

## **Implantable Cardioverter Defibrillator Therapy in Hypertrophic Cardiomyopathy: A SIMPLE Substudy Authors**

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2 **Implantable Cardioverter Defibrillator Therapy in Hypertrophic**  
3 **Cardiomyopathy: A SIMPLE Substudy**  
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1 **Abstract**

2 **Background:** Patients with hypertrophic cardiomyopathy (HCM) are considered to  
3 be at high risk for elevated defibrillation thresholds, peri-procedural complications,  
4 and failed appropriate shocks.

5 **Objective:** To determine the value of defibrillation testing in HCM patients  
6 undergoing ICD implantation.

7 **Methods:** Defibrillation thresholds, perioperative complications, and long-term  
8 outcomes were compared between patients with HCM, and those with ischemic or  
9 dilated cardiomyopathy (ICM/DCM) enrolled in the SIMPLE trial. In patients with  
10 HCM, outcomes were also compared between those randomized to DT versus no  
11 DT.

12 **Results:** Adequate defibrillation safety margin without system change was achieved  
13 in 46/52 (88.5%) HCM and in 948/1047 (90.5%) ICM/DCM patients ( $p=0.63$ ).  
14 Perioperative complications occurred in 1/52 (1.9%) HCM patients with DT, in  
15 comparison to 67/1047 (6.4%) ICM/DCM patients with DT ( $p=0.37$ ) or to 3/42 (7.1%)  
16 HCM patients without DT ( $p=0.32$ ). During follow-up, there was no significant  
17 difference between HCM vs. ICM/DCM patients in terms of all-cause mortality  
18 (adjusted-HR 1.02, 95% CI 0.45-2.34), composite of arrhythmic death or failed  
19 appropriate shock (adjusted-HR 0.33, 95% CI 0.04-2.42), inappropriate shocks  
20 (adjusted-HR 1.64, 95% CI 0.69-3.89) or system complications (adjusted-HR 1.93,  
21 95% CI 0.88-4.27). All-cause mortality (HR 0.26, 95% CI 0.03-2.20), appropriate (HR  
22 0.24, 95% CI 0.03-2.05) and inappropriate shocks (HR 2.13, 95% CI 0.51-8.94) were  
23 similar in HCM patients without or with DT.

24 **Conclusion:** We did not find any difference in intraoperative defibrillation efficacy,  
25 perioperative complications, and long-term outcomes between patients with HCM

1 and with ICM/DCM. DT did not improve intraoperative or clinical shock efficacy in  
2 HCM patients.

3 **Keywords:** hypertrophic cardiomyopathy, HCM, implantable cardioverter defibrillator,  
4 ICD, defibrillation testing, SIMPLE

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ACCEPTED MANUSCRIPT

## 1 Introduction

2 Implantable cardioverter defibrillators (ICDs) are indicated for selected patients with  
3 hypertrophic cardiomyopathy (HCM), either for primary or secondary prevention of  
4 sudden cardiac death [1,2]. The majority of HCM patients undergoes ICD  
5 implantation for primary prevention [2,3] with American and European guidelines  
6 recommending individual sudden cardiac death risk stratification [1,2,4]. At the time  
7 of ICD insertion, patients with HCM are considered to be prone to have elevated  
8 defibrillation thresholds necessitating additional measures such as re-programming,  
9 lead re-positioning, or insertion of additional ICD leads [5-8]. Previous studies also  
10 indicate that HCM patients have an increased risk of peri-procedural complications  
11 [3, 9-11], and that their clinical course may be complicated by a higher incidence of  
12 failed appropriate ICD therapy [10,12] or inappropriate shocks [6,10,13].

13 SIMPLE was the largest randomized trial demonstrating that routine defibrillation  
14 testing (DT) at the time of ICD insertion does not improve shock efficacy or reduce  
15 mortality [14,15]. Moreover, elevation in postoperative troponin levels in patients  
16 undergoing DT were associated with worse long-term outcomes [16]. Based on the  
17 results of the SIMPLE trial, ICDs are implanted without DT in the majority of patients;  
18 however, the necessity of DT specifically for HCM patients is still under debate. The  
19 2015 HRS/EHRA/APHRS/SOLAECE consensus statement on optimal ICD  
20 programming and testing did not provide clear guidelines or recommendations  
21 regarding defibrillation testing in patients with HCM [17].

22 The database of the SIMPLE trial provides a unique opportunity to evaluate the  
23 aforementioned clinical issues associated with ICD therapy in patients with HCM.

24

25

## 1 **Methods**

2 This is a secondary analysis from the SIMPLE trial (Shockless IMPLant Evaluation,  
3 ClinicalTrials.gov number: NCT00800384). A detailed description of study design [14]  
4 and results have been published previously [15]. Briefly, SIMPLE was a single-  
5 blinded, randomized, multicentre, non-inferiority clinical trial enrolling 2,500 patients  
6 who were receiving their first ICD either for primary or secondary prevention, with or  
7 without cardiac resynchronization therapy. Patients were randomized to have either  
8 defibrillation testing (testing group) or not (no-testing group). Implanters were  
9 expected to position the ICD left-hand side and to provide a sensed R-wave of at  
10 least 5.0 mV and acceptable high-voltage impedance. In the defibrillation testing (DT)  
11 group, the protocol required induction of ventricular fibrillation in order to demonstrate  
12 either one successful arrhythmia termination at 17J or two successful terminations at  
13 21J. In case the initial system configuration did not achieve the predefined  
14 defibrillation safety margin, the ICD had to be re-configured and DT repeated.

15 The primary efficacy endpoint of SIMPLE was the composite of arrhythmic death or  
16 failed appropriate shock (i.e., a shock that did not terminate a spontaneous episode  
17 of ventricular tachycardia or fibrillation). All-cause mortality was the most important  
18 secondary outcome. The primary safety composite was assessed at 30 days after  
19 ICD implantation to evaluate the safety of defibrillation testing, and it included death,  
20 myocardial infarction, stroke, systematic or pulmonary embolism, heart failure, need  
21 for chest compressions or an aortic ballon pump during implantation, use of intra-  
22 operative vasoconstrictors, non-elective intubation, arterial-line complications,  
23 unplanned stay in the ICU, other anoxic brain injury, pneumothorax, cardiac  
24 perforation, ICD infection, or aspiration pneumonia.

1 The study protocol was approved by the institutional review boards of all participating  
2 centres.

3 **Categorization of patients by the underlying cardiac disease.** Patients were  
4 categorized by the investigator according to their underlying cardiac disease as  
5 having coronary artery disease, hypertrophic (HCM) or dilated cardiomyopathy  
6 (DCM), primary electrical disorder (Brugada syndrome, Long-QT syndrome,  
7 catecholaminergic polymorphic ventricular tachycardia), and/or arrhythmogenic RV  
8 cardiomyopathy. Clinical indication for ICD implantation was also recorded (i.e.  
9 primary vs. secondary prevention). The population of interest of the current analysis  
10 comprised patients with HCM. If patients had HCM and another diagnosis (i.e.  
11 ICM), they were still classified as HCM. The control group consisted of a pooled  
12 cohort of patients with ischemic cardiomyopathy or dilated cardiomyopathy  
13 (ICM/DCM) who were randomized to undergo DT.

14 **Clinical endpoints.** In the current analysis we compared peri-operative  
15 complications (as the primary safety endpoint of the original study) and defibrillation  
16 thresholds between HCM patients and patients with ICM/DCM within the DT arm,  
17 and between HCM patients with and without DT. Long-term clinical outcomes such  
18 as all-cause mortality, composite of arrhythmic death or failed appropriate shock,  
19 appropriate shock, inappropriate shock, and system revision between HCM patients  
20 and ICM/DCM patients and in HCM patients with and without DT were also  
21 compared.

22 **Statistical analysis.** All analyses were based on the intention-to-treat principle  
23 unless otherwise specified. Endpoint events including deaths, shocks, and safety  
24 outcomes were adjudicated by an adjudication committee that was unaware of  
25 treatment allocation. All data were entered in a central database kept at the

1 Population Health Research Institute, Hamilton, Canada. Categorical variables were  
2 compared using Chi-square test or Fisher's exact test and continuous variables using  
3 two-sample t-test. To assess the risk of clinical outcomes between patient groups the  
4 Cox proportional hazards regression model was used. The models were unadjusted  
5 and adjusted for potential confounders including age, gender, primary prevention ICD  
6 indication, NYHA class, LVEF, atrial fibrillation, hypertension, stroke/TIA, diabetes  
7 and impaired renal function. Survival curves were constructed according to the  
8 Kaplan-Meier method. Statistical analyses were performed with SAS version 9.4  
9 software (SAS Institute, Inc., Cary, NC, USA). Two-sided p values <0.05 were  
10 considered statistically significant.

11

## 12 **Results**

13 **Patient characteristics.** From the total of 2,500 randomized ICD recipients of the  
14 SIMPLE trial, 95 (3.8%) patients had a diagnosis of HCM. A total of 2177 (87.1%)  
15 patients with ICM/DCM constituted the control group (Table 1). As expected, patients  
16 in the ICM/DCM cohort were generally older and had more often symptomatic heart  
17 failure or other relevant comorbidities, such as hypertension, diabetes or chronic  
18 kidney disease, compared to HCM patients. HCM patients received more often dual  
19 chamber devices while more ICM/DCM patients were implanted with single chamber  
20 or CRT-D systems. The mean value of the sensed R-wave at implantation was  
21  $16.7\pm 6.8$  mV for HCM patients compared to  $15.0\pm 6.2$  mV in ICM/DCM cohort  
22 ( $p=0.023$ ).

23 There were no statistically significant differences in the baseline characteristics of  
24 HCM patients with (N=53) and without defibrillation testing (N=42)(Supplementary  
25 Table 1).



1 **Defibrillation thresholds.** An adequate defibrillation safety margin without system  
2 change was achieved in comparable proportions of HCM and ICM/DCM patients  
3 (88.5% vs. 90.5%,  $p=0.626$ )(Table 2). The success rate for achieving the predefined  
4 safety margin without system change or with additional surgical (i.e. the RV lead  
5 reposition, addition or removal of a coil, addition of a subcutaneous array) or  
6 programming efforts (i.e. SVC coil off, can off, reversed polarity) was also similar  
7 between patients in the HCM and control groups (92.3% vs. 93.4%,  $p=0.772$ ).

8 **Perioperative complications.** The rate of perioperative complications (primary  
9 safety outcome) assessed at 30 days post implant did not significantly differ between  
10 patients with HCM and ICM/DCM who underwent DT (1/52 vs. 67/1047,  
11  $p=0.367$ )(Table 3).

12 Comparing perioperative complications between HCM patients with and without DT,  
13 no significant difference was observed (primary safety outcome: 1/52 vs. 3/42,  
14  $p=0.321$ ; secondary safety outcome: 0/52 vs. 3/42,  $p=0.086$ )(Supplementary Table  
15 2).

16 **Long-term outcomes.** The mean follow-up duration in SIMPLE was  $3.1 \pm 1.0$  years.  
17 Crude Kaplan-Meier analysis demonstrated lower all-cause mortality (HR 0.32, 95%  
18 CI 0.14-0.72), lower incidence of arrhythmic death or failed appropriate shock (HR  
19 0.23, 95% CI 0.06-0.93), and lower rate of appropriate shocks (HR 0.38, 95% CI  
20 0.17-0.86) in HCM patients compared to patients with ICM/DCM (Table 4A;  
21 Supplementary Figure 1A-B; Figure 1A). There was no significant difference in the  
22 crude rate of inappropriate shocks (HR 1.14, 95% CI 0.56-2.32) or system revision  
23 (HR 0.78, 95% CI 0.39-1.58)(Table 4A; Figure 1B). The comparison of HCM and  
24 ICM/DCM patients adjusted for confounding factors revealed no significant difference  
25 in all-cause mortality (adjusted HR 1.02, 95% CI 0.45-2.34), composite of arrhythmic

1 death or failed appropriate shock (adjusted HR 0.33, 95% CI 0.04-2.42), rate of  
2 inappropriate shocks (adjusted HR 1.64, 95% CI 0.69-3.89) or system complications  
3 (adjusted HR 1.93, 95% CI 0.88-4.27)(Table 4A; Supplementary Figure 1A-B; Figure  
4 1B). However, there was a trend towards less appropriate ICD therapies in HCM  
5 patients compared to the ICM/DCM cohort (adjusted HR 0.44, 0.17-1.12,  
6  $p=0.08$ )(Table 3A; Figure 1A).

7 There was no significant difference between the HCM patients without versus with  
8 DT in terms of all-cause mortality (HR 0.26, 95% CI 0.03-2.20), appropriate (HR 0.24,  
9 95% CI 0.03-2.05) or inappropriate ICD shocks (HR 2.13, 95% CI 0.51-8.94)(Table  
10 4B). The composite of arrhythmic death or failed appropriate shock occurred in two  
11 HCM patients with DT versus none in the non DT group (Table 4B).

12

## 13 Discussion

14 **Main findings.** In this pre-specified secondary analysis of the SIMPLE trial, we did  
15 not find any difference in outcomes for patients with HCM compared to patients with  
16 ICM or DCM. We also confirmed the overall results of SIMPLE in the sub-group of  
17 patients with HCM; specifically, there was no significant difference between HCM  
18 patients with and without DT in terms of perioperative complications, clinical shock-  
19 efficacy, or all-cause mortality. Therefore, the results of the main SIMPLE trial apply  
20 to patients with HCM in whom it appears safe to conduct ICD implantation without  
21 DT.

22 **Defibrillation thresholds.** High risk for elevated defibrillation thresholds  
23 necessitating additional measures such as re-programming, re-positioning or  
24 implanting additional ICD leads have been reported for patients with HCM in several

1 previous observational studies [5-8]. A weak correlation with LV wall thickness  
2 [5,8,11] or QRS duration and defibrillation threshold [7] was also described.

3 These results are in contrast with more recent, single-center observations from Quin  
4 et al. [18] and Francia et al. [19] who did not find a difference in defibrillation  
5 thresholds between HCM and control groups; left ventricular hypertrophy or QRS  
6 duration were not associated with elevated defibrillation thresholds.

7 Our study is the first to describe clinical outcomes in patients enrolled in a large,  
8 multicenter, controlled, randomized trial and supports the findings of the latter two  
9 studies. An adequate defibrillation safety margin without ICD system change was  
10 achieved in the similar proportion of HCM patients as in the control group of patients  
11 with ICM/DCM.

12 **ICD-related complications.** The incidence of perioperative complications ranges  
13 from 2-18% [5,6,9-11] and depends largely on the definition used. For instance,  
14 Schinkel et al. reported in a meta-analysis of ICD studies in HCM patients a system-  
15 related complication rate of 15% (3.4%/year), which included perioperative  
16 complications and complications during follow-up [3].

17 The perioperative complication rate for HCM and ICM/DCM patients in the present  
18 analysis were 1.9% and 6.4%, respectively ( $p=n.s.$ ). Need for system revision in  
19 HCM patients during long-term follow-up was low at 2.8%/year.

20 **Long-term outcomes.** For HCM patients implanted with an ICD, all-cause mortality  
21 rate ranged from 0.5% up to 2.25% per year [3,5,6,10,20,21]. We found an  
22 annualized all-cause mortality rate of 1.9% in HCM patients, not significantly different  
23 from that in ICM/DCM patients.

24 The evaluation of shock efficacy by determining failed appropriate shock incidence  
25 seems to be particularly relevant in the HCM population. There is only one prior study

1 comparing shock efficacy for spontaneous VT/VF in HCM patients with and without  
2 DT [19]. This study compromised 66 patients in whom ICD shock efficacy was 75%  
3 at first attempt and 12 out of 12 VT/VF in 7 patients were successfully converted with  
4  $\geq 1$  shocks. The present analysis confirms this finding with a very low rate of  
5 arrhythmic death or failed appropriate shock (0.6%/year). Our study expands these  
6 observations by comparing HCM patients with ICM/DCM patients where again no  
7 significant differences between the two patient groups after adjusting for confounders  
8 were found.

9 Previous studies have reported incidences of appropriate ICD discharges of 2.3-  
10 11%/year [5,6,9-11,20,22]. In our patient population, appropriate ICD discharges  
11 occurred at an annual incidence of 2.0% with a trend towards less appropriate ICD  
12 therapies in HCM patients compared to the ICM/DCM cohort.

13 Prior studies have reported relatively high rates of inappropriate ICD therapies in  
14 HCM patients, predominantly due to supraventricular arrhythmias or T-wave  
15 oversensing [3,6,10,13,20]. For instance, in a recently published report from the  
16 Swedish ICD registry, inappropriate ICD shock occurred in 14.3%, which was mainly  
17 triggered by atrial fibrillation/flutter or ectopic tachycardia (56.5%) [13]. However, this  
18 study reports an outcome of registry patients recruited between 1995 and 2012.  
19 Therefore, programming of the devices was probably different from current standards  
20 focused on minimization of inappropriate therapy. In our study, there was a low  
21 incidence of 2.8% per year, not significantly different from the one observed in  
22 patients with ICM/DCM.

23 Whether newer ICD technologies such as the subcutaneous ICD will further improve  
24 device efficacy and safety in HCM patients remains to be determined [23,24].

1 **Limitations.** Classification of the underlying cardiac disease within the SIMPLE trial  
2 relied on the judgement of the investigator with no pre-specified definitions applied.  
3 The typical clinical variables used for risk stratification in HCM guidelines [1,2,4] were  
4 not collected in a systematic fashion. The relatively small number of patients with  
5 HCM in the SIMPLE trial resulted in low statistical power to detect differences in  
6 outcomes; however, this is the largest report based on a randomized patient  
7 population with prospectively collected data and blinded endpoint adjudication to  
8 evaluate DT in patients with HCM.

## 10 **Conclusions**

11 In this retrospective analysis of the SIMPLE trial, the rate of ICD-related  
12 complications and long-term outcomes in HCM patients were not significantly  
13 different from those observed in patients with ICM/DCM. Moreover, routine  
14 defibrillation testing did not seem to be associated with beneficial clinical effects in  
15 HCM patients.

## 17 **Disclosures**

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1 **Tables**2 **Table 1** Baseline characteristics of patients with HCM and with ICM/DCM

	All (N=2272)	HCM (N=95)	ICM/DCM (N=2177)	P Value
Age, mean±SD	63.6±10.8	57.0±14.0	63.9±10.5	<0.001
Gender (Male), n(%)	1864 (82.0)	63 (66.3)	1801 (82.7)	<0.001
BMI, mean±SD	28.0±4.9	28.3±4.7	28.0±4.9	0.524
ICD implanted for primary prevention, n(%)	1708 (75.2)	76 (80.0)	1632 (75.0)	0.266
NYHA class				<0.001
I/II, n(%)	935 (41.2)	21 (22.1)	914 (42.0)	
III/IV, n(%)	754 (33.2)	7 (7.4)	747 (34.3)	
LVEF, mean±SD	30.5±11.4	56.6±17.8	29.5±9.7	<0.001
Atrial fibrillation, n(%)	526 (23.2)	25 (26.3)	501 (23.0)	0.455
Hypertension, n(%)	1481 (65.2)	42 (44.2)	1439 (66.1)	<0.001
Previous stroke/TIA, n(%)	245 (10.8)	6 (6.3)	239 (11.0)	0.152
Diabetes, n(%)	703 (30.9)	17 (17.9)	686 (31.5)	0.005
Impaired renal function, n(%)	454 (20.0)	6 (6.3)	448 (20.6)	<0.001
Amiodarone use, n(%)	347 (15.3)	9 (9.5)	338 (15.5)	0.108
ACE inhibitor, n(%)	1665 (73.3)	28 (29.5)	1637 (75.2)	<0.001
ARB, n(%)	390 (17.2)	17 (17.9)	373 (17.1)	0.847
Beta-blocker, n(%)	2041 (89.8)	72 (75.8)	1969 (90.4)	<0.001
Aldosterone antagonist, n(%)	897 (39.5)	10 (10.5)	887 (40.7)	<0.001
Oral anticoagulant, n(%)	468 (20.6)	13 (13.7)	455 (20.9)	0.089
Digitalis, n(%)	282 (12.4)	5 (5.3)	277 (12.7)	0.031
Type of ICD				<0.001
VVI-ICD, n(%)	1005 (44.2)	32 (33.7)	973 (44.7)	
DDD-ICD, n(%)	575 (25.3)	56 (58.9)	519 (23.8)	
CRT-ICD, n(%)	676 (29.8)	6 (6.3)	670 (30.8)	
Dual coil ICD lead, n(%)	1322 (58.2)	54 (56.8)	1268 (58.2)	0.786
Implant R-wave, mean±SD	15.1±6.3	16.7±6.8	15.0±6.2	0.023

3 *ACE = angiotensin-converting-enzyme, ARB = angiotensin II receptor antagonist, BMI = body mass index, DCM = dilated*  
4 *cardiomyopathy, DT = defibrillation testing, HCM = hypertrophic cardiomyopathy, ICD = implantable cardioverter defibrillator, ICM =*  
5 *ischaemic cardiomyopathy, LVEF = left ventricular ejection fraction, NYHA = New York Heart Association functional classification, SD*  
6 *= Standard deviation, TIA = transient ischemic attack*

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1 **Table 2** Comparison of defibrillation testing between HCM patients and ICM/DCM  
 2 patients

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	All (N=1099*)	HCM (N=52*)	ICM/DCM (N=1047*)	P Value
Adequate defibrillation safety margin achieved without any change	994 (90.4)	46 (88.5)	948 (90.5)	0.626
Achieved with additional efforts				
RV lead reposition/Add or remove of coil/Add subcutaneous array	8 (0.7)	0 (0.0)	8 (0.8)	>0.999
SVC coil programmed out/Can programmed off/Polarity reversed	24 (2.2)	2 (3.8)	22 (2.1)	0.315
Not achieved with additional efforts				
RV lead reposition/Add or remove of coil/Add subcutaneous array	18 (1.6)	1 (1.9)	17 (1.6)	0.585
SVC coil programmed out/Can programmed off/Polarity reversed	16 (1.5)	1 (1.9)	15 (1.4)	0.542

4 \* Included only patients who underwent defibrillation testing as per study protocol. One HCM patient randomized to DT did not receive  
 5 DT. Two patients with HCM did not achieve adequate defibrillation safety margin and no additional efforts were made (protocol  
 6 deviation).

7 DCM = dilated cardiomyopathy, HCM = hypertrophic cardiomyopathy, ICM = ischaemic cardiomyopathy, RV = right ventricular, SVC =  
 8 superior vena cava  
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1 **Table 3** Comparison of perioperative complications between HCM patients and  
 2 ICM/DCM patients (subjects undergoing DT)

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	All (N=1099†)	HCM (N=52†)	ICM/DCM (N=1047†)	P Value
Primary safety Composite*, n(%)	68 (6.2)	1 (1.9)	67 (6.4)	0.367
Secondary safety Composite**, n(%)	47 (4.3)	0 (0.0)	47 (4.5)	0.164
Death, n(%)	5 (0.5)	0 (0.0)	5 (0.5)	>0.999
Stroke, n(%)	3 (0.3)	0 (0.0)	3 (0.3)	>0.999
Non-CNS systemic embolism, n(%)	2 (0.2)	0 (0.0)	2 (0.2)	>0.999
Pulmonary embolism, n(%)	1 (0.1)	0 (0.0)	1 (0.1)	>0.999
Myocardial infarction, n(%)	1 (0.1)	0 (0.0)	1 (0.1)	>0.999
Heart failure needing inotropes or diuretics, n(%)	23 (2.1)	0 (0.0)	23 (2.2)	0.622
Intraoperative hypotension, n(%)	7 (0.6)	0 (0.0)	7 (0.7)	>0.999
Need for chest compression, n(%)	4 (0.4)	0 (0.0)	4 (0.4)	>0.999
Non-elective intubation, n(%)	5 (0.5)	0 (0.0)	5 (0.5)	>0.999
Aspiration pneumonia, n(%)	1 (0.1)	0 (0.0)	1 (0.1)	>0.999
Unplanned stay in ICU, n(%)	1 (0.1)	0 (0.0)	1 (0.1)	>0.999
Pneumothorax, n(%)	12 (1.1)	0 (0.0)	12 (1.1)	>0.999
Pericarditis, cardiac perforation or tamponade, n(%)	9 (0.8)	1 (1.9)	8 (0.8)	0.355
Device infection, n(%)	3 (0.3)	0 (0.0)	3 (0.3)	>0.999
Arterial-line complication, n(%)	1 (0.1)	0 (0.0)	1 (0.1)	>0.999
Anoxic brain injury, n(%)	0 (0.0)	0 (0.0)	0 (0.0)	-

4 \* Included all complications

5 \*\* Included all complications from table except for aspiration pneumonia, pneumothorax, Pericarditis/cardiac perforation/cardiac  
6 tamponade, device infection and anoxic brain injury

7 † Included only patients who had an ICD implanted. 1 HCM patient did not receive ICD.

8 CNS = central nervous system, DCM = dilated cardiomyopathy, DT = defibrillation testing, HCM = hypertrophic cardiomyopathy, ICM =  
9 ischaemic cardiomyopathy

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1 **Table 4A** Risk of clinical outcomes in patients with HCM and with ICM/DCM

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Clinical outcomes	Overall		HCM		ICM/DCM		Unadjusted		Adjusted*	
	n/N	Rate (%/yr)	n/N	Rate (%/yr)	n/N	Rate (%/yr)	HR (95% CI)	P value	HR (95% CI)	P value
All-cause mortality	406/2272	5.8	6/95	1.9	400/2177	5.9	0.32 (0.14-0.72)	0.006	1.02 (0.45-2.34)	0.959
Arrhythmic Death or Failed appropriate shock	186/2272	2.7	2/95	0.6	184/2177	2.8	0.23 (0.06-0.93)	0.04	0.33 (0.04-2.42)	0.275
Appropriate shock	337/2272	5.3	6/95	2.0	331/2177	5.4	0.38 (0.17-0.86)	0.02	0.44 (0.17-1.12)	0.084
Inappropriate shock	165/2272	2.5	8/95	2.8	157/2177	2.5	1.14 (0.56-2.32)	0.72	1.64 (0.69-3.89)	0.261
System revision	234/2272	3.6	8/95	2.8	226/2177	3.6	0.78 (0.39-1.58)	0.493	1.93 (0.88-4.27)	0.102

3 \* Adjusted for age, gender, primary prevention, NYHA class, LVEF, atrial fibrillation, Hypertension, stroke/TIA, diabetes and impaired renal function

4 DCM = dilated cardiomyopathy, HCM = hypertrophic cardiomyopathy, ICM = ischaemic cardiomyopathy

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7 **Table 4B** Risk of clinical outcomes in HCM patients with and without DT

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Clinical outcomes	Overall		No DT		DT		No DT vs. DT	
	n/N	Rate (%/yr)	n/N	Rate (%/yr)	n/N	Rate (%/yr)	HR (95% CI)	P value
All-cause mortality	6/95	1.9	1/42	0.7	5/53	2.9	0.26 (0.03-2.20)	0.215
Arrhythmic Death or Failed appropriate shock	2/95	0.6	0/42	0.0	2/53	1.2	-	-
Appropriate shock	6/95	2.0	1/42	0.7	5/53	3.1	0.24 (0.03-2.05)	0.192
Inappropriate shock	8/95	2.8	5/42	4.0	3/53	1.8	2.13 (0.51-8.94)	0.300

9 DT = defibrillation testing, HCM = hypertrophic cardiomyopathy

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1 **Figure legends**

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3 **Figure 1A** Kaplan-Meier curves of appropriate shock by HCM vs. ICM/DCM

4 **Figure 1B** Kaplan-Meier curves of inappropriate shock by HCM vs. ICM/DCM

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