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Subcutaneous implantable cardioverter defibrillator and defibrillation testing: a propensity-matched pilot study

S-ICD and defibrillation testing

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ABSTRACT

Background

To date, only few comparisons between subcutaneous implantable cardioverter defibrillator (S-ICD) patients undergoing vs. not undergoing defibrillation testing (DT) at implantation (DT+ vs DT-) have been reported.

Objective

Aim of the study was to compare long-term clinical outcomes of two propensity-matched cohorts of DT+ and DT- patients.

Methods

Among consecutive S-ICD patients, implanted across 17 centers from January 2015 to October 2020, DT- patients were 1:1 propensity-matched for baseline characteristics with DT+ patients. The primary outcome was a composite of ineffective shocks and cardiovascular mortality. Appropriate and inappropriate shock rates were deemed secondary outcomes.

Results

Among 1290 patients, a total of 566 propensity-matched patients (n=283 DT+; n=283 DT-) served as study population. Over a median follow-up of 25.3 months, no significant differences in primary outcome event rates were found (n=10 DT+ vs n=14 DT-; p=0.404) as well as for ineffective shocks (n=5 DT- vs n=3 DT+; p=0.725). At multivariable Cox regression analysis, DT performance was neither associated with a reduction of the primary combined outcome, nor of ineffective shocks at follow-up. A high PRAETORIAN score was positively associated with both the primary outcome (HR=3.976 [1.339–11.802] p=0.013) and ineffective shocks alone at follow-up (HR=19.030 [4.752–76.203] p=0.003).

Conclusion

In two cohorts of strictly propensity-matched patients, DT performance was not associated with significant differences in cardiovascular mortality and ineffective shocks. The

PRAETORIAN score resulted capable of correctly identifying a large percentage of the patients at risk of ineffective shock conversion in both cohorts.

ClinicalTrials.gov Identifier=NCT0473876

Keywords: defibrillation testing; S-ICD; praetorian score; sudden cardiac death; propensity matching.

INTRODUCTION

In the last decade, the subcutaneous implantable cardioverter defibrillator (S-ICD) has become an established alternative to transvenous implantable cardioverter defibrillators (TV-ICD) among patients without indications for pacing or resynchronization therapy[1]. Although defibrillation testing (DT) was once required at the time of TV-ICD implantation, this practice is nowadays no longer routinely recommended[1]. As the S-ICD is a more recent technology, DT is instead deemed to be necessary in these patients. The predominant role of DT is related to the assessment of appropriate sensing of ventricular arrhythmias (VAs), as well as to the assurance of adequate defibrillation energy requirements needed for effective termination of ventricular tachycardia (VT) and ventricular fibrillation (VF), thereby testing system integrity at implant, which is crucial to deliver effective defibrillation. The clinical utility of DT during ICD implants has been gradually questioned[2]. Arguments against DT encompass the risks of DT-related complications, and mostly the inability to predict shock efficacy and long-term outcomes[3–5]. Indeed, the real safety margin of a 80J S-ICD has been suggested to be largely superior to a 40J DT in nearly 90% of patients, thus questioning the role of defibrillation testing as per the manufacturer recommendation[6]. The latest consensus statement recommends the use of defibrillation testing in patients undergoing S-ICD implantation[1], while after the SIMPLE[7] and NORDIC-ICD trials[8], implanting a TV-ICD without performing DT is considered standard clinical practice for most patients.

Recent studies have shown that a new risk stratifying tool (the PRAETORIAN score, PS) may help to identify patients with S-ICD at high risk of conversion failure[9], and that DT seems not to impact the safety of defibrillation therapy and overall patients' survival[10]. Therefore, the need for routine DT implementation in S-ICD systems has been furtherly questioned, even if this lack of association between DT and effective defibrillation, as well as long-term survival outcomes, reflect findings derived only from registries or non-randomized

111 studies[10–12]. This study aims to present long-term outcomes of two multicentered, propensity-
112 matched cohorts of patients implanted with S-ICD, according to performance of DT.

METHODS

The ELISIR project (Experience from the Long-term Italian S-ICD registry) is a European, multi-center, open-label, independent, and physician-initiated observational registry, currently involving 17 Centers[10]. This manuscript has been approved by the institutional review board and has been drafted in accordance with the tenets of the Helsinki Declaration, as revised in 2013.

Registry population

From January 2015 to October 2020, all consecutive patients meeting current guideline indications for ICD implantation and undergoing implantation of a S-ICD device (*Boston Scientific*) at 17 European institutions were enrolled in the registry. Patients were divided into two cohorts, according to the performance of DT at the time of implant. For patients undergoing DT (DT+ group), VF was induced using transthoracic 50 Hz burst pacing. No specifics regarding shock energy output were given per-protocol: the majority (91.2%) of the enrolled DT+ group received a first 65J shock with a standard shock polarity, and a 65J shock with a reverse shock polarity was then given in case of conversion-failure. The remaining (8.8%) patients were instead performed with a < 65J incremental shock protocol, as per previously reported clinical practice[6]. Briefly, in those cases, a first shock at 40J in direct polarity was delivered; in the case of ineffective defibrillation, a second shock was delivered at 80J, followed by external rescue shocks. Additional defibrillation testing using energies between 40J - 80J, or testing reverse polarity, were left to the discretion of the implanting physician. No specifics regarding DT setting were given per protocol: the use of either general anesthesia or deep sedation was left at the discretion of each single operator.

Study population

The aim of the current study was to compare the clinical outcomes of two propensity-matched cohorts of DT+ and DT- patients. From the overall registry population, all patients with both a follow-up time shorter than 6 months from implantation and no primary outcome events in the available follow-up were excluded. A total of 329 DT- patients were present in the registry at the time of the study. DT- patients were 1:1 propensity-matched for age, gender, specific arrhythmic substrate, LVEF, primary or secondary prevention implantation with patients from the DT+ cohort. After matching, the final study population was composed of two cohorts (DT+ and DT- cohorts, respectively), of 283 propensity-matched patients each (**Figure-1**). All patients with ineffective shocks during long-term follow-up in the DT- cohort present in the registry were included in the current study.

Data collection

In addition to the variables used for propensity matching, we collected data regarding demographics, personal medical history, cardiovascular risk factors, and peri-procedural information. If a post-implant 2-views chest X-ray was available, the PS was calculated and patients were classified at low-, intermediate-, and high-risk of conversion failure in accordance to the score definition[9]. Briefly, according to its definition, PS was calculated following four steps: 1) the number of coil widths of fat tissue between the nearest half of the S-ICD coil and the sternum ribs was determined (≤1 coil-width=30 points; 2 coil-widths=60 points; 3 coil-widths=90 points; >3 coil-widths=150 points); 2) the position of the S-ICD generator in relation to the mid-line was determined (generator on or posterior of the mid-line=x1; anterior of the mid-line=x2; ½ length anterior=x4); 3) the amount of fat tissue between the nearest point of the generator and the thoracic wall was determined (< 1 generator-width=x1; ≥1 generator-width=x1.5); 4) in patients with a BMI of ≤25 kg/m2, 40

points were subtracted in the case of a score of ≥90 in step 4. Patients with a PS <90, 90<150 or ≥150 were regarded having a low, intermediate or high-risk of conversion failure, respectively. Follow-up strategy was left to each center's policy, with most patients being evaluated at 1-, 6-, 12- months, and every 6 months thereafter. All device therapy delivered over the entire follow-up, both appropriate and inappropriate interventions, and/or arrhythmia recorded during in-hospital and/or remote follow-up and/or in-clinic device interrogation were collected, as well as cardiovascular and overall mortality.

Outcome definition

The primary outcome of the study was defined as a composite of ineffective shocks and cardiovascular mortality during follow-up; an ineffective shock was defined as a shock therapy delivered by an S-ICD on an adequately recognized shockable rhythm, incapable of correctly cardioverting the patient. As secondary outcomes, ineffective, appropriate, and inappropriate shock rates, as well as the combined rates of appropriate and inappropriate shocks across the two cohorts were assessed.

Statistical analysis

Continuous variables were reported as mean±standard deviation (s.d.) or as median [inter-quartile range (1^{st}-3^{rd} quartile)] if normally or non-normally distributed, respectively. Categorical variables were reported as count (%). Propensity matching has been performed using the nearest neighbor method without replacement, using common support and a caliber set at 0.005. Comparisons have been performed using a X^2 test or a Fisher's Exact Test between categorical variables, and a Student's t test or a Mann-Whitney U-test between numerical variables, as appropriate according to their distribution. Event-free survival was plotted using Kaplan-Meier estimates and a log-rank test was used to compare them. A Cox

188 regression was used to assess the associations between baseline and procedural characteristics
189 and clinical outcomes. Univariable analyses were performed at first; all variables reaching a
190 threshold p-value 0.10 were then fit into a multivariable model to adjust for confounders. A
191 two-sided p-value <0.05 was considered significant throughout the manuscript. Analysis has
192 been performed using STATA 14.0 (StataCorp LLC, College Station, TX).
193

RESULTS

Baseline characteristics of the study population

From an overall registry population of 1290 patients, a total of 566 propensity-matched patients (n=283 DT+; n=283 DT-) were extracted from the registry and enrolled in the current study, to serve as study population. After propensity-matching, the two cohorts resulted comparable for both matched and unmatched baseline data (median age 55 [46–64] vs 56 [48–64], p=0.273; males 78.1% vs 79.2%, p=0.759; primary prevention 78.5% vs 77.4%, p=0.761; in the DT+ and DT- cohort, respectively). No significant differences between underlying etiology were found in the two groups after matching. Matching-related bias reduction has been reported in **Table-S1** and **Figure-S1**. Complete baseline characteristics of the DT+ and DT- cohorts have been reported in **Table-1**.

Peri-procedural characteristics

The implantation technique was similar between the two groups, with the two-incision technique (93.6% vs 90.5%, p=0.262) and intramuscular placement (83.0% vs 83.4%, p=0.910) being the most commonly performed. **Table-S2** summarizes reasons for DT avoidance. Both the shock and conditional zone programming were similar in the two cohorts; the standard shock polarity was chosen in 98.9% (n=267) and 98.5% (n=266) of patients (p=0.865) in the DT+ and DT- cohorts, respectively. The primary sensing vector was the most frequently set at implant (65.7% vs 69.3%, p=0.865), with 80J maximum output for 1st shock therapy programmed in all patients (this data was available in 80.7% of the entire cohort). Adequate radiological imaging to calculate a PS was available in 410 (72.4%) patients, with the overall study population resulting mostly at a low risk of conversion failure (n=339); no significant differences in the risk distribution were observed (p=0.339). An extensive listing of peri-procedural characteristics of the two cohorts is reported in **Table-S3.**

Outcomes during follow-up

Over a median follow-up of 25.3 [15.2–38.5] months, 47 complex ventricular arrhythmias (n=33 VT; n=14 VF) were adequately recognized and treated in the two cohorts representing similar rates of appropriate shocks (7.8% vs 8.8%; p=0.648). A total of 24 (4.2%) patients presented a primary outcome event (n=10 in the DT + cohort, n=14 in the DT – cohort); we did not observe any significant difference in primary outcome event rates between the two cohorts (p=0.404) (**Figure-2A**). Eight ineffective shocks (1st shock in all cases) were reported, without any statistically significant difference between the two cohorts (n=5 in the DT- cohort vs n=3 DT+ cohort; p=0.725) (**Figure-2C**). Multiple shocks were required for adequate cardioversion in 6 patients, while in two patients an adequate cardioversion was not achieved (n=1 from DT- cohort, who received cardio-pulmonary resuscitations maneuvers and was rescued by a successful in-hospital external DC shock; n=1 from DT+ cohort, resulting in patient's death). A PS was available in all patients in whom ineffective shocks were reported, and its distribution resulted as follows: n=1 PS of 30; n=1 PS of 60; n=2 PS of 120; n=2 PS of 180; n=1 PS of 270; n=1 PS of 300. Fifty-two inappropriate S-ICD therapies were delivered during follow-up (n=22 in the DT- cohort, n=30 in the DT+ cohort; p=0.244), with atrial fibrillation (n=26) and T wave oversensing (n=18) representing the most common triggers. The overall follow-up data has been reported in **Table-2**.

Primary outcome, ineffective, inappropriate and appropriate shocks predictors

DT performance was neither associated with a reduction of the primary combined outcome, nor of ineffective shocks at follow-up. A high PS was positively associated with both the primary outcome (HR=3.976 [1.339–11.802] p=0.013) and ineffective shocks at follow-up (HR=19.030 [4.752–76.203] p=0.003). AF was significantly associated with appropriate shocks at follow-up (HR=1.731 [1.276–2.350] p<0.001), while age and primary prevention

were negatively associated with this secondary outcome; as for inappropriate shocks, only age resulted to be significant in negatively predicting this secondary outcome at multivariate analysis (HR=0.971 [0.951–0.991] p=0.006). The main findings of multivariate analysis for all study outcomes have been reported in **Table-3**. The whole output of the regression for the primary and secondary outcomes has been reported in **Table-S4/S5.**

DISCUSSION

Our multicenter study presents long-term outcomes from 566 propensity-matched patients undergoing S-ICD implantation, with and without the performance of DT at the time of implant, extracted from the largest unsponsored S-ICD registry. Among an overall population of 1290 patients, propensity matching was performed for age, gender, arrhythmic substrate, LVEF, and primary/secondary prevention for S-ICD placement.

The main results of the study were as follows:

- Over a median follow-up of 25.3 months, the DT+ and DT- cohorts resulted comparable in terms of a combined outcome of cardiovascular mortality and ineffective shocks;
- A total of eight ineffective shocks were observed, with a comparable distribution in the two cohorts. Six out of eight ineffective shocks were experienced in patients with a moderate or high risk of ineffective conversion estimated by the novel PS;
- DT performance was neither associated with a reduction in the primary outcome nor in the rate of ineffective shocks;
- Among the unmatched variables, a high-risk status as per post-implantation PS was the only strong independent predictor for both the primary combined outcome of the study and ineffective shocks during follow-up.

Rationale, study population, and main results

Current available studies directly assessing the impact of DT performance on the long term efficacy of S-ICD therapies are limited to the small sample sized previous experiences[10-12]. These studies did not find any significant difference in long-term outcomes between the patients receiving and not receiving DT at implant. However, limited sample sizes and/or the presence of baseline differences between the two cohorts prevented the presentation of

stronger evidence on the topic. In order to address the impact of DT on long-term outcomes on patients implanted with S-ICD, we derived two cohorts of propensity-matched patients, according to the performance of DT at the time of implantation. As expected from the strict matching strategy employed, the 566 propensity-matched patients resulted highly balanced at the post-matching assessment, with only a very low and statistically nonsignificant residual bias. This is of paramount importance, since age, sex and mostly underlying cardiac conditions may have an obvious significant impact on overall mortality and ICD-related outcomes, as also assessed in randomized trials enrolling TV-ICD patients[13,14].

Outcomes and DT

In current clinical practice, DT is usually performed at the time of implantation, theoretically aiming to assess the extent of the defibrillation safety margin. Nonetheless, this strategy presents several limitations, mostly due to the probabilistic nature of DT, which results from the variations of the amount of tissue in its vulnerable period at the moment of the shocks[15]. Indeed, during failed shocks, the volume of myocardium in its vulnerable phase is known to be significantly larger than during successful defibrillation shocks, with identical near-threshold shock strengths. During VF, the amount of myocardium in its vulnerable period changes at any moment, so that several VF inductions might be potentially required to establish the true defibrillation threshold, with potential inconsistent or inconclusive results[15,16]. Indeed, according to standard settings, S-ICD deliver 80J shocks. Thus, this programming assures a consistent safety margin beyond the "traditional" energy of up to 65J, which may therefore result in a failure to predict the real rate of ineffective shocks by DT (i.e., underestimating truly successful VF conversions). Moreover, recent observations highlighted that the safety margin of the current S-ICD release is $\geq$ 40J in nearly 90% of patients (far greater than in TV-ICD recipients), somehow reducing DT usefulness as an

estimate of patient safety at follow-up[6]. Furthermore, clinical arrhythmias are often different from those induced during DT; these arrhythmias may indeed be triggered by a framework of conditions (i.e. stress-induced ischemia, a high adrenergic drive, acidosis due to heart failure or other concomitant illnesses) which can dramatically increase ventricular defibrillation threshold and promote arrhythmia recurrences, heavily impacting on shock conversion efficacy. These conditions are difficult to be replicated in the controlled conditions of DT, that represents "a best-of-cases scenario". Additionally, DT performance requires anesthesiologic support and, although uncommon, complications associated with DTs have been reported[10,17,18]. Hence, the possibility of forgoing DT after S-ICD implantation has been postulated[19].

The present manuscript represents an incremental step towards reducing some concerns regarding the need of DT performance after S-ICD implantations, further expanding the preliminary data previously presented by our group. In our study, the DT+ and DT- cohorts were comparable both regarding the primary outcome as well as regarding ineffective shock rates. In addition, DT performance at implant was not significantly associated with a reduction in the combined primary outcome or in ineffective shocks. The results of our study are in line with and strengthen the currently available preliminary experiences assessing this topic[11,12]. Although not a randomized trial, this study represents the largest and most robust comparison between two DT+ and DT- cohorts, with strict propensity-matching, implemented in order to minimize unaccounted baseline bias between the cohorts, and representing the nearest analysis to a randomized clinical trial. According to our data, patients in whom a DT was not performed (i.e. due to an advanced and clinical unstable situation and/or to patient refusal) do not seem to be at higher risk of ineffective shock conversion and/or cardiovascular mortality. The upcoming PRAETORIAN-DFT trial will provide the final evidence needed to forego DT in S-ICD placement.

PRAETORIAN score

The PS is a recent risk score stratification tool introduced by *Quast* et al.[9], potentially harboring the capability of an immediate post-procedure risk stratification for shock conversion failure. The overall risk derived by the PS in our cohort was mostly low, indicating a good overall quality of the implantations in these expert centers. As reported by the work from *Quast* et al.[9], patients implanted in large-volume centers by expert proceduralists should result in a low risk of DT failure.

A pivotal experience from *Francia* et al.[20] recently assessed the impact of device placement technique on PS and S-ICD conversion effectiveness at implant. In their report, the combination of a two-incision technique and intramuscular device allocation allowed to obtain a deeper coil placement and a more posterior generator deployment, preventing a too anterior misplacement of the S-ICD can; this resulted in lower PS for patients implanted with this technique. In their experience, although being associated with a lower post-shock impedance, interestingly, the PS did not correlate with conversion failure at 65J[20]. Of the eight patients experiencing ineffective shocks during follow-up in our study, three underwent DT at implantation, correctly converting a device-induced VF. All three had a high PS (180, 270, and 300, respectively), which is associated with a high risk of conversion failure. Overall, six out of eight patients with an ineffective conversion at follow-up had a high PS, consistently with the observation that lower scores are associated with a higher safety margin[6]. Our findings and data reported by *Francia* et al. are in disagreement only if DT is considered an absolute proxy for real-world shock interventions capability. Given the different characteristics of DT-induced and clinical arrhythmias, the PS may in fact not correlate with DT results, while still retaining a high predictive value for clinical conversion failure. In our cohort, an elevated PS proved to be a strong independent predictor of both the primary combined outcome and of ineffective conversion. Nevertheless, it should be

mentioned that, as this tool has been conceived, it represents a pure post-procedural evaluation, which can only lead to an early (but not immediate) S-ICD repositioning when a high-risk of conversion failure is detected, requiring a full re-intervention and potentially resulting in patient discomfort. Further analyses on this topic and on its eventual earlier intra-procedural evaluation are definitely needed, but our preliminary data on this novel tool seem very promising.

Study limitations

This is an observational non-randomized study with a relative low incidence of ineffective shocks experienced during follow-up; the observed results need to be validated by larger upcoming prospective randomized clinical trials, one of which is currently ongoing (PRAETORIAN-DFT). However, to our knowledge, the presented DT- cohort is the largest description of a long-term follow-up cohort of patients undergoing S-ICD implantation without DT performance available to date, and, although relatively underpowered, it should be considered as a pilot study. Finally, it should be noted that our findings are mostly derived from high-volume centers, with expert proceduralists working at referral centers for S-ICDs. Since defibrillation energy requirements, as well as ineffective shocks and PS, may be very dependent on S-ICD device/lead positioning and individual proceduralist's skills, these findings may not be directly replicable in lower volume centers.

CONCLUSIONS

In two cohorts of propensity-matched patients, DT performance was not associated with a significant difference in the primary combined outcome of cardiovascular mortality and ineffective shocks over a median follow-up of 25.2 months. The PS was capable of correctly identifying a large percentage of the patients at risk of ineffective shock conversion in both cohorts. Randomized controlled studies, with a larger sample size and longer duration of follow-up, are highly needed to further validate these results.

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437 **Table-1**
438

Baseline characteristics of the study cohort

	DT+ (n=283)	**DT- (n=283)**	p
Age (years), median [IQR]	55 [46–64]	56 [48–64]	0.273
Male, n (%)	221 (78.1)	224 (79.2)	0.759
BMI, median [IQR]	25.7 [23.5–28.7]	26.0 [23.1–28.0]	0.813
Diabetes, n (%)	62 (21.9)	71 (25.1)	0.372
Hypertension, n (%)	146 (51.6)	129 (45.6)	0.153
Sport practice, n (%)	10 (3.5)	15 (5.3)	0.306
LVEF (%), mean±s.d.	33.9±13.1	34.7±12.2	0.442
Chronic kidney disease, n (%)	32 (11.3)	37 (13.1)	0.521
Dialysis, n (%)	9 (3.2)	10 (3.5)	0.815
Primary Prevention Implant, n (%)	222 (78.5)	219 (77.4)	0.761
Underlying Cardiac Disease			
Ischemic cardiomyopathy, n (%)	*119 (42.0)*	*120 (42.4)*	0.932
Dilatative cardiomyopathy, n (%)	*93 (32.9)*	*94 (33.2)*	0.929
Hypertrophic cardiomyopathy, n (%)	*10 (3.5)*	*9 (3.2)*	0.816
Arrhythmogenic cardiomyopathy, n (%)	*7 (2.5)*	*7 (2.5)*	1.000
Brugada syndrome, n (%)	*11 (3.9)*	*13 (4.6)*	0.676
Idiopathic ventricular fibrillation, n (%)	*12 (4.2)*	*11 (3.9)*	0.831
Other, n (%)	*31 (11.0)*	*29 (10.2)*	0.784
Atrial fibrillation, n (%)	77 (27.2)	86 (30.4)	0.403
Beta-blockers, n (%)	235 (83.1)	240 (84.8)	0.567
Amiodarone, n (%)	31 (11.0)	38 (13.4)	0.368

439
440 BMI=body mass index; DT=defibrillation testing; LVEF=left ventricular ejection fraction

441 **Table-2**
442

Follow-up data			
	DT+ (n=283)	**DT- (n=283)**	p
Follow-up time (months), median [IQR]	25.1 [15.9–36.3]	25.5 [15.1–41.0]	0.273
Primary outcome events, n (%)	10 (3.5)	14 (5.0)	0.404
Cardiovascular mortality, n (%)	*7 (2.5)*	*9 (3.2)*	*0.612*
Ineffective shock, n (%)	*3 (1.1)*	*5 (1.8)*	*0.725*
Appropriate shocks, n (%)	22 (7.8)	25 (8.8)	0.648
Sustained VT, n (%)	*16 (5.6)*	*17 (6.0)*	*0.858*
Ventricular fibrillation, n (%)	*6 (2.1)*	*8 (2.8)*	*0.583*
Inappropriate shocks, n (%)	30 (10.6)	22 (7.8)	0.244
Atrial fibrillation, n (%)	*15 (5.3)*	*11 (3.9)*	*0.422*
TWO, n (%)	*10 (3.5)*	*8 (2.8)*	*0.632*
Myopotentials, n (%)	*3 (1.1)*	*2 (0.7)*	*0.653*
Lead Noise, n (%)	*1 (0.3)*	*0*	*1.000*
VAD interference, n (%)	*1 (0.3)*	*1 (0.3)*	*1.000*

443
444 DT=defibrillation testing; TWO=T-Wave Oversensing; VAD=ventricular assist device;
445 VT=ventricular tachycardia

446 **Table-3**
447
448

Multivariate analysis for study outcomes

	Primary combined outcome			Ineffective shocks			Appropriate shocks			Inappropriate shocks		
	aHR	C.I.	p	aHR	C.I.	p	aHR	C.I.	p	aHR	C.I.	p
Age				0.963	[0.920–1.008]	0.108	0.970	[0.951–0.989]	**0.003**	0.971	[0.951–0.991]	**0.006**
Male												
Ischemic CM										0.792	[0.405–1.546]	0.494
Hypertension										0.559	[0.281–1.110]	0.096
BMI												
Diabetes												
AF	1.674	[0.733–3.822]	0.221				1.731	[1.276–2.350]	**<0.001**			
Primary prevention							0.330	[0.180–0.603]	**<0.001**			
LVEF												
DT performance												
High risk at PS	3.976	[1.339–11.802]	**0.013**	19.030	[4.752–76.203]	**<0.001**						

449
450 AF=atrial fibrillation; BMI=body mass index; CM=cardiomyopathy; DT=defibrillation testing; LVEF=left ventricular ejection fraction;
451 PS=PRAETORIAN score.

FIGURE LEGEND

Figure-1. Workflow chart showing the selection process for the study population.

Figure-2. Panel A) Between the DT+ and DT- cohort, no significant differences in terms of survival from combined ineffective shocks and cardiovascular mortality (primary outcome) were observed. Panel B–C–D) Survival from B) appropriate, C) inappropriate, and D) combined appropriate and inappropriate shocks (secondary outcomes) did not differ between the DT+ and DT- cohorts.