 (84%)	292 (80%)	0.296
Ejection Fraction	33.1 ± 13.9	35.1 ± 16.7	0.138
NYHA			
Class I	36 (18%)	68 (19%)	0.832
Class II	63 (31%)	115 (32%)	0.968
Class III	86 (43%)	157 (43%)	0.958
Class IV	12 (6%)	14 (4%)	0.246
Non-ischemic cardiomyopathy	88 (44%)	167 (46%)	0.652
Ischemic cardiomyopathy	102 (51%)	161 (44%)	0.130

Previous myocardial infarction	63 (31%)	138 (38%)	0.124
Prior PCI	58 (29%)	102 (28%)	0.818
Prior CABG	39 (19%)	54 (15%)	0.157
Coronary artery disease	109 (54%)	171(47%)	0.093
Primary valvular heart disease	43 (21%)	23 (6%)	<0.001*
Syncope	50 (25%)	78 (21%)	0.340
Ventricular Tachycardia	74 (37%)	114 (31%)	0.177
Cardiac arrest	37 (18%)	54 (15%)	0.263
Indication for pacemaker	74 (37%)	50 (14%)	<0.001*
History of CVA	34 (17%)	37 (10%)	0.020*
Chronic lung disease	24 (12%)	35 (10%)	0.381
Diabetes	69 (34%)	132 (36%)	0.662
Hypertension	148 (74%)	224 (61%)	0.003*
CKD (eGFR <60)	76 (38%)	101 (28%)	0.013*
On renal dialysis	7 (3%)	16 (4%)	0.603
History of smoking	96 (48%)	186 (51%)	0.428
Paroxysmal AF	112 (56%)	-	-
Persistent AF	54 (27%)	-	-
Permanent AF	35 (17%)	-	-
CHA_2DS_2-VASc score	3.9 ± 1.8	3.3 ± 1.9	<0.001*
ICD indication			
Primary prevention	140(70%)	279 (76%)	0.078
Secondary prevention	61 (30%)	86 (24%)	0.078
ICD type			
Single chamber or subcutaneo	30 (15%)	88 (24%)	0.010*

	us			
	Dual Chamber	77 (38%)	146 (40%)	0.693
	CRT-D	94 (47%)	131 (36%)	0.011*
Laboratories				
	Hemoglobin	12.7 ± 2.2	12.6 ± 2.0	0.523
	Blood urea nitrogen	26.1 ± 14.3	22.1 ± 11.8	<0.001*
	Serum creatinine	1.40 ± 1.2	1.23 ± 1.2	0.127
ECG characteristics				
	PR	193.9 ± 43.4	176.4 ± 36.8	<0.001*
	QRS duration	124.0 ± 32.5	121.7 ± 32.2	0.446
	QT	440.2 ± 69.5	436.1 ± 53.5	0.440
Systolic blood pressure		125.6 ± 20.7	122.1 ± 19.1	0.043*
Diastolic blood pressure		72.1 ± 14.2	70.4 ± 12.4	0.147
Discharge Medications				
	ACE inhibitor	94 (47%)	198 (54%)	0.080
	ARB	48 (24%)	84 (23%)	0.831
	MRA	48 (24%)	92 (25%)	0.694
	Beta-blocker	172 (86%)	330 (90%)	0.058
	Calcium channel blocker	13 (6%)	10 (3%)	0.032*
	Diuretic	148 (74%)	224 (61%)	0.004*
	Aspirin	125 (62%)	245 (67%)	0.215
	Statin	133 (66%)	227 (62%)	0.370
	VKA	88 (44%)	39 (11%)	<0.001*
	DOAC	60 (30%)	6 (2%)	<0.001*

	Amiodarone	43 (21%)	24 (7%)	<0.001*

*= statistically significant p value of less than or equal to 0.05

ACE, angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass graft; CKD, chronic kidney disease; CRT-D, cardiac resynchronization therapy defibrillator; CVA, cerebrovascular accident; DOAC, direct oral anticoagulant; eGFR, estimated glomerular filtration rate; MRA, mineralocorticoid receptor antagonist; NYHA, new york heart association; PCI, percutaneous coronary intervention; PI, pacific islander; VKA, vitamin K antagonist

Table 2. Statistically significant clinical factors associated with a baseline history of atrial fibrillation in ICD patients at the time of implant after multivariate adjustment.

Variable	Adjusted odds ratio	95% confidence interval	P value
Ejection fraction	0.97*	0.95-1.00	0.011
Dual-chamber ICD	2.11	1.12-3.96	0.02
Weight	1.06†	1.03-1.09	<0.001
Hispanic	0.48	0.24-0.98	0.044
PR interval	1.14‡	1.06-1.22	0.001
Valvular heart disease	6.19	2.41-15.8	<0.001
Hypertension	2.09	1.01-4.31	0.046
Creatinine	1.44§	1.03-2.02	0.033
Previous myocardial infarction	0.40	0.20-0.79	0.008
Body mass index	0.82**	0.74-0.91	<0.001

For quantitative variables odds ratios are expressed as the following:
* per 1% in ejection fraction
† per 1kg in weight
‡ per 10msec in PR interval
§ per 1mg/dL in creatinine
** per 1kg/m^2 in body mass index

Table 3. Event rates for clinical outcomes in follow-up in patients with and without a baseline history of atrial fibrillation.

	Baseline history of AF n=201	No baseline history of AF n=365	HR (95% CI)	P value	Adjusted HR† (95% CI)	P value
ATP	50 (25%)	62 (17%)	1.49 (1.03-2.17)	0.035*	1.84 (1.19-2.85)	0.006*
Appropriate shock	34 (17%)	37 (10%)	1.59 (1.00-2.54)	0.050*	1.80 (1.05-3.09)	0.032*
Inappropriate shock	20 (10%)	17 (5%)	2.12 (1.11-4.05)	0.023*	3.72 (1.78-7.77)	0.0001*
HF readmission	64 (32%)	88 (24%)	1.27 (0.92-1.75)	0.140	1.13 (0.78-1.63)	0.529
All cause mortality	27 (13%)	33 (9%)	1.29 (0.78-2.13)	0.325	1.10 (0.61-2.00)	0.738

*= statistically significant p value of less than or equal to 0.05

† Hazard ration (HR) adjusted for age, sex, renal clearance, ejection fraction, QRS duration, CRT, NYHA, use of beta-blocker

AF, atrial fibrillation; ATP, anti-tachycardia pacing; CI, confidence interval; HF, heart failure; HR, hazard ratio

Supplementary Data Table 1. In-hospital outcomes after ICD implantation stratified by a baseline history of atrial fibrillation versus no baseline history of atrial fibrillation.

Adverse event	Total	AF (n=201)	No AF (n=365)	P value
Length of hospital stay (implant to discharge), days	-	2.2 (4.3)	2.2 (5.3)	0.997
Any complication	25	10 (5%)	15 (4%)	0.632
In-hospital mortality	4	1 (<1%)	3 (<1%)	0.659

AF, atrial fibrillation

Supplementary Data Table 2. Sub-analysis of inappropriate shocks in follow up
in patients with and without a baseline history of atrial fibrillation.

2011-2012	Baseline history of AF n=54	No baseline history of AF n=94	HR (95% CI)	P value	Adjusted HR† (95% CI)	P value
Inappropriate shock	10 (19%)	5 (5%)	3.78 (1.29-11.06)	0.015 *	6.47 (1.80-23.31)	0.004 *
2013-2018	Baseline history of AF n=147	No baseline history of AF n=271	HR (95% CI)	P value	Adjusted HR† (95% CI)	P value
Inappropriate shock	10 (7%)	12 (4%)	1.44 (0.62-3.33)	0.394	2.35 (0.85-6.50)	0.101

*= statistically significant p value of less than or equal to 0.05

† Hazard ration (HR) adjusted for age, sex, renal clearance, ejection fraction, QRS duration, CRT, NYHA, use of beta-blocker

AF, atrial fibrillation; CI, confidence interval; HR, hazard ratio

Figures:

Fig. 1a-e Kaplan-Meier curves for ATP, appropriate shock, inappropriate shock, HF readmission, and all-cause mortality stratified by the presence of baseline atrial fibrillation versus no atrial fibrillation

Fig. 1a

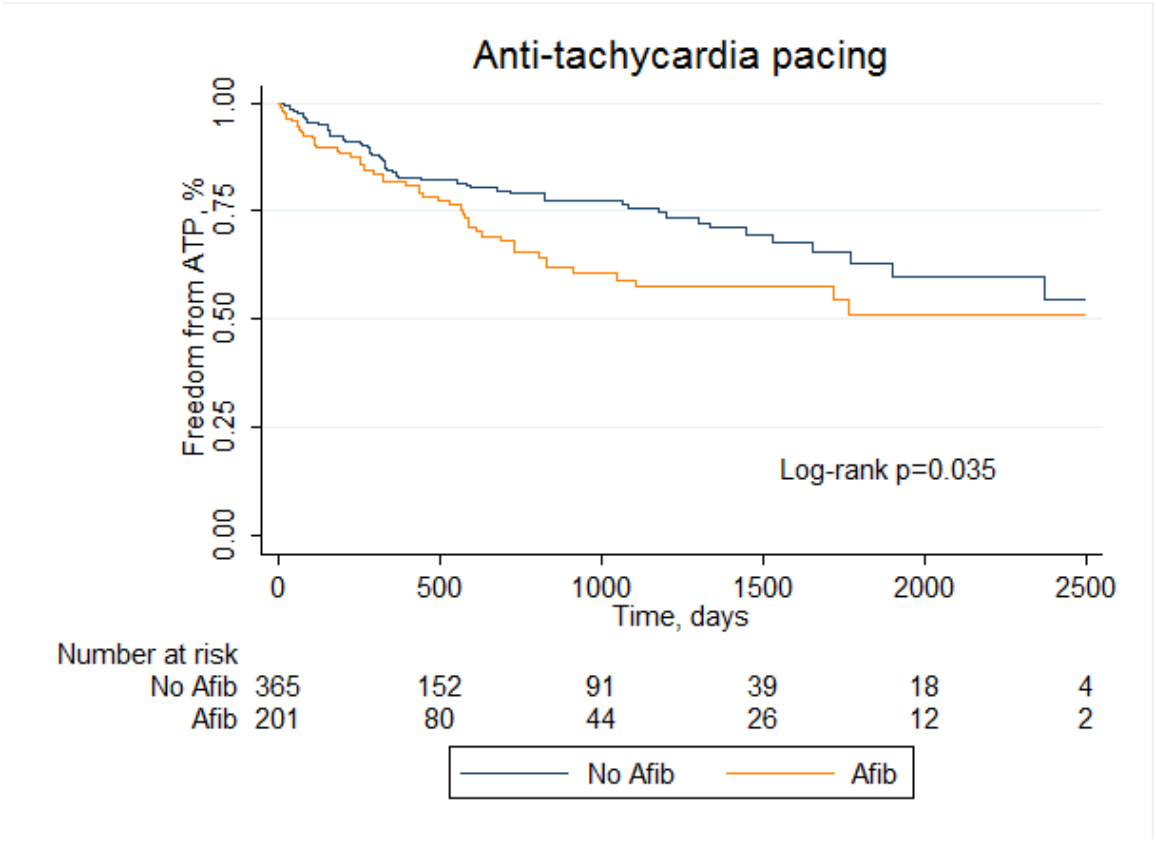

Anti-tachycardia pacing
Freedom from ATP, %
0.00
0.25
0.50
0.75
1.00
Log-rank p=0.035
0
500
1000
1500
2000
2500
Time, days
Number at risk
No Afib 365 152 91 39 18 4
Afib 201 80 44 26 12 2
No Afib
Afib

Fig. 1b

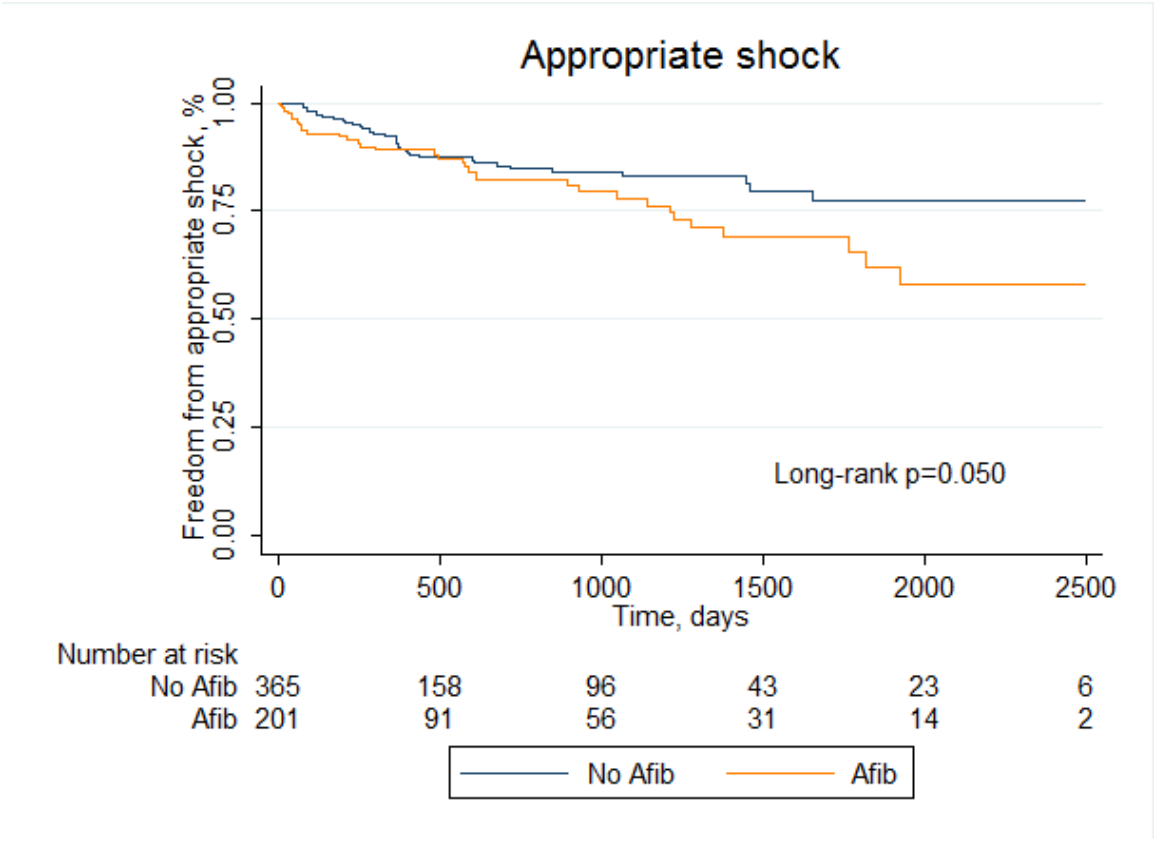

Appropriate shock
Freedom from appropriate shock, %
0.00
0.25
0.50
0.75
1.00
Long-rank p=0.050
0
500
1000
1500
2000
2500
Time, days
Number at risk
No Afib 365 158 96 43 23 6
Afib 201 91 56 31 14 2
No Afib
Afib

Fig. 1c

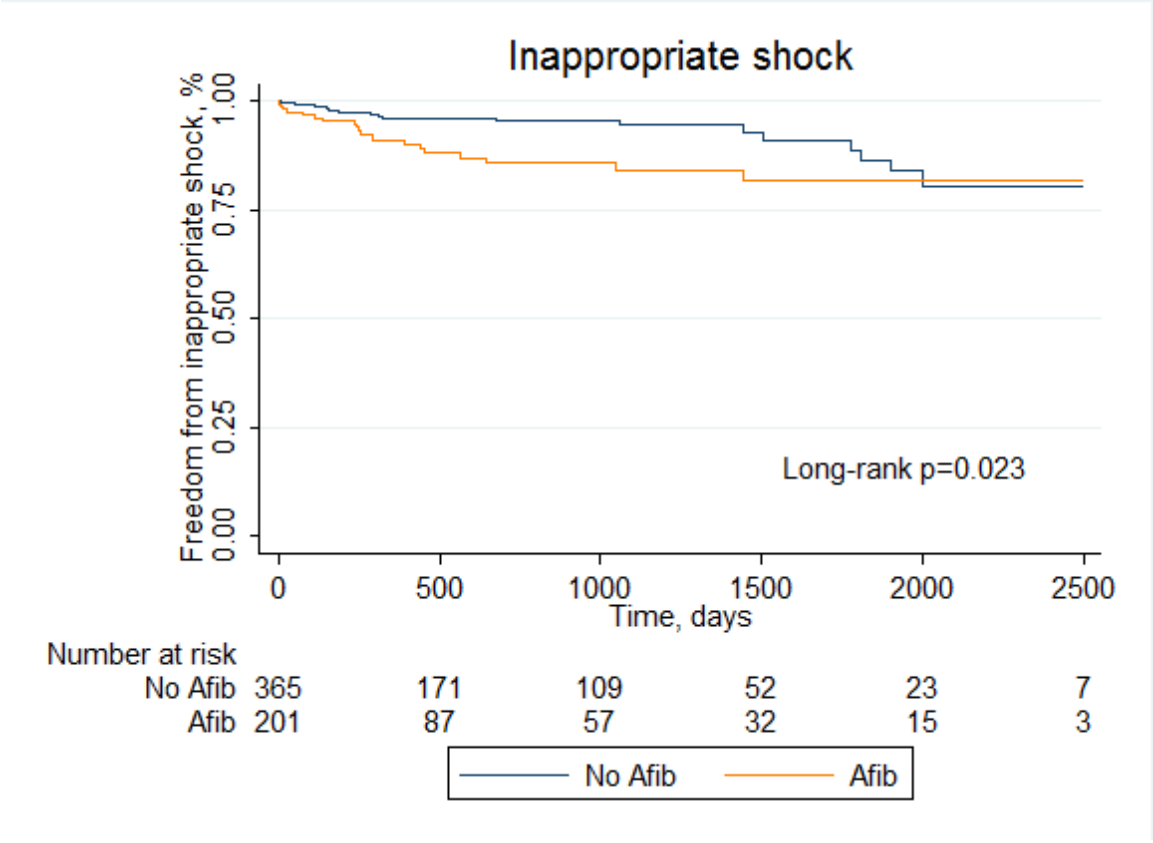

Inappropriate shock
Freedom from inappropriate shock, %
0.00
0.25
0.50
0.75
1.00
Long-rank p=0.023
0
500
1000
1500
2000
2500
Time, days
Number at risk
No Afib 365 171 109 52 23 7
Afib 201 87 57 32 15 3
No Afib
Afib

Fig. 1d

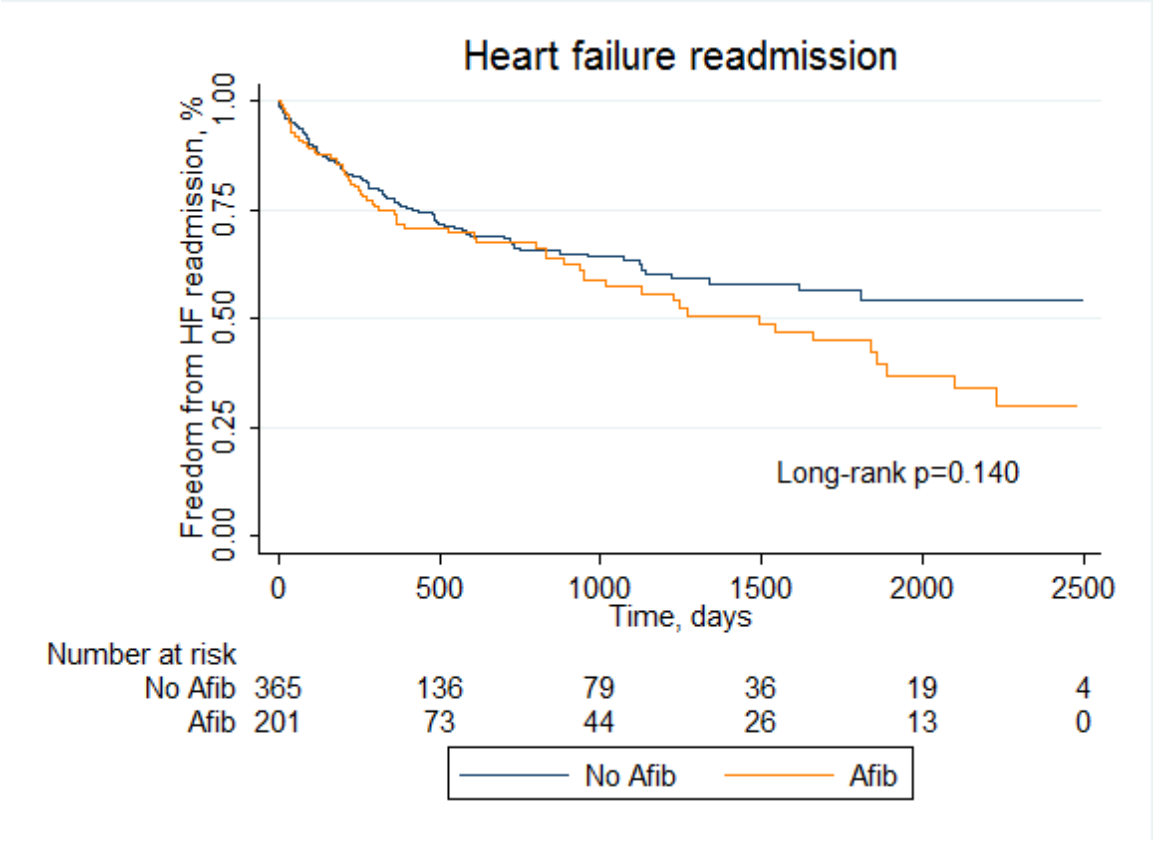
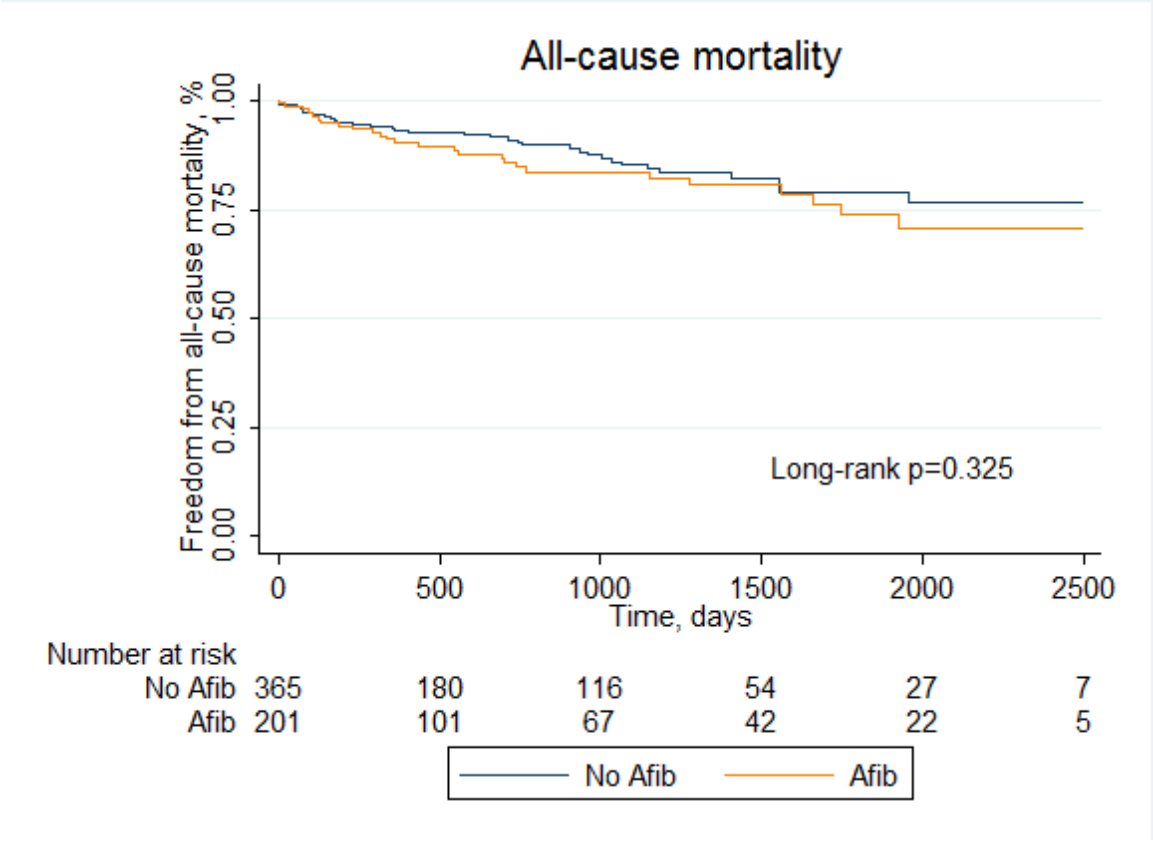

Heart failure readmission
Freedom from HF readmission, %
0.00
0.25
0.50
0.75
1.00
Long-rank p=0.140
0
500
1000
1500
2000
2500
Time, days
Number at risk
No Afib 365 136 79 36 19 4
Afib 201 73 44 26 13 0
No Afib
Afib

Fig. 1e


All-cause mortality
Freedom from all-cause mortality, %
0.00
0.25
0.50
0.75
1.00
Long-rank p=0.325
0
500
1000
1500
2000
2500
Time, days
Number at risk
No Afib 365 180 116 54 27 7
Afib 201 101 67 42 22 5
No Afib
Afib

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