Defibrillator shocks and their impact on objective and subjective patient outcomes: results from the painfree SST clinical trial

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Abstract: BACKGROUND: The impact of ICD shock on device-measured activity and patient reported outcomes is unknown. OBJECTIVE: The purpose of this study was to analyze the acute and long-term effects of ICD shock on objective behavioral data (i.e., device-based physical activity) and subjective patient reported outcomes (e.g., quality of life and shock anxiety). METHODS: The PainFree SST clinical trial included 2,770 patients with a single or dual-chamber ICD, or cardiac resynchronization defibrillator (CRT-D) who were followed for 22 ± 9 months. Participants completed measures of quality of life (EuroQol 5-D [EQ5D]) and shock anxiety (Florida Shock Anxiety Scale [FSAS]) at baseline, bi-annual visits, and monthly for 6 months following an ICD shock. Daily physical activity data were obtained from a built-in device accelerometer. RESULTS: Average daily activity was 185.3 ± 119.4 minutes/day. Activity was significantly reduced after an ICD shock ($p<0.0001$) and recovered to a normal level after approximately 90 days. ICD shock was also associated with decreased quality of life (EQ5D Health Score) and increased EQ5D anxiety scores, but it did not impact mobility, self-care, activity, or pain. Similarly, shock anxiety (FSAS) increased in shocked patients and remained significantly elevated at 24 months, regardless of appropriate or inappropriate shock delivery. CONCLUSIONS: ICD shocks have a long-lasting, adverse impact on both objective, device-measured physical activity and subjective patient reported outcomes of quality of life and shock anxiety. Successful management of ICD patients requires attention to clinically relevant behavioral and psychological outcomes to expedite recovery and return to activities of daily living.

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Abstract

Background: The impact of ICD shock on device-measured activity and patient reported outcomes is unknown.

Objective: The purpose of this study was to analyze the acute and long-term effects of ICD shock on objective behavioral data (i.e., device-based physical activity) and subjective patient reported outcomes (e.g., quality of life and shock anxiety).

Methods: The PainFree SST clinical trial included 2,770 patients with a single or dual-chamber ICD, or cardiac resynchronization defibrillator (CRT-D) who were followed for 22 ± 9 months. Participants completed measures of quality of life (EuroQol 5-D [EQ5D]) and shock anxiety (Florida Shock Anxiety Scale [FSAS]) at baseline, bi-annual visits, and monthly for 6 months following an ICD shock. Daily physical activity data were obtained from a built-in device accelerometer.

Results: Average daily activity was 185.3 ± 119.4 minutes/day. Activity was significantly reduced after an ICD shock ($p<0.0001$) and recovered to a normal level after approximately 90 days. ICD shock was also associated with decreased quality of life (EQ5D Health Score) and increased EQ5D anxiety scores, but it did not impact mobility, self-care, activity, or pain. Similarly, shock anxiety (FSAS) increased in shocked patients and remained significantly elevated at 24 months, regardless of appropriate or inappropriate shock delivery.

Conclusions: ICD shocks have a long-lasting, adverse impact on both objective, device-measured physical activity and subjective patient reported outcomes of quality of life and shock anxiety. Successful management of ICD patients requires attention to clinically relevant behavioral and psychological outcomes to expedite recovery and return to activities of daily living.

Key words: Quality and Outcomes, Electrophysiology, Mental Health, Exercise, Quality of Life, Implantable Cardioverter Defibrillator

Clinical Trial Registration: URL: http://clinicaltrials.gov Unique Identifier: NCT00982397

Introduction

The implantable cardioverter defibrillator (ICD) reduces mortality in patients at risk for life-threatening arrhythmias.[1] However, the fear of experiencing spontaneous arrhythmias and frequent device-delivered shock therapies may lead some patients to limit their daily activities or avoid physical exertion, which could adversely impact their health and quality of life.[2]

Previous studies of health-related quality of life in ICD patients have generally relied on subjective, self-report data that is susceptible to recall bias. Results from these studies have found that while ICD shocks are associated with increased anxiety in smaller, single-institution studies, this is not uniformly the case in larger multicenter trials, suggesting a need for improved methodology and precision measurement of the effect of ICD shock on the patient experience.[3, 4] Objective behavioral data associated with ICD shock has also been lacking despite the fact that modern ICDs are capable of collecting longitudinal physical activity data. Device-measured physical activity has been associated with mortality and hospitalization,[4-6] and could be combined with subjective patient outcomes to provide a more robust examination of the impact of ICD shock on patient activity and quality of life.

In this study, we analyzed data from the PainFree SST clinical trial to prospectively examine the acute and long-term effects of ICD therapies on daily activity, quality of life, and shock anxiety.

Methods

Study Overview and Patient Population

PainFree SST was a large multicenter clinical trial designed to evaluate improved device detection algorithms to reduce ICD shock (SmartShock® technology). The study design and primary results have been published elsewhere.[7, 8] In brief, PainFree SST enrolled 2,790 patients from 150 centers worldwide implanted with a Medtronic Protecta® (Medtronic

plc, Minneapolis, MN, USA) single or dual-chamber ICD, or cardiac resynchronization defibrillator (CRT-D), between September 2009 and August 2012. This included new implants, upgrades, and replacements. Twenty patients were subsequently excluded from all analyses for various reasons, resulting in a final study cohort of 2,770 patients. All patients provided written informed consent. Study protocols and procedures were approved by the ethics committee or institutional review board at all participating sites.

Data Collection

Patients were seen at enrollment (at the time of ICD implant prior to hospital discharge) and twice annually thereafter. Device data on patient activity and arrhythmia episodes treated with a shock or anti-tachycardia pacing (ATP) were extracted. Available electrocardiograms were reviewed and adjudicated by an independent episode review committee (ERC). Shock anxiety and quality of life data were collected at baseline, bi-annual visits, and monthly for 6 months following an ICD shock. This intensive follow-up approach allowed for closer examination of the immediate and long-term effects of ICD shock from the patient's perspective.

Measures

Patient activity data were obtained from the internal ICD accelerometer located in the device generator. As the body moves, internal sensors generate an electrical signal that is proportional to acceleration of the generator. A proprietary algorithm interprets the electrical signal and classifies each minute as active or non-active. The algorithm is calibrated to detect walking at a slow pace as active. A daily summary score for total activity in minutes per day is automatically calculated and stored in the device. The use of device-detected accelerometer data has been validated as an objective measure of daily activity in previous studies of ICD patients.[6, 9-11]

Quality of life was assessed with the EuroQol 5-D (EQ5D) questionnaire, a five-dimension measure of perceived health status (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) based on a three-point response (no problems, some problems, extreme problems). Additionally, the EQ5D includes a visual analog scale (VAS) which provides a composite health status score referred to as the EQ5D Health Score. Higher EQ5D Health Scores indicate better self-reported health.

Shock anxiety was assessed with the Florida Shock Anxiety Scale (FSAS), a 10-item validated, widely used measure of ICD-specific adjustment that assesses feared stimuli and avoidance behaviors (e.g., "I am scared to exercise because it may increase my heart rate and cause my device to fire").[5] Respondents rated items on a five-point scale. Items were summed according to scoring guidelines to obtain a total score ranging from 10 to 50, with higher values indicating greater shock anxiety. FSAS questionnaires were included in the analysis when at least 7 of the 10 questions were answered. For questionnaires with missing answers the summary score was normalized by multiplying with 10/(number of answered questions).

Statistics

Quality of life was prospectively defined as a secondary objective in PainFree SST. Activity was later added as an outcome parameter.

Categorical parameters are presented with count and percentage, or percentage alone. For statistical comparison between two groups, a Fisher's exact test or a Cochran-Mantel-Haenszel test for trend was used. Continuous parameters are presented with mean value and standard deviation, and compared between groups using a Student's t-test.

Daily activity records for all patients included device type, time since implant, being hospitalized (yes/no), experienced earlier shocks (yes/no), and time since most recent shock. Analysis of activity used linear mixed regression models with daily values as unit of analysis. These had a random intercept for patient and an auto-regressive structure for correlation of

subsequent measurements from individual patients. A sandwich variance estimator was used as an additional correction for repeated measurements in patients. A base model included device type and time since implant as a piecewise linear covariate with knots at selected time-points post-implant (30, 60, 90, and 365 days post-implant). Follow-up data were restricted to the first 24 months. Subsequent analyses were done adding variables to the base model. The effect of hospitalization was estimated as the average difference in activity between days hospitalized and days not hospitalized, corrected for device type and time since implant. The effect of ICD shocks was assessed from an indicator variable identifying whether or not there was an earlier shock and a piecewise linear covariate for time since shock with knots at 30, 60 and 90 days post-shock. The effect of ATP was analyzed similarly. Analyses of the effect of shocks and ATP were corrected for device type, time since implant, and the effect of hospitalization. Effects are reported with 95% confidence intervals (CI).

Analysis of FSAS and EQ5D Health Score used a similar modeling approach with patient visit as the unit of analysis, using a compound symmetry correlation structure. Local regression (LOESS) was used for the figures. Statistical analysis of the different dimensions of EQ5D before and after shock used ordinal logistic regression models with GEE variance adjustment that included all questionnaires from baseline and scheduled follow-up visits with an indicator variable for earlier shocks.

All analyses were done in SAS version 9.4 (SAS Institute, Cary, NC, USA). P-values <0.05 were considered significant.

Results

Baseline Characteristics

A total of 2,770 patients were followed for 22 ± 9 months. Clinical characteristics of the patients are shown in Table 1. ICD shock was more prevalent among patients who were male, implanted for secondary prevention, taking anti-arrhythmic drugs, or had a prior history of

atrial fibrillation (AF). Compared to patients with only appropriate shocks, patients with any inappropriate shock were more likely to have a history of AF, and less likely to have a history of coronary artery disease, atrioventricular block, coronary artery bypass grafting, or myocardial infarction.

In total, 915 arrhythmic episodes were extracted from device memory, in which 289 patients received ICD shocks (0.21 episodes per patient year). This included 804 episodes for which electrocardiograms were available and that were adjudicated: 115 inappropriately shocked episodes in 70 patients and 689 appropriately shocked episodes in 234 patients. Additionally, there were 111 shocked episodes in 17 patients where electrocardiograms were not available due to limited device memory. For 15 of these 17 patients, there were other shocked episodes that had electrocardiograms available. Finally, 19 patients reported ICD shocks only at visits for which no device memory data was available. In total, 308 patients had shocks.

There were 6,017 arrhythmic episodes in 388 patients for which ATP was delivered (1.37 episodes per patient year). There were 1162 hospitalizations in 589 patients reported.

Association Between ICD Shock and Physical Activity

Daily activity data were available for 2,555 patients. Average daily physical activity was 185.3 ± 119.4 minutes per day.

Patient Activity Trends Over Time and the Acute Effects of Shock

There was a clear rise in physical activity during the first 90 days post-implant (+88.6 minutes/day, CI: 85.4 to 91.8, $p<0.0001$) followed by a gradual decline (-14.9 minutes/day between 3 and 24 months, CI: -17.7 to -12.1, $p<0.0001$).

Pre-shock activity levels of patients that experienced ICD shock during follow up did not differ significantly from activity levels of patients who did not receive shocks (193.6 ± 119.4 minutes/day vs 185.8 ± 119.0 minutes/day, $p=0.61$). Patients with a CRT-D device

were less active than ICD patients, 164.4 ± 110.7 versus 198.4 ± 122.6 minutes/day ($p<0.0001$; see Supplementary Figure S1 for activity values from baseline to 24 months). Corrected for device type there was no difference between primary and secondary prevention patients. Hospitalization was associated with a significant reduction in daily physical activity (75.3 ± 84.6 minutes/day in hospital compared to 185.9 ± 119.2 minutes/day out of hospital, $p<0.0001$).

The acute effects of ICD shock on activity are illustrated in Figure 1A. The data show that activity was significantly reduced after an ICD shock (-23.7 minutes/day when corrected for device type, time since implant, and the effect of hospitalization, CI: -30.2 to -17.2, $p<0.0001$) and recovered as time since shock increased (at 30 days post-shock, activity increased +10.1 minutes/day, CI: 4.1 to 16.0, $p=0.0010$). Post-shock activity reduction did not differ significantly between shocks with a hospitalization and shocks without a hospitalization (22.9 minutes/day vs. 19.6 minutes/day; $p=0.61$, Supplemental Figure 2).

Number of Prior Shocks

Activity reduction was associated with the number of prior ICD shocks, with 21.1 minutes/day decrease when there was exactly 1 prior shock, 27.4 minutes/day after 2-5 shocks, and 33.8 minutes/day after more than 5 shocks ($p=0.018$).

Appropriate vs. Inappropriate Shock

Activity reduction did not differ significantly between appropriate and inappropriate shocks (24.6 minutes/day, CI: 17.9 to 31.2, vs 20.2 minutes/day, CI: 6.0 to 34.5; $p=0.26$, Supplemental Figure 3).

Antitachycardia Pacing (ATP)

Figure 1B illustrates physical activity in the days before and after low-voltage pacing therapy (ATP). Activity was significantly reduced after ATP (-5.8 minutes/day relative to the

patient's overall average activity, CI: -11.4 to -0.13, p=0.045), although the magnitude of the effect is much smaller than for shocks.

Association Between ICD Shock and Quality of Life

Quality of life scores (EQ5D Health Score) before and after ICD shock are shown in Figure 2. Baseline average on the EQ5D Health Score was 66.8 ± 19.2. The EQ5D Health Score was lower for CRT-D patients than for ICD patients (64.8 ± 19.1 vs 67.9 ± 19.2, p<0.0001). Corrected for device type, there was no difference between primary and secondary prevention patients and there was also no difference in EQ5D Health Score at baseline between patients that did and did not experience subsequent ICD shock (67.5 ± 18.3 vs 66.7 ± 19.3; p=0.50).

Quality of Life Trends Over Time and the Acute Effects of Shock

Follow-up Health Score assessments were generally higher than baseline (de novo implants +7.0 points at 12 months; CI: 6.1 to 7.9, p=0.004), however there were significant decreases during hospitalization (-7.6 points; CI: -10.3 to -4.9, p<0.0001) and when there had been any earlier shock (-3.6 points; CI: -5.1 to -2.1, p<0.0001, Table 2).

The acute effects of ICD shock on quality of life were also examined by comparing the last assessment before and the first assessment after a patient's first shock episode. These data demonstrated a significant decrease in overall Health Score (68.2 ± 19.3 vs 65.2 ± 20.5; p = 0.029). EQ5D subscale scores before and after shock are reported in Supplemental Table 1. Shocks significantly impacted Anxiety/Depression, but not Mobility, Self-Care, Usual Activity, or Pain/Discomfort. Quality of life was also examined monthly for 6 months after the shock event (Figure 4 in the Data Supplement). Post-shock EQ5D Health Score increased as time since shock progressed, signifying improved perceived health (p=0.017).

Number of Prior Shocks

The number of prior shocks was associated with the Health Score such that, more shocks were associated with worse quality of life (p=0.01). The Health Score was reduced by 2.1 points when there was 1 prior shock, by 4.3 points after 2-5 shocks, and by 6.4 points after >5 shocks.

Appropriate vs. Inappropriate Shock

The decrease in Health Score was seen only after appropriate shocks (-3.9 points; p<0.0001); there was not a decrease after inappropriate shocks (-0.9 points; CI: -3.8 to 2.0, p=0.55).

Association Between ICD Shock and Shock Anxiety

Shock anxiety scores (FSAS scores) before and after ICD shock are presented in Figure 3. At baseline, the average FSAS score was 16.6 ± 8.0, comparable to existing norms.[5] There were no differences between ICD and CRT-D patients, nor between primary and secondary prevention. No baseline differences in FSAS scores were found between patients with and without subsequent shock (16.9 ± 7.6 vs 16.6 ± 8.0; p=0.69).

Shock Anxiety Trends Over Time and the Acute Effects of Shock

Follow-up FSAS assessments were generally lower than baseline (-2.8 points; CI: -3.1 to -2.5, p<0.0001) and not different during hospitalization (+1.0 points; CI: -0.4 to 2.3, p=0.17), but were significantly increased when there had been any earlier shock (+3.2 points; CI: 2.6 to 3.7, p<0.0001, Table 2).

The acute effects of ICD shock on shock anxiety were examined monthly for 6 months after the shock event (Figure 4). In patients with a prior ICD shock, proximity to the event was significantly associated with FSAS scores, such that greater time since shock was associated with lower FSAS scores and decreased shock anxiety (-0.4 points per months; CI: -0.5 to -0.3, p < 0.0001). However, even > 6 months after the ICD discharge, shock anxiety remained increased (+1.9 points; CI: 1.1 to 2.7, p<0.0001).

Number of Prior Shocks

The number of prior shocks had a significant impact on the FSAS score (p=0.002), FSAS scores increased by 3.3 points when there was 1 prior shock, 2.4 points after 2-5 shocks, and 5.3 points when there were >5 prior shocks. A higher number of shocks (1 shock vs. >5 shocks) was associated with a significant increase in shock anxiety (p=0.0074).

Appropriate vs. Inappropriate Shock

The increase in shock anxiety was larger after appropriate shocks compared to inappropriate shocks (3.3 vs 1.1 points; p=0.009), but was not significantly different when the patient was hospitalized (4.6 vs 3.0 points; p=0.11).

Discussion

This study is the first prospective examination of the acute and chronic effects of ICD shock on objective behaviors (i.e. accelerometer detected physical activity) and subjective quality of life outcomes (i.e. self-reported quality of life and shock anxiety) in a large, international cohort of ICD patients. The principal findings from this study are that ICD shock has immediate and long-term adverse effects on global and disease-specific quality of life. Furthermore, baseline device-detected daily physical activity was low in most ICD patients (approximately 3 hours per day) and significantly declined after ICD shock. Activity gradually increased as time since shock progressed and returned to pre-shock levels after approximately 90 days.

By integrating multiple diagnostic parameters to assess quality of life in ICD patients, the current study addresses major limitations of previously published trials. The Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) demonstrated the deleterious effect of ICD shock on quality of life in the month following a shock using a generic quality of life metric.[12] Our study extends these findings by describing both the acute and long-term impact of shock on behavioral and psychological recovery in ICD patients. Notably, our analyses

299 also accounted for device type, ICD indication, device-delivered therapy (shock vs. low
300 voltage pacing), hospitalization, and single vs. multiple ICD shocks. Collectively, these data
301 suggest that declines in quality of life after ICD shock persist beyond 30 days post-shock and
302 may be influenced by significant reductions in daily physical activity, increased general
303 anxiety, and shock anxiety. Generic components of health-related quality of life including
304 mobility, self-care, activity, and pain were not sensitive to these changes, suggesting that
305 shock anxiety and device-based activity data may be more useful measures of ICD-specific
306 outcomes.

307 The current study builds on earlier work demonstrating the reliability, utility, and
308 significance of device-detected activity data as a prognostic indicator of clinical outcomes.[9,
309 10, 13] In a study of heart failure patients with implanted cardiac devices, Cowie et al. found
310 low levels of device-detected activity to be independently associated with a 2.5-fold increase
311 in risk for hospitalization within the next 30 days.[13] Additionally, recent data from the
312 ALTITUDE Activity Study demonstrated lower baseline physical activity was associated
313 with a 40% absolute increase in mortality 4 years after implant.[10] Low levels of baseline
314 physical activity found in this study (185.3 ± 119.4 minutes per day) are comparable to
315 activity data reported by Kramer et al. (107.5 ± 66.2 minutes per day). However, that study
316 did not adjust for hospitalization in their activity analyses and thus, our findings provide
317 important clarification of hospital vs. non-hospital activity data.

318 Results from the current study also demonstrate the immediate and lasting effects of
319 ICD shock on physical activity and illustrate the significant amount of time (approximately 3
320 months) it takes patients to return to baseline levels of activity after ICD shock. Given the
321 known associations between low levels of physical activity, psychological functioning, and
322 adverse cardiac events, it is reasonable to assume that ICD patients who experience shock
323 and a prolonged decline in physical activity may have an increased risk for hospitalization,

morbidity, and mortality. Whether device activity could serve as a behavioral "early warning" system to prevent adverse outcomes is unknown but potentially viable, and could be examined in future research.

Limitations

Several limitations should be considered when interpreting these findings. First, the use of self-reported measures is subject to multiple sources of bias including self-presentation bias, the effects of practice or fatigue, and regression to the mean. Second, ICD accelerometers do not provide information concerning activity intensity or type of movement. Third, participants in this study were enrolled in a clinical trial of a single vendor using one brand of ICDs. Moreover, there was no independent validity check on the accelerometer data but such data exists in the literature.[11] Additionally, our sample included patients from the original Painfree SST trial with new implants, upgrades, and replacements and it is possible that device history or prior shock may have influenced study outcomes. However, we note that 67% of our sample was de novo implants. Finally, it is possible that the higher frequency of measurement of activity compared to FSAS and EQ5D measurement frequency contributed to the increased sensitivity to capture the effect of a shock.

Conclusions

This large prospective study of ICD patients demonstrated that ICD shock has immediate and long-term effects on objective and subjective indicators of health, including device measured physical activity, quality of life, and shock anxiety. These results lend further credibility to consideration of patient activity as an important quality of life outcome and support the need for further research and targeted patient and provider interventions to optimize clinical management.

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348

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401 **Figure Legends**

402 **Figure 1.** Averaged daily activity in relation to time before or after ICD shock (panel A) or
403 ATP therapy (panel B). The horizontal line represents the overall average activity excluding
404 measurements from the first 90 days post-implant or within 90 days before and 90 days after
405 a shock.

406

407 **Figure 2.** Quality of life (EQ5D Health Score) at scheduled follow-up visits, before and after
408 ICD shock. The horizontal line represents the average Health Score from scheduled follow-
409 up visits when there was no earlier shock.

410

411 **Figure 3.** Shock anxiety (FSAS scores) before and after ICD shock. The increase of the score
412 after a shock is significant ($p<0.0001$), indicating worse shock anxiety following ICD shock.
413 The horizontal line represents the average FSAS score from scheduled follow-up visits when
414 there was no earlier shock.

415

416 **Figure 4.** FSAS score decreases when the ICD shock is longer ago, signifying lower anxiety
417 ($p<0.0001$). The horizontal line represents the average FSAS score from scheduled follow-up
418 visits when there was no earlier shock.

419 **Tables**

420 **Table 1:** Patient Characteristics

421

Patient Characteristics	**All patients (N = 2770)**	**Any Shock (N = 308)**	**Inappropriate Shock (N = 70)**
Demographics and Clinical Presentation			
Geography			
North America	1129 (41%)	93 (30%)	18 (26%)
Europe	1056 (38%)	134 (44%)	28 (40%)
Other	585 (21%)	81 (26%)	24 (34%)
Male	2200 (79%)	265 (86%)	55 (79%)
Age (years)	65 ± 12	64 ± 13	62 ± 13
LVEF (%)	32 ± 13	33 ± 14	36 ± 16
QRS (ms)	126 ± 33	128 ± 33	121 ± 28
Secondary prevention	847 (31%)	151 (49%)	23 (33%)
NYHA class			
I	419 (15%)	58 (19%)	14 (20%)
II	1104 (40%)	124 (40%)	28 (40%)
III	853 (31%)	85 (28%)	19 (27%)
IV	38 (1%)	4 (1%)	0 (0%)
No Heart Failure	354 (13%)	36 (12%)	8 (11%)

Patient Characteristics	All patients (N = 2770)	Any Shock (N = 308)	Inappropriate Shock (N = 70)
History			
Coronary artery disease	1745 (63%)	185 (60%)	30 (43%)
Myocardial infarction	1048 (38%)	118 (38%)	14 (20%)
Congestive heart failure	1060 (38%)	98 (32%)	19 (27%)
Hypertension	1444 (52%)	145 (47%)	35 (50%)
Valve dysfunction	697 (25%)	83 (27%)	14 (20%)
Coronary artery bypass graft (CABG)	658 (24%)	75 (24%)	8 (11%)
Previous device, any	923 (33%)	96 (31%)	22 (31%)
Arrhythmias and Conduction Defects			
Atrial fibrillation	818 (30%)	119 (39%)	35 (50%)
Ventricular tachycardia, (incl. non-sustained)	991 (36%)	171 (56%)	37 (53%)
AV block	404 (15%)	45 (15%)	2 (3%)
Left bundle branch block	699 (25%)	75 (24%)	16 (23%)
Right bundle branch block	215 (8%)	35 (11%)	6 (9%)
Device			
CRT-D	1071 (39%)	113 (37%)	22 (31%)
DR ICD	948 (34%)	114 (37%)	26 (37%)
VR ICD	751 (27%)	81 (26%)	22 (31%)

Patient Characteristics	All patients (N = 2770)	Any Shock (N = 308)	Inappropriate Shock (N = 70)
Medication			
ACE-inhibitor or ARB	2133 (77%)	240 (78%)	58 (83%)
Beta-Blocker	2370 (86%)	263 (85%)	63 (90%)
Diuretic	1886 (68%)	206 (67%)	48 (69%)
Statin	1673 (60%)	186 (60%)	35 (50%)
Anti-Arrhythmic	519 (19%)	88 (29%)	13 (19%)

Numbers are n (%) or mean ± standard deviation.

Abbreviations: ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; AV: atrio-ventricular; CRT-D: cardiac resynchronization therapy defibrillator; DR-ICD: dual-chamber implantable cardioverter defibrillator; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; VR-ICD: single chamber implantable cardioverter defibrillator.

429 **Table 2**. The effect of hospitalization and ICD shock on EQ5D Health Score and FSAS

	EQ5D Health Score value / change (CI)	p-value	FSAS value / change (CI)	p-value
Baseline ICD patients*	65.8 (64.9 to 66.7)		17.3 (16.9 to 17.6)	
CRT-D	- 2.3 (-3.5 to -1.1)	0.0001	--	(0.10)**
Follow-up (12 months)*	+ 7.0 (6.1 to 7.9)	< 0.0001	- 2.8 (-3.1 to -2.5)	< 0.0001
In hospital	- 7.6 (-10.3 to -4.9)	< 0.0001	--	(0.13)**
Earlier shock	- 3.6 (-5.1 to -2.1)	< 0.0001	+ 3.2 (2.6 to 3.7)	< 0.0001

430 Abbreviations: CRT-D= Cardiac resynchronization therapy defibrillator; FSAS=Florida
431 Shock Anxiety Scale; ICD=Implantable cardioverter defibrillator
432 *For de novo implanted patients
433 **Variable removed from final model; p-value from expanded model
434 †For example, the average EQ5D Health Score of a CRT-D patient at 12 months after device
435 implantation would be 65.8 – 2.3 + 7.0 = 70.5. If such patient had a prior shock and was
436 hospitalized, the Health Score would be (3.6+7.6=) 11.2 points lower.

Figure 1A

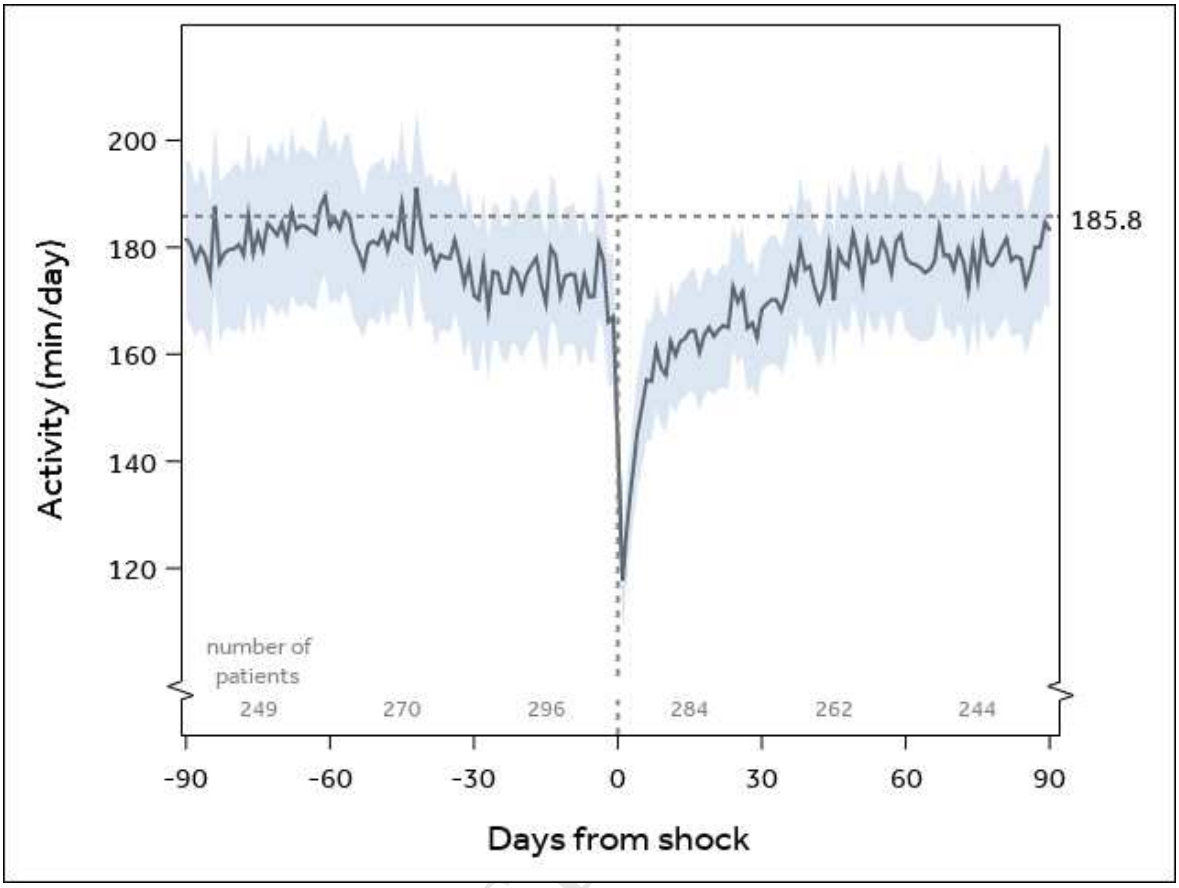

Figure 1B

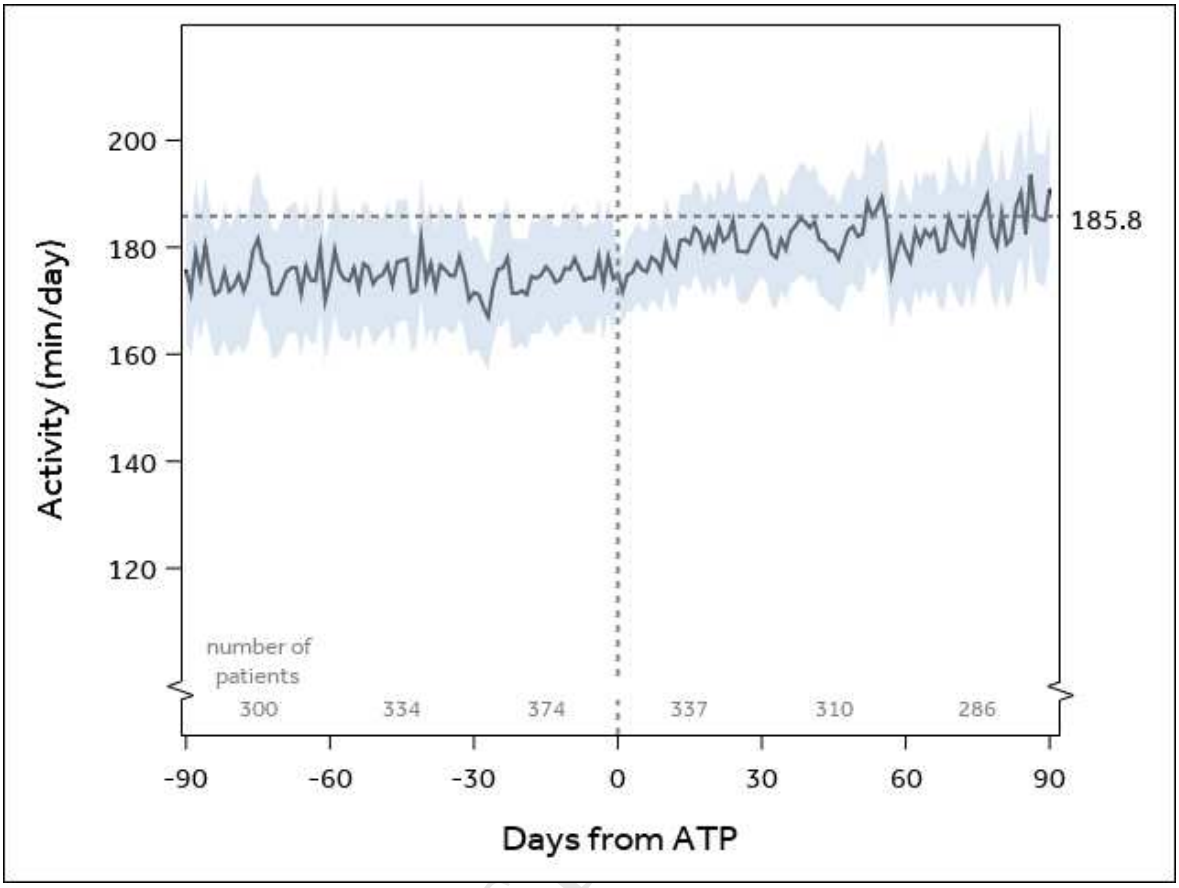

Figure 2

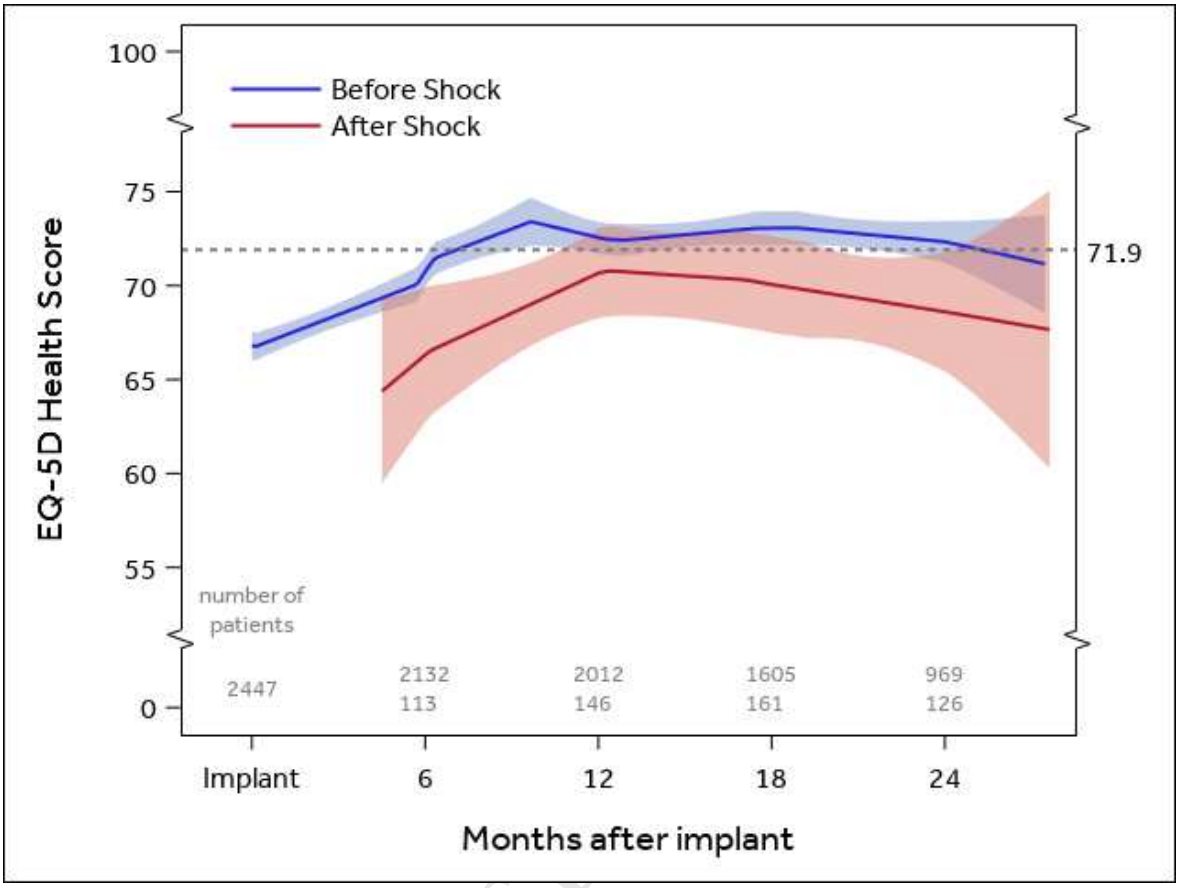

Figure 3

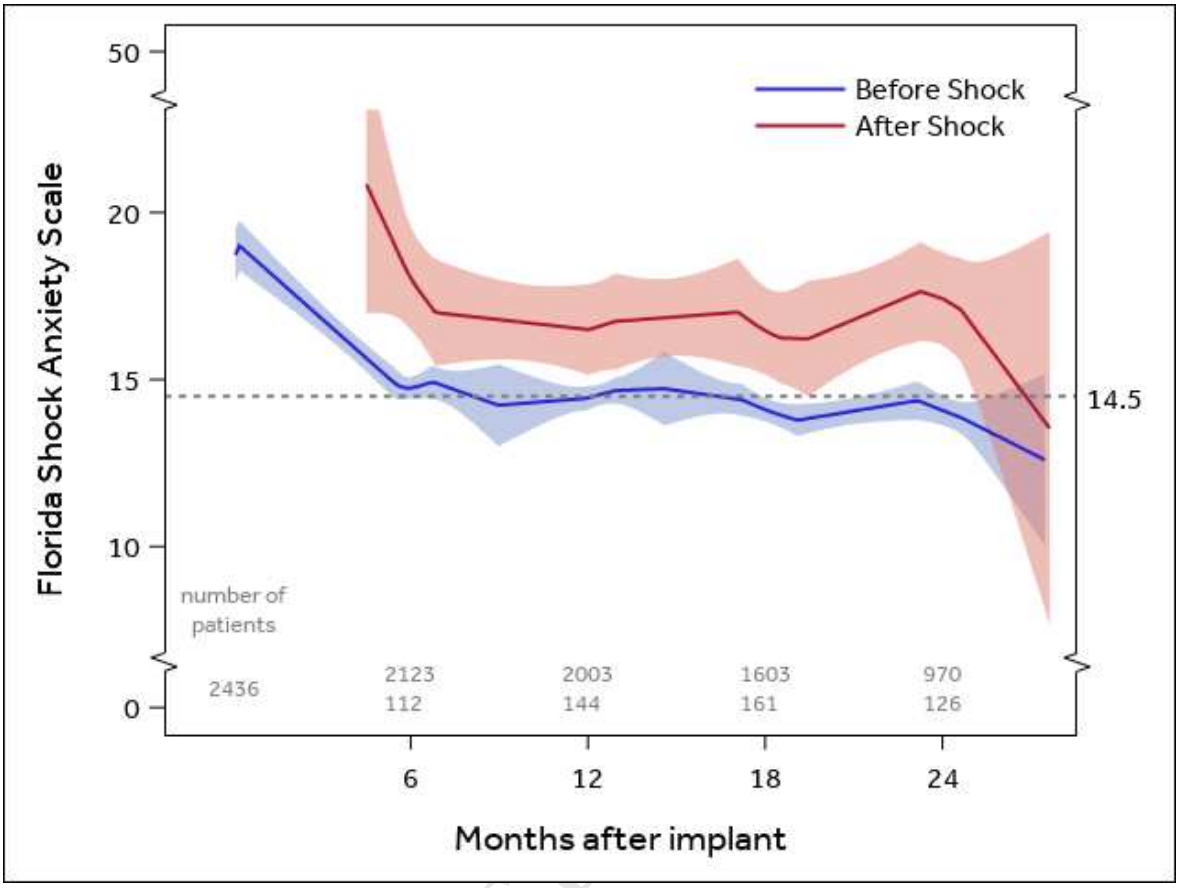

Figure 4