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# Predictors of subcutaneous ICD shocks and prognostic impact in patients with structural heart disease

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**Short title: prognostic impact of subcutaneous ICD shocks**

## **Abstract**

### **Background:**

We aimed to assess long-term outcomes in S-ICD recipients with structural heart disease, especially focusing on shock incidence, predictors and associated prognoses.

### **Methods:**

In this multicenter registry-based study, we retrospectively included all patients who underwent S-ICD implantation in 3 tertiary centers. The prognostic impact of S-ICD shock was assessed with a composite outcome that included all-cause death and hospitalization for heart failure.

### **Results:**

A total of 351 patients with underlying cardiomyopathy were included. In multivariable Fine and Gray regression models, secondary prevention, LVEF, conditional shock threshold, and QRS duration appeared to be independent predictors of appropriate S-ICD shock occurrence. In the multivariate Cox regression model adjusted for age, baseline LVEF, underlying cardiomyopathy subtype, NYHA class and appropriate shocks were significantly associated with increased composite prognostic outcome risk (HR: 2.61, 95% CI: 1.21 to 5.65,  $p=0.014$ ), whereas inappropriate shocks were not (HR: 1.35, 95% CI: 0.75 to 4.48,  $p=0.18$ ). The analysis of each component of the composite prognostic outcome highlighted that the occurrence of appropriate shocks was associated with an increased risk of hospitalization for heart failure (HR: 3.10, 95% CI: 1.26 to 7.58,  $p=0.013$ ) and a trend for mortality (HR: 2.19, 95% CI: 0.78 to 6.16,  $p=0.14$ ).

### **Conclusions:**

Appropriate S-ICD shocks were associated with a 3-fold increase in acute heart failure admission, whereas inappropriate shocks were not. Conditional shock threshold programming is an independent predictor of S-ICD shock, and its prognostic impact should be further investigated in patients with structural heart disease.

*Key words: Subcutaneous ICD; shock; sudden cardiac death; structural heart disease*

## **Summary**

Limited data report long-term outcomes in S-ICD recipients with structural heart disease. This multicenter study provides evidence suggesting that appropriate shock is associated with incident heart failure, whereas inappropriate shock is not. The conditional shock threshold is a strong independent predictor of appropriate shocks. Its prognostic impact should be further investigated.

## INTRODUCTION

Implantable cardioverter defibrillators (ICDs) have become the standard of care for preventing sudden cardiac death in terms of primary and secondary prevention (1). Subcutaneous ICDs (S-ICDs) are an alternative to the conventional transvenous ICD (TV-ICD) system, and they do not need a transvenous lead, thereby avoiding endocardial lead-related complications (2–4). Although initial registries have shown low complication rates and high effectiveness of ventricular tachycardia (VT)/ventricular fibrillation (VF) conversion in patients with a wide range of indications, long-term outcomes in patients with structural heart disease are lacking, especially regarding shock incidence and related mortality (4,5). In the past, patients with TV-ICD shocks have been shown to have increased mortality and incident heart failure in previous studies compared to ICD patients without documented shocks, which has led to device programming guidelines to reduce the incidence of appropriate and inappropriate shocks (6–9). Recent studies suggest that S-ICD shocks do not seem to cause myocardial injury (10). No data regarding prognostic outcomes associated with S-ICD shocks are available despite an important rise of S-ICD implantations. Though clinical characteristics of implanted patients might differ between S-ICD and TV-ICD, the aim of this study was to investigate the incidence, predictors and prognostic impact of S-ICD shocks assessed in a multicenter registry of S-ICD recipients with underlying structural heart disease.

## **METHODS**

### **Study design and definitions.**

In this multicenter registry-based study, we retrospectively included all patients who underwent S-ICD implantation from September 2012 to December 2018 in three tertiary centers (Lille University Hospital, Nancy University Hospital and Nantes University Hospital). The study was approved by the local ethics committee board. Patients with idiopathic ventricular arrhythmia, channelopathy or ventricular arrhythmia related to spastic angina were excluded.

The clinical baseline characteristics at S-ICD implantation were collected for all patients. Secondary prevention was defined as a history of resuscitated cardiac death due to ventricular tachyarrhythmias or sustained monomorphic VT or VF. S-ICD programming parameters were recorded after implantation. The Subcutaneous ICD programming provides for a shock zone where rhythms are analyzed strictly based on heart rate analysis without rhythm discrimination. An optional conditional shock zone also can be programmed. It uses a discrimination algorithm to classify rhythms as either shockable or non-shockable, if they are deemed to be supraventricular arrhythmias. The SMART Pass algorithm, which uses a digital high-pass (9-Hz) filter to avoid cardiac oversensing was activated when available.

Subcutaneous ICD shock occurrence data was collected based on in-hospital emergency appointments, hospitalization, scheduled appointments or remote monitoring follow-up. Shocks were considered appropriate if the triggering rhythm was determined to be ventricular fibrillation or ventricular tachycardia. Inappropriate triggers of ICD shocks included

supraventricular tachycardias; P, R or T wave oversensing lead fracture artifacts; or electromagnetic interference.

The prognostic impact of S-ICD shocks was assessed with a composite outcome that included all-cause death, hospitalization for heart failure. All clinical events were adjudicated by 2 investigators or by 3 investigators in the case of disagreement, according to prespecified definitions.

### **Statistical analysis**

Quantitative variables are expressed as the means (standard deviations) in the case of a normal distribution or medians (interquartile range, IQR) otherwise. Normality of the distributions was assessed using histograms and the Shapiro-Wilk test. Categorical variables are expressed as numbers (percentages). For detailed Statistical Analysis methods, see Supplementary Materials.

Statistical testing was performed at the two-tailed  $\alpha$  level of 0.05. Data were analyzed using the SAS software package, release 9.4 (SAS Institute, Cary, NC).

## **RESULTS**

### **Study population.**

Between September 2012 and December 2018, 456 patients underwent S-ICD implantation in the three tertiary centers. Among these patients, 351 had underlying cardiomyopathy. The study flow chart is shown in Figure 1. The mean ( $\pm$  SD) age was  $44.3 \pm 15.1$  years, 76% of patients were male, 73% underwent implantation for primary prevention and 15.5% had previously received TV-ICD implantation prior to S-ICD implantation (18 TV-ICD infections and 36 lead fractures). The mean LVEF was  $44.8\% \pm 18.6$  (Table S1 in Supplementary Materials). Ischemic, hypertrophic and dilated cardiomyopathy represented 82.9% of all etiologies (33.3%, 28.2% and 21.4%, respectively) (Figure 2). Sixty-three percent of patients had an enabled SMART Pass algorithm, and most patients had a programmed conditional shock threshold  $\geq 200$  bpm (87%).

### **S-ICD shock incidence and characteristics**

After a median follow-up of 28 months (IQR, 21; 41 months), 65 (18.5%) patients received appropriate or inappropriate shocks. A total of 196 S-ICD shocks occurred, with 146 appropriate shocks in 39 patients (11%) and 50 inappropriate shocks in 32 patients (9%). Six patients experienced both appropriate and inappropriate shocks. Seventy-two (49.3%) appropriate shocks were due to monomorphic VT, 54 (37%) to VF and 20 (13.7%) to polymorphic VT (Figure 3A). Among the inappropriate shocks, 21 (38.9%) were due to T-



wave oversensing, 25 (53.7%) were due to artifacts, and 4 (7.4%) were due to supraventricular tachycardia (Figure 3B).

The cumulative incidence of any shock was 12.3% (95% CI: 9.1 to 16.1) at 12 months, 15.5% (95% CI: 11.7 to 19.6) at 24 months, and 21.2% (95% CI: 16.2 to 26.2) at 36 months. The cumulative incidence of appropriate shock was 6.6% (95% CI: 4.3 to 9.6) at 12 months, 8.7% (95% CI: 5.9 to 12.1) at 24 months, and 12.3% (95% CI: 8.5 to 16.8) at 36 months. The cumulative incidence of inappropriate shock was 5.7% (95% CI: 3.6 to 8.6) at 12 months, 7.4% (95% CI: 4.9 to 10.6) at 24 months and 9.4% (95% CI: 6.2 to 13.4) at 36 months (Figure 4).

### **S-ICD shock predictors**

In univariate analysis, the overall S-ICD shock predictors were secondary prevention (HR in the first 12 months of follow-up: 2.52, 95% CI: 1.39 to 4.59,  $p=0.002$ ), LVEF (HR per one SD decrease from 12 month to end of follow-up: 2.05, 95% CI: 1.26 to 3.33,  $p=0.003$ ), a lower conditional shock threshold (for a threshold < 200 bpm HR: 2.44, 95% CI: 1.32 to 4.47,  $p=0.004$ ), previous endocardial ICD (HR: 1.85, 95% CI: 1.04 to 3.28,  $p=0.035$ ), alternate vector programming (HR: 2.27, 95% CI: 1.16 to 4.45,  $p=0.017$ ), SMART Pass not enabled (HR: 2.31, 95% CI: 1.37 to 3.87,  $p=0.002$ ), QRS duration (per one SD increase, HR: 1.40, 95% CI: 1.12 to 1.74,  $p=0.002$ ) and dyslipidemia (HR: 1.73, 95% CI: 1.05 to 2.85,  $p=0.032$ ) (Table S2 in Supplementary Materials).

In multivariate analysis, the independent predictors of overall S-ICD shocks were secondary prevention, LVEF, SMART Pass not enabled, alternate vector programming and dyslipidemia, which remained independently associated with S-ICD shock occurrence (Table 1, Model 1).

In multivariate analysis, the independent predictors of appropriate shocks were LVEF, secondary prevention, conditional shock threshold, and QRS duration (Table 1, Model 2).

For inappropriate shocks, the independent predictors were a history of atrial fibrillation, SMART Pass not enabled, alternate vector programming and hypertension (Table 1, Model 3).

### **Prognostic impact of S-ICD shocks**

The composite prognostic outcome that included all-cause mortality and hospitalization for heart failure occurred in 56 patients (26 deaths, 43 hospitalizations for heart failure). Eleven patients underwent heart transplantation.

In the multivariable Cox regression model that included S-ICD shock as a time-dependent covariate as well as age, LVEF, underlying cardiomyopathy and NYHA class as prespecified confounders, the occurrence of appropriate shocks was significantly associated with an increased risk of the composite prognostic outcome (HR: 2.61, 95% CI: 1.21 to 5.65,  $p=0.014$ ), whereas the occurrence of inappropriate shocks was not (HR: 1.35, 95% CI: 0.75 to 4.48,  $p=0.18$ ). The analysis of each component of the composite prognostic outcome highlighted that the occurrence of appropriate shocks was associated with an increased risk of hospitalization for heart failure (HR: 3.10, 95% CI: 1.26 to 7.58,  $p=0.013$ ) and a trend for mortality (HR: 2.19, 95% CI: 0.78 to 6.16,  $p=0.14$ ). In contrast, inappropriate shocks were not significantly associated with hospitalization for heart failure (HR: 0.78, 95% CI: 0.17 to 3.35,

p=0.73) despite there be an associated trend towards increased mortality (HR: 2.99, 95% CI: 0.98 to 9.09, p=0.053) (Table 2).

### **Impact of S-ICD programming**

Considering the prognostic impact of appropriate S-ICD shocks and the impact of S-ICD programming on S-ICD shocks occurrence, the clinical impact of S-ICD programming was assessed. Ten percent of patients (n=35) had a programmed conditional shock threshold < 200bpm, 46% (n= 163) between 200 and 220 bpm and 41% (n=143)  $\geq$  220bpm. Three percent of patients (n=10) had no conditional shock zone programmed. Eight patients presented a syncope and 1 patient underwent external cardioversion for a slow VT. All these patients had a conditional shock threshold > 200bpm. Among patients who received appropriate shocks for monomorphic VT, 11/24 (46%) had a conditional shock threshold < 200bpm and presented lower VT frequencies than patients with conditional shock threshold  $\geq$  200bpm (195 $\pm$ 16 bpm versus 225 $\pm$ 21 bpm, p<0.0001).

In unadjusted analysis, the conditional shock threshold was associated with an increased risk for the composite prognostic outcome (HR: 2.65, 95% CI: 1.42 to 4.90, p = 0.002), which was mainly driven by an increased risk of mortality (3.88, 95% CI: 1.66 to 9.02, p=0.002). However, after adjustment for LVEF, underlying cardiomyopathy subtype and NYHA class, the conditional shock threshold was no longer associated with the composite prognostic outcome (table 3).

## DISCUSSION

This study provides contemporary data on shock incidence and long-term outcomes related to S-ICD shocks in patients with structural heart disease. In this cohort, we demonstrate that (i) S-ICD shocks are common events with a 3-year cumulative incidence of 21.2% with 9.4% of inappropriate shocks ; (ii) reduced LVEF, secondary prevention, QRS duration and conditional shock threshold programming are independent predictors of appropriate shocks; (iii) atrial fibrillation, alternate vector programming and SMART Pass algorithms that are not enabled are independent predictors of inappropriate shocks; and (iv) appropriate S-ICD shocks are independent predictors of incident heart failure, whereas inappropriate shocks are not.

We first report a cumulative incidence of 12.3% for appropriate shocks and 9.4% for inappropriate shocks at 3 years. This result is consistent with previous S-ICD registries with a cumulative incidence of 11.7% for inappropriate shocks at 3 years as reported by Boersma et al in the EFFORTLESS registry (5) despite a higher rate of structural heart disease in our cohort.

As expected, LVEF and secondary prevention were identified as predictors of appropriate S-ICD shocks, which is consistent with the findings from previous TV-ICD studies (11,12). More surprisingly, we identified the conditional shock threshold as a predictor of appropriate shock. The effect of ICD programming on shock incidence has been well described in TV-ICD. In 2008, Wilkoff et al. demonstrated in the PREPARE trial that delayed therapy programming significantly reduced the incidence of ICD shock with a similar rate of arrhythmic syncope (13). In the analysis from the EFFORTLESS registry, Boersma et al. did not find the conditional shock threshold to be a predictor of shock in S-ICD recipients, unlike our results (5). Of note, EFFORTLESS included a significant proportion of patients without

structural heart disease which may result in a lower incidence of expected “slow” VT. Such discrepancy might be related to that point. In our cohort, S-ICD programming was determined at the discretion of the physician, and it is plausible that a lower conditional shock threshold was programmed in patients with advanced heart failure because of a higher risk of slow VT. However, after adjustment for LVEF and underlying cardiomyopathy, our results demonstrated that the programmed threshold was still an independent predictor of appropriate shock. Interestingly, we found that the conditional shock threshold was associated with total mortality, however, after adjustment for LVEF and NYHA class, this association was no longer found. Taken together, these data question the interest of a low conditional shock threshold (*i.e.*, less than 200 bpm) in patients with advanced heart failure. Controlled trials would thus be of interest to investigate the incidence of syncope and prognosis associated with S-ICD programming.

Although inappropriate shocks in the MADIT-II trial were primarily due to AF or SVT episodes (80%), T-wave or artifact oversensing was the main cause of S-ICD shock in previous registries (5,14). Our findings are consistent with these results and provide data showing the effectiveness of the SMART Pass algorithm for preventing inappropriate shocks. In our study, the use of alternate vector programming was also an independent predictor of inappropriate shock. This result is in line with a subgroup analysis of data from the EFFORTLESS registry describing alternate vector programming as most vulnerable to the occurrence of inappropriate ICD shock (20). Thus, this finding should encourage physicians to avoid alternate vector programming as much as possible.

Previous studies have investigated the prognostic impact of TV-ICD shocks, suggesting its prognostic relevance and accelerating poor outcomes in patients with structural heart disease. Poole et al. found a fivefold increase in ICD shocks and death in SCD-HeFT (6). More recently, MacIntyre et al. demonstrated in a cohort of TV-ICD recipients that a single ICD

shock was associated with a 2-fold increase in the risk of heart failure admissions (15). To our knowledge, no study has evaluated whether this association between the incidence of acute heart failure and ICD shocks exists in patients with an S-ICD. We have found a 2.6-fold increase in the risk of hospitalization for heart failure in patients receiving appropriate S-ICD shock.

In our study, 12% of patients experienced hospitalization for heart failure and the mortality was 7%, which is lower than TV-ICDs cohorts (6). However, in TV-ICD studies, patients displayed a more depressed LVEF at baseline with a higher rate of mortality and incident acute heart failure compared to our population of patients. This point is probably related to the criteria used to implant S-ICDs rather than TV-ICDs (*i.e.*, no need for resynchronization therapy or pacing). Therefore, patients with structural heart disease undergoing S-ICD implantation currently display a lower risk than TV-ICD patients, and the findings of our study should be carefully extrapolated to all patients with structural heart disease.

However, assessing factors related to adverse outcomes in such populations remains of interest for identifying high-risk patients and associated therapeutic strategies. While our data suggest that the occurrence of an appropriate S-ICD shock should warn physicians of the risk for acute heart failure, we also provide data suggesting that inappropriate S-ICD shocks are not associated with such outcomes. This differential effect observed according to the type of shock suggests that appropriate shocks could be the hallmark of advanced heart disease, whereas inappropriate shocks are not. Unlike TV-ICD patients in whom the main cause of inappropriate shocks is represented by supraventricular tachycardia, most of inappropriate shocks in S-ICD patients are T-wave and artifact oversensing. Considering supraventricular tachycardia as a hallmark of advanced heart failure, the deleterious effect of inappropriate therapy observed in TV-ICD patients would thus no longer be considered as a shock-related effect.

Clinical findings related to the deleterious effect of TV-ICD shocks are also supported by histological data reporting myocardial damage induced by intraventricular defibrillation (16,17). Therefore, advanced structural heart disease would be associated with a higher incidence of appropriate shocks, which may, in turn, alter the prognosis of TV-ICD patients. In contrast, S-ICD shocks do not seem to induce myocardial damage. Recently, D'Onofrio et al. investigated troponin release after S-ICD shocks delivered at the time of implantation. Interestingly, no troponin increase was observed, suggesting that subcutaneous defibrillation may not induce myocardial injury (10). The differential effect of endo versus subcutaneous shock on patient prognosis is still unknown but could be different. To address this point, randomized trials are required to assess the prognostic impact of TV-ICDs versus S-ICDs in patients with advanced heart failure.

### **Study limitations**

Our study has some limitations. First, our data reflect practice in French centers, and we do not know whether these findings are generalizable for practices in other parts of the world, especially considering S-ICD programming. On the other hand, the very high follow-up rate and the adjudication of clinical events can be considered strengths of the study. Regarding our study sample size and number of cases of S-ICD shocks that occurred during follow-up, we cannot exclude the risk of overfitting in multivariable analyses of S-ICD shock predictors as well as a loss of power for identifying independent predictors. The results of the preoperative screening were not available for all patients and therefore were not included in our analysis, especially for inappropriate therapy. Finally, given the low incidence of total mortality in our cohort, larger studies are required to confirm the impact of S-ICD shock on this outcome.

## **CONCLUSION**

In patients with structural heart disease, appropriate S-ICD shocks were associated with a 3-fold increase in acute heart failure admission, whereas inappropriate shocks were not. Appropriate shock predictors are related to the severity of the underlying cardiomyopathy and the programmed conditional shock threshold. The prognostic impact of conditional shock threshold programming should be further investigated in patients with advanced heart failure.

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**Figure 1. Population flow chart**

*LQT: long QT syndrome; VF: ventricular fibrillation; CPVT: catecholaminergic polymorphic ventricular tachycardia*

**Figure 2. Overview of underlying cardiomyopathies**

*Overview of underlying cardiomyopathies. ARVC: arrhythmogenic right ventricular cardiomyopathy; LV: left ventricle*

**Figure 3. S-ICD shock characteristics**

*S-ICD: subcutaneous implantable cardioverter defibrillator; VT: ventricular tachycardia; VF: ventricular fibrillation*

**Figure 4. Cumulative incidence of implantable cardioverter–defibrillator (ICD) shocks**

**Table 1. Multivariate analysis of predictors of implantable cardioverter–defibrillator (ICD) shocks**

Predictors	SHR (95% CI)	p
<b>Model 1: any shocks</b>		
LVEF per SD decrease		0.003 <sup>1</sup>
0 to 12 months	1.14 (0.83 to 1.59)	0.41
12 months to end of follow-up	2.17 (1.36 to 3.58)	<0.001
Alternate vector programmed	2.52 (1.31 to 4.85)	0.005
Secondary prevention		0.024 <sup>1</sup>
0 to 12 months	2.27 (1.19 to 4.32)	0.012
12 months to end of follow-up	1.76 (0.77 to 4.03)	0.18
QRS duration per SD increase	1.26 (0.98 to 1.61)	0.073
SMART Pass not enabled	2.44 (1.40 to 4.35)	0.001
Dyslipidemia	1.71 (1.01 to 2.90)	0.045
<b>Model 2: appropriate shocks</b>		
Secondary prevention		0.003 <sup>1</sup>
0 to 12 months	4.05 (1.73 to 9.45)	0.001
12 months to end of follow-up	2.35 (0.82 to 6.65)	0.11
QRS duration per SD increase	1.49 (1.09 to 2.02)	0.011
LVEF per SD decrease		0.013 <sup>1</sup>
0 to 12 months	1.15 (0.72 to 1.85)	0.55
12 months to end of follow-up	2.32 (1.31 to 4.34)	0.004
Conditional shock threshold <200 bpm	2.63 (1.06 to 6.7)	0.036
<b>Model 3: inappropriate shocks</b>		
Atrial fibrillation	3.06 (1.32 to 7.09)	0.009
Alternate vector programmed	3.09 (1.14 to 8.31)	0.026
SMART Pass not enabled	3.3 (1.56 to 7.14)	0.002
Hypertension	2.53 (1.15 to 5.59)	0.021

*SHRs were calculated using backward-stepwise multivariable Fine and Gray regression models using p-value >0.10 as a removal criterion after handling missing values by multiple imputation. Candidate predictors in model 1 were dyslipidemia, conditional shock threshold ( $\geq 200$  vs.  $< 200$ ), underlying cardiomyopathy, secondary prevention (as time-dependent coefficient), LVEF (as time-dependent coefficient), previous endocardial ICD, alternate vector, not enabled SMART Pass, and QRS duration. Candidate predictors in model 2 were NYHA classification (III vs. I+II), conditional shock threshold ( $\geq 200$  vs.  $< 200$ ), underlying cardiomyopathy, secondary prevention (as time-dependent coefficient), LVEF (as time-dependent coefficient), previous endocardial ICD, not enabled SMART Pass, and QRS duration. Candidate predictors in model 3 were sex, hypertension, atrial fibrillation, alternate vector programming and not enabled SMART Pass. <sup>1</sup> p-value for overall effect. Abbreviations: ACE= angiotensin-converting enzyme; AIC=Akaike information criterion; CI=confidence interval; ICD=implantable cardioverter-defibrillator; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association; SD=standard deviation; SHR=subhazard ratio.*

**Table 2. Association between implantable cardioverter–defibrillator (ICD) shocks and death and/or hospitalization heart failure**

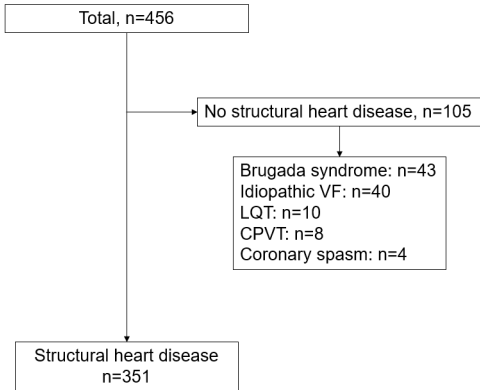
ICD shocks	Patients at risk <sup>1</sup>	HR (95% CI) <sup>2</sup>	P <sup>2</sup>	Adjusted HR (95% CI) <sup>2,3</sup>	P <sup>2,3</sup>
<b>Composite prognostic outcome</b>					
Any shocks					
No	8792	1.00 (ref.)	-	1.00 (ref.)	-
≥1	1345	3.32 (1.76 to 6.25)	<0.001	2.74 (1.40 to 5.34)	<b>0.003</b>
Appropriate shocks					
No	9388	1.00 (ref.)	-	1.00 (ref.)	-
≥1	749	3.80 (1.86 to 7.77)	<0.001	2.61 (1.21 to 5.65)	<b>0.014</b>
Inappropriate shocks					
No	9515	1.00 (ref.)	-	1.00 (ref.)	-
≥1	622	1.37 (0.48 to 3.86)	0.56	1.35 (0.75 to 4.48)	0.18
<b>Mortality</b>					
Any shocks					
No	9165	1.00 (ref.)	-	1.00 (ref.)	-
≥1	1585	4.10 (1.74 to 9.64)	0.072	2.95 (1.23 to 7.05)	<b>0.015</b>
Appropriate shocks					
No	9866	1.00 (ref.)	-	1.00 (ref.)	-
≥1	884	3.51 (1.28 to 9.60)	0.014	2.19 (0.78 to 6.16)	0.14
Inappropriate shocks					
No	10001	1.00 (ref.)	-	1.00 (ref.)	-
≥1	749	2.99 (1.00 to 8.90)	0.049	2.99 (0.98 to 9.09)	0.053
<b>Hospitalization for heart failure</b>					
Any shocks					
No	8792	1.00 (ref.)	-	1.00 (ref.)	-
≥1	1345	2.73 (1.28 to 5.81)	0.009	2.48 (1.10 to 5.58)	<b>0.028</b>
Appropriate shocks					
No	9388	1.00 (ref.)	-	1.00 (ref.)	-
≥1	749	3.44 (1.47 to 8.02)	0.004	2.62 (1.02 to 6.70)	<b>0.044</b>
Inappropriate shocks					
No	9515	1.00 (ref.)	-	1.00 (ref.)	-
≥1	622	0.86 (0.20 to 3.64)	0.84	0.78 (0.17 to 3.35)	0.73

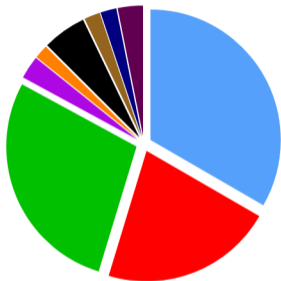
<sup>1</sup> expressed as patients-months. <sup>2</sup> Cox regression model including ICD shocks as time-dependent covariates. <sup>3</sup> adjusted for age, LVEF, underlying cardiomyopathy and NYHA classification. Abbreviations: CI=confidence interval; HR=subhazard ratio; ICD=implantable cardioverter–defibrillator; LVEF=left ventricular ejection fraction; NYHA= New York Heart Association.

**Table 3. Association between implantable cardioverter–defibrillator (ICD) conditional shock threshold programming and death and/or hospitalization heart failure**

	<b>HR (95% CI)<sup>1</sup></b>	<b>P</b>	<b>Adjusted HR (95% CI)<sup>2</sup></b>	<b>P<sup>2</sup></b>
Prognostic composite outcome	2.65 (1.42 to 4.90)	0.002	1.07 (0.54 to 2.13)	0.84
Total mortality	3.88 (1.66 to 9.02)	0.002	1.63 (0.60 to 4.41)	0.33
Hospitalization for heart failure	1.97 (0.91 to 4.26)	0.084	0.69 (0.29 to 1.60)	0.38

*1 Cox's regression model 2 adjusted for age, LVEF, underlying cardiomyopathy and NYHA classification. Abbreviations: CI=confidence interval; HR=subhazard ratio; ICD=implantable cardioverter–defibrillator; LVEF=left ventricular ejection fraction; NYHA=new york heart association*

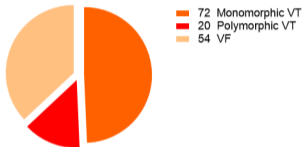
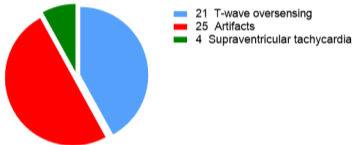




- 117 Ischemic cardiomyopathy
- 99 Hypertrophic cardiomyopathy
- 75 Dilated cardiomyopathy
- 19 Congenital heart disease
- 10 ARVC
- 7 LV non-compaction
- 7 Myocarditis-related cardiomyopathy
- 6 Valvular heart disease
- 11 Other

**Total=351patients**



**A****Causes of appropriate ICD shocks****Total=146 shocks****B****Causes of inappropriate ICD shocks****Total= 50 shocks**

