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Worldwide experience with a totally subcutaneous implantable defibrillator: early results from the EFFORTLESS S-ICD Registry

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Aims The totally subcutaneous implantable-defibrillator (S-ICD) is a new alternative to the conventional transvenous ICD system to minimize intravascular lead complications. There are limited data describing the long-term performance of the S-ICD. This paper presents the first large international patient population collected as part of the EFFORTLESS S-ICD Registry.

Methods and results The EFFORTLESS S-ICD Registry is a non-randomized, standard of care, multicentre Registry designed to collect long-term, system-related, clinical, and patient reported outcome data from S-ICD implanted patients since June 2009. Follow-up data are systematically collected over 60-month post-implant including Quality of Life. The study population of 472 patients of which 241 (51%) were enrolled prospectively has a mean follow-up duration of 558 days (range 13–1342 days, median 498 days), 72% male, mean age of 49 $\pm$ 18 years (range 9–88 years), 42% mean left ventricular ejection fraction. Complication-free rates were 97 and 94%, at 30 and 360 days, respectively. Three hundred and seventeen spontaneous episodes were recorded in 85 patients during the follow-up period. Of these episodes, 169 (53%) received therapy, 93 being for Ventricular Tachycardia/Fibrillation (VT/VF). One patient died of recurrent VF and severe bradycardia. Regarding discrete VT/VF episodes, first shock conversion efficacy was 88% with 100% overall successful clinical conversion after a maximum of five shocks. The 360-day inappropriate shock rate was 7% with the vast majority occurring for oversensing (62/73 episodes), primarily of cardiac signals (94% of oversensed episodes).

Conclusion The first large cohort of real-world data from an International patient S-ICD population demonstrates appropriate system performance with clinical event rates and inappropriate shock rates comparable with those reported for conventional ICDs. Clinical trial registration URL: http://www.clinicaltrials.gov. Unique identifier NCT01085435.

Keywords Subcutaneous ICD • Ventricular arrhythmias • Cardiac arrest • Primary prevention • Secondary prevention

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Introduction

Sudden cardiac death (SCD) occurs in ~50 000–70 000 patients annually in the UK, proportionate numbers of patients in other European countries and >350 000 patients in the USA.[1] Implantable cardioverter-defibrillators (ICDs) were first introduced into clinical practice in 1980[2] and since then multiple randomized, multicentre trials have shown significant survival benefits in primary and secondary prevention populations.[3–6] Despite the recognized mortality benefit, there are significant co-morbidities associated with ICD therapy especially in young primary prevention patients due to the high incidence of acute and chronic transvenous lead complications.[7,8] These include systemic infections, acute and chronic displacement, pneumothorax, cardiac perforation, and tamponade as well as inappropriate shocks associated with insulation failure or lead fractures.[9,10] Cumulative data suggest that there may be at least a 20% risk of transvenous lead failure at 8–10 years post-implant[11,12] and complication rates may also be higher in the paediatric ICD population where long term (5–12 year) reports indicate rates of at least 40%.[13,14] Since complications increase with multiple procedures, this further places younger ICD patients at considerable risk of long-term device-related morbidities.

The entirely subcutaneous ICD system (S-ICD System, Cameron Health/Boston Scientific) was developed to provide an alternative to the transvenous ICD system, as it is implanted with no transvenous/epicardial leads. Early studies demonstrating its feasibility and safety have been published[15] as well as small cohorts, single country, and individual case studies.[16–21] However to date, there is no long-term 'real-world' data demonstrating the performance of the system in a multicentre, heterogeneous ICD population. The purpose of the ongoing *E*valuation o*F* *FactORs* Impac*T*ing *CL*inical Outcome and Cost *E*ffectiveneS*S* of the S-ICD (EFFORTLESS S-ICD) Registry is to document clinical-, system-, and patient-related outcome data from S-ICD patients implanted since the commercial release of the S-ICD.[22] This paper documents the early results from the EFFORTLESS S-ICD Registry.

Methods

Registry design

The EFFORTLESS S-ICD Registry is an observational, non-randomized, standard of care evaluation currently being conducted in geographies outside the USA where the S-ICD is approved for use and distribution since CE Marking in 2009.[22] The Registry is conducted according to the Helsinki Declaration and ISO 14155:2009. Currently seven countries are actively participating (The Czech Republic, Denmark, Germany, Italy, The Netherlands, New Zealand and the UK). All the patients provide informed consent according to National and Institutional regulations. Patients are followed as per Institutional standards for up to 60-months post-implant. All scheduled and unscheduled follow-ups for the first-year post-implant are recorded, while in years 2–5 post-implant there is a minimum annual follow-up data requirement (including all adverse events, spontaneous arrhythmia episodes, and programming changes). Patients are enrolled prospectively and retrospectively.[22]

Specific contraindications include class I indications for permanent pacing, pace-terminable ventricular tachycardia, and previously implanted functional unipolar pacing system.

Induced and spontaneous episodes

Owing to the variability in acute defibrillation testing protocols at each clinical site, successful conversion efficacy at implant is defined for the Registry as at least one successful conversion of an induced ventricular arrhythmia at ≤80J. Two patients were tested only at energies <65J, all other patients had at least one Defibrillation Threshold Test (DFT) performed at ≥65J. A total of 10 patients had any testing done at <65J. All spontaneous episodes with documented stored electrogram evidence were evaluated to determine whether they were ventricular or supraventricular as opposed to noise or extra-cardiac physiological activity. Delivery of shock therapy was deemed appropriate if delivered to a ventricular arrhythmia (VT/VF) at a rate within the programmed conditional or shock zone. Therapy was labelled inappropriate if delivered to sinus rhythm (e.g. for T-wave oversensing; myocardial potentials; Electro-magnetic interference (EMI)) or to any supraventricular arrhythmia (SVT) including those with an intrinsic rate within the conditional and programmed shock zone.

Statistical and data analysis

Baseline demographics and clinical variables, including medical history, risk factors, co-morbidities, and NYHA functional class for heart failure, are presented as available. Continuous variables are summarized as means, standard deviations, medians, and ranges. Categorical variables are summarized as frequencies and percentages. Two-sided *P*-values for the difference between prospective and retrospective cohorts were determined using a Student's *t*-test for numerical comparisons and using Pearson's χ^2 test for categorical comparisons. Complication-free rates are analysed using the Kaplan–Meier (KM) estimate. All statistical analyses were performed and independently validated using SAS Enterprise Guide, version 5.1 (SAS 9.3). A two-sided *P*-value of <0.05 was considered significant.

Results

Patient demographics

Baseline patient characteristics, medications at the time of initial implant of the S-ICD System, cardiac history, and co-morbidities for all enrolled patient are summarized in *Table 1*. There is a broad spectrum of patients with a significant proportion of congenital heart disease, ion channelopathy and non-ischaemic cardiomyopathy patients, distinguishing this population from standard ICD cohorts. The characteristics of the three patients withdrawn due to inclusion/exclusion criteria violation are not included in the analysis.

The mean age of patients at implant was 49 ± 18 years (range 9–88 years), the majority was male (72%) and the mean left ventricular ejection fraction was 42% ± 19%. The majority of study patients (63%) had a primary prevention indication of which 40% were ischaemic. Documented co-morbidities included congestive heart failure (29%), hypertension (24%), ischaemic heart disease (37%), diabetes (12%), renal disease (9%), and atrial fibrillation (17%). Sixty-seven patients (15%) had been previously implanted with a transvenous ICD system and 13 patients had a concomitant pacemaker.

Patient status

The data set presented reflects the information available at the time of analysis (data cut-off 23 April 2013) from 472 patients with at least an enrolment and/or implant data set in the database. Patients were enrolled between 2 Feb 2011 and 15 Apr 2013 at 29 clinical sites in Europe and New Zealand (see *Figure 1*). A total of 241 patients

Table 1 Baseline patient characteristics at the time of initial subcutaneous implantable defibrillator system implant[a]

Characteristic	Retrospective		Prospective		ALL		*P*-value[b]
	n	Value	*n*	Value	*n*	Value	
Age at implant, years	216	47 ± 18	234	51 ± 17	450	49 ± 18	0.02
Age range, years		9–86		15–88		9–88	
Male, *n* (%)	216	149 (69)	234	174 (74)	450	323 (72)	0.21
LVEF, %	164	44 ± 18	184	40 ± 19	348	42 ± 19	0.045
QRS interval, ms	191	104 ± 21	215	109 ± 32	406	107 ± 28	0.07
Primary prevention, *n* (%)	216	141 (65)	233	141 (61)	449	282 (63)	0.30
Clinical disease, *n* (%)	214		231		445		
Ischaemic cardiomyopathy		70 (33)		96 (42)		166 (37)	0.05
Idiopathic VF		16 (7)		18 (8)		34 (8)	0.90
Inherited channelopathies		36 (17)		24 (10)		60 (13)	0.05
Congenital heart disease		24 (11)		9 (4)		33 (7)	0.003
Non-ischaemic cardiomyopathy		63 (29)		76 (33)		139 (31)	0.43
Dilated		19		24		43	
HCM		29		29		58	
ARVC		5		12		17	
Myocarditis		2		0		2	
Non-dilated		2		3		5	
Other		6		8		14	
Other		5 (2)		8 (3)		13 (3)	0.48
Comorbidities, *n* (%)							
Hypertension	212	50 (24)	234	56 (24)	446	106 (24)	0.93
Atrial fibrillation	209	27 (13)	233	49 (21)	442	76 (17)	0.01
Congestive heart failure	211	53 (25)	232	75 (32)	443	128 (29)	0.09
NYHA I		11		13		24	
NYHA II		19		33		52	
NYHA III		9		25		34	
Diabetes	210	19 (9)	234	34 (15)	444	53 (12)	0.08
Kidney disease	210	14 (7)	233	25 (11)	443	39 (9)	0.13
Concomitant pacemaker	214	5 (2)	233	8 (3)	447	13 (3)	0.49
Previous transvenous ICD	214	30 (14)	233	37 (16)	447	67 (15)	0.58
Cardiac medications, *n* (%)	214	167 (78)	234	200 (86)	448	367 (82)	0.04
Beta-blocker		125 (75)		155 (78)		280 (76)	0.09
ACE/ARBs		98 (59)		124 (62)		222 (61)	0.13
Diuretic		71 (43)		91 (46)		162 (44)	0.21
Anticoagulant/antiplatelet		98 (59)		124 (62)		222 (61)	0.13
Statins/other lipid lowering		31 (19)		55 (28)		86 (23)	0.02

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker, ARVC, arrhythmogenic right ventricular dysplasia with risk for sudden cardiac death; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator, LVEF, left ventricular ejection fraction, NYHA, New York Heart Association heart failure classification, S-ICD, subcutaneous implantable cardioverter-defibrillator; VF, ventricular fibrillation.

[a]Values are number of patients *n*(percentage, %) or mean ± standard deviation unless otherwise noted.

[b]*P*-value computed for difference between prospective and retrospective cohorts.

(51%) were enrolled prospectively and of these, 232 (96%) were included in the Quality of Life substudy that will be reported later. The mean follow-up duration of all implanted patients ($n = 456$) was 558 days with a range of 13–1342 days (median = 498 days) giving a cumulative follow-up duration of 254 578 days. A small number of the patients have already previously been reported as part of local, S-ICD experience reports.[17] *Figure 2* shows the status of the Retrospective and Prospective patients in the Registry. Of the patients included, six were withdrawn prior to implant due to inclusion/exclusion criteria violations ($n = 3$), patient decision ($n = 1$), and investigator decision ($n = 2$). Nine patients have died during the course of the Registry (2%). None of the deaths occurred in the peri-operative period (i.e. within 30-day post-implant) although one remains of unknown cause due to lack of documentation.

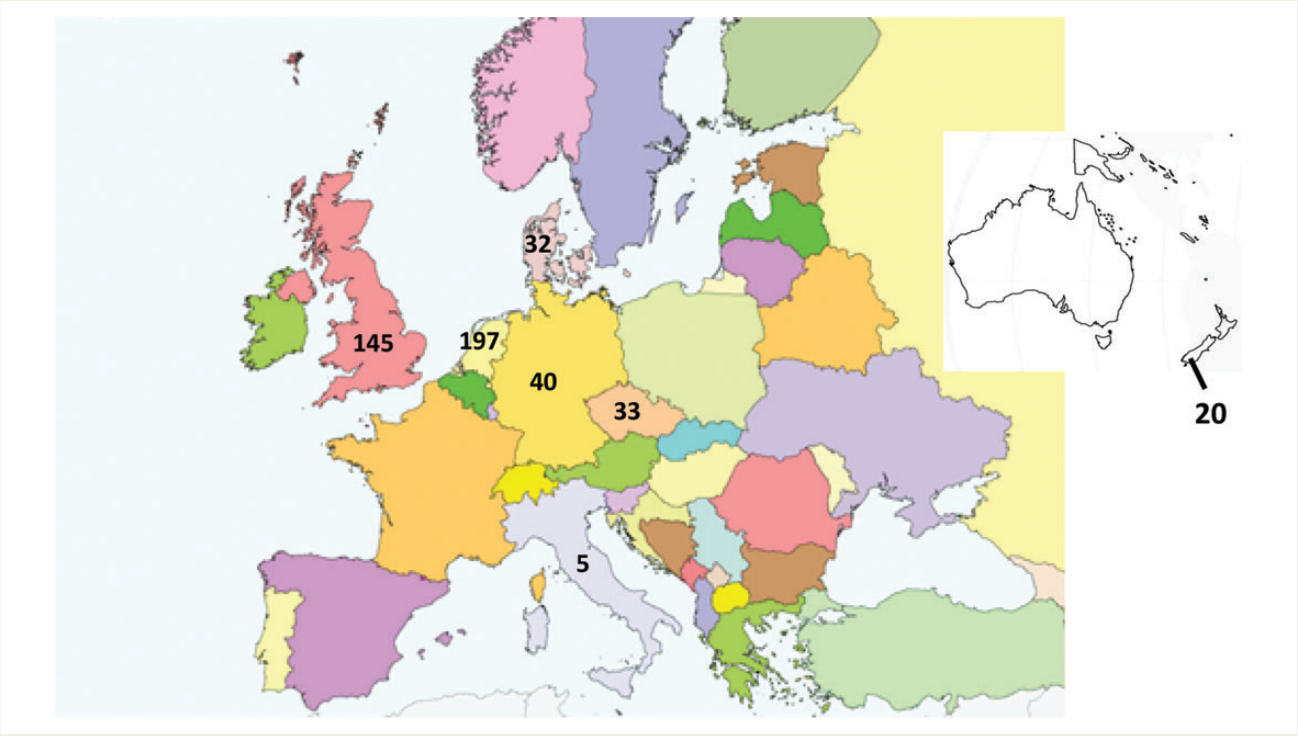


Figure 1 EFFORTLESS Subcutaneous Implantable Defibrillator Registry enrolment by country in Europe and Australasia (inset).

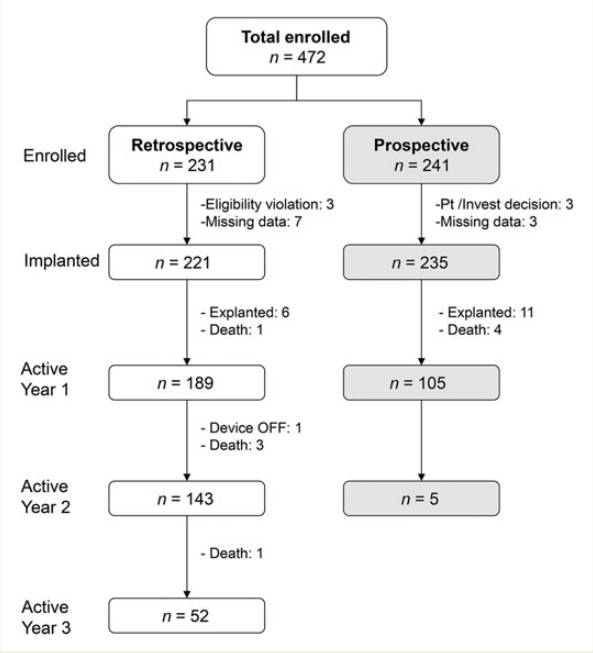


Figure 2 Patient flow chart for EFFORTLESS Subcutaneous Implantable Defibrillator Registry.

Of the remaining 8 patients, 4 died from pump failure, 1 from kidney disease, 1 from respiratory failure, and 1 from bronchopneumonia and stroke secondary to heart failure. One patient died after an apparent extended period of asystole/bradycardia followed by an appropriately detected and treated VF episode that failed to convert. The patient received an additional 11 shocks, none of which was able to convert the arrhythmia. In this patient, the defibrillation test directly after implant had been successful. None of the deaths has been reported to be related to the S-ICD system or implant procedure.

Explants have been documented in 17 patients (3.7%) due to infection ($n = 8$), decubitus/erosion ($n = 1$), heart transplant ($n = 1$), failure to convert induced episodes at initial implant ($n = 1$), failure to convert spontaneous episodes ($n = 1$), inappropriate sensing ($n = 1$), elective decision after inappropriate shocks ($n = 1$), replacement of the S-ICD system by a transvenous ICD system due to recurrent VT ($n = 2$) and patient decision due to pain ($n = 1$). Additionally, one patient had the device turned OFF due to T-wave oversensing and recurrent inappropriate therapy. One-year follow-up was completed in 294 patients (189 retrospective; 105 prospective) with 143 and 52 retrospective patients reaching 2- and 3-year follow-up, respectively. Five prospective patients have reached 2-years of follow-up.

Implant procedure

Where procedural information was available, general anaesthesia was used in the majority of S-ICD implantation procedures (273/432; 63%) with an average procedure time ('skin to skin') of 69 $\pm$ 27 min (median 61 min). No distinction was made in the database between procedure times that were solely for implant of the S-ICD vs. those that included additional procedures such as concomitant removal of a transvenous system or implant of a pacemaker. In the majority of cases where information was available no cardiac imaging was used for placement of the S-ICD system (310/356; 87%).

Implant conversion testing

Four hundred and ten of 456 patients had available documented VT/VF conversion testing data performed either acutely or within days of implant. In eight cases information was incomplete, while in nine patients VT/VF was not inducible. Of the 393 patients with complete data, in all but 1 patient VT/VF was successfully converted (99.7%). Seven of these patients had an initial conversion failure that required one or more procedures to reposition the system to become successful. A shock energy of ≤65J was successful in 95% of patients. The 95% CI for DFT conversion efficacy is 99.7% (99.2, 100%).

Spontaneous episodes

Appropriate therapy

A total of 317 spontaneous episodes in 85 individual patients were recorded during the follow-up, of which 169 episodes received therapy in 59 patients (see *Table 2* and *Figure 3*). Of the 145 classified untreated episodes, 93 were adjudicated as inappropriate sensing, 37 were non-sustained VT/VF, 12 were non-sustained SVT above discrimination zone (three are unclassified).

Table 2 Spontaneous episodes recorded and classified by the subcutaneous implantable defibrillator system

S-ICD system performance	Number of episodes	Number of patients (% of 456)
Therapy delivered	169	59 (13)
Appropriate therapy	93	33 (7.2)
VT/VF discrete episodes	51	29
VT/VF 'storm' episodes	40	4
VT/VF conversion prior to shock	2	2
Inappropriate therapy[a]	73	32 (7.0)
SVT above discrimination zone	10	6
Inappropriate sensing (cardiac)[b]	58	24
Inappropriate sensing (non-cardiac)	4	4
VF/SVT discrimination error	1	1
Rhythm unclassified[c]	3	1
Therapy withheld[d]	145	61 (13)
Episode unclassified[e]	3	3
Total	317	85 (19)

SVT, supraventricular tachyarrhythmia; VF, ventricular fibrillation; VT, ventricular tachyarrhythmia.
[a]Three patients had multiple episodes of different types. Two patients had episodes of both cardiac and non-cardiac inappropriate sensing and one patient had episodes of cardiac oversensing and discrimination error.
[b]Oversensing due to P-waves, wide QRS, T-waves, low amplitude signal, and unspecified.
[c]Unclassified episodes where treatment was provided, but no S-ECG source documentation was retained in order to make a full classification of the treated episode.
[d]Appropriate charge with spontaneous termination of VF/VT, inappropriate charge for SVT above discrimination zone or inappropriate sensing.
[e]Unclassified episodes that could not be classified as either treated or un-treated episodes due to incomplete data at the time of data cut.

Non-sustained episodes of VT/VF

There were 37 episodes of non-sustained VT/VF which did not last longer than the initial detection phase of the device algorithms and therefore were not treated. Two VT/VF episodes spontaneously converted after confirmation and charging but prior to delivery of a shock.

Sustained episodes of VT/VF

Ninety-one episodes (53%) in 33 patients were classified as sustained VT/VF—51 were discrete episodes ($n = 29$ patients) and 40 were episodes recorded during VT/VF 'storms' (defined as ≥3 treated VF/VT episodes within 24 h). Of the 51 discrete episodes receiving therapy, 45 converted to sinus rhythm either immediately or within a few seconds after the first shock (type 2 break, $n = 3$) giving a first shock conversion efficacy of 88%. In the remaining 6 episodes, >1 shock was required to achieve cardioversion to sinus rhythm. The overall shock conversion efficacy per protocol definition of successful conversion within one device-defined episode and five shocks was 96% (49/51 episodes). However, in one patient defined as a failure per protocol, conversion occurred shortly after the fifth shock (but outside of the Electrogram storage time) and in the second, a short period of undersensing resulted in an episode being ended inappropriately by the device after two failed shocks, only to be re-initiated immediately after with one subsequent, successful shock. Clinically, therefore the discrete VT/VF conversion efficacy was 100% since all episodes were converted.

Six VT/VF storm events in 4 patients resulted in the 40 episodes. One renal dialysis patient had multiple VT/VF storm events over a period of 17-month post-implant and subsequently died due to pump failure. In one case of a patient with Loeffler's syndrome, the VF storm was preceded by a 10 min period of bradycardia (lowest heart rate of 28/min in the 60 s pre-arrest). The VF that subsequently developed was not successfully defibrillated, and the patient died. This unusual patient had obliteration of the RV and LV apices by a mass and was not deemed suitable for a standard ICD system. At implant VF had been sensed appropriately and cardioverted at 65J.

Inappropriate shocks

A total of 73 inappropriate shocks were recorded in 32 patients over an average follow-up of 18 months (360 day inappropriate shock rate of 7%, *Table 2* and *Figure 3*). The majority of inappropriate shocks was due to oversensing (85%) most frequently of cardiac signals (94% of oversensed episodes) mainly consisting of T waves or low amplitude signals (31 and 53% of cardiac oversensed episodes, respectively). In four patients, inappropriate shocks were due to noise or EMI while six patients had inappropriate therapy due to SVT rates that crossed into the shock-only zone. There was one episode of discriminator error, in which morphology was impacted by a clipped signal.

Impact of programming

Four hundred and thirty-one patients had their device programming documented at implant. Three hundred and fifty-seven (82%) had dual zone programming and 74 (17%) had single zone shock-only programming. Supplementary material online, *Appendix S1* shows

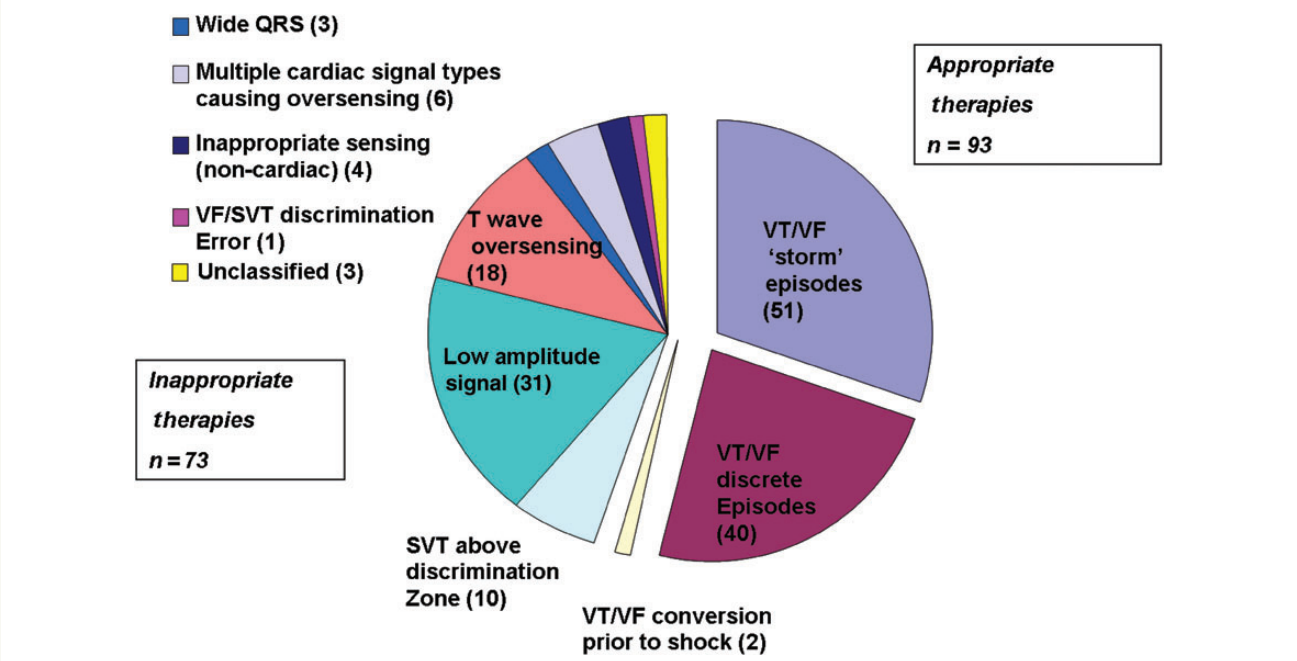


Figure 3 Proportion of appropriate and inappropriate therapies and their aetiologies (three other unclassified treated episodes are excluded in the figure as they that could not be classified as either treated or untreated episodes). Numbers in brackets represent number of patients.

Table 3 Subcutaneous implantable defibrillator system and/or implant procedure-related complications requiring intervention

Complication	Number of events	Patients *n* (%)
Erosion or extrusion of implanted electrode or pulse generator	4	4 (0.9)
Haematoma	1	1 (0.2)
Failure to convert spontaneous VF episode	1	1 (0.2)
Inability to communicate with device	1	1 (0.2)
Inappropriate shock: oversensing	2	2 (0.4)
Incision/superficial infection	2	2 (0.4)
Near syncope/dizziness/shortness of breath/confusion	1	1 (0.2)
Pleural effusion	1	1 (0.2)
Pneumothorax	1	1 (0.2)
Premature battery depletion	1	1 (0.2)
Shock delivered for non-VT/VF	1	1 (0.2)
System infection	12	11 (2.4)
Suboptimal electrode position/electrode movement	5	5 (1.1)
Suboptimal pulse generator position	1	1 (0.2)
Suture discomfort	1	1 (0.2)
Total complications (% of 456)	35	29 (6.4)

the distribution of all programming at implant. Three hundred sixty-two patients (84%) were programmed with a shock zone of ≥220 b.p.m. Similar proportions of patients were programmed with primary (50%) and secondary (39%) sensing vectors and very few were programmed with the alternative sensing vector (10%). Almost all the patients (94%) were programmed with gain set at 1×. As previously stated, 32 patients (7.0%) received a total of 73 inappropriate shocks. Only nine patients (2%) experienced recurrent inappropriate shocks following initial interventions (reprogramming and/or exercise test-guided adjustments and one medication change). Eight of these nine patients experienced recurrent shocks with the same underlying cause for the initial shock. Two patients had the device explanted due to the inability to completely mitigate inappropriate therapy and one patient had the device programmed OFF. Dual zone programming had a 6.4% inappropriate shock rate (23/357) while single zone programming had a 12% rate (9/74) [$P = 0.09$, (Pearson's χ^2 test)]. The former prevented all but one inappropriate shock for AF/SVT. Supplementary material online, *Appendix S2* shows the programming at the time of inappropriate shock for each episode.

Time to therapy

Time to therapy was defined as the interval starting 2000 ms after the last induction artefact and ending at the onset of the shock deflection on a standard ECG recording. Owing to the limited availability of data for retrospective patients, it was only recorded for inductions performed in prospectively enrolled patients and for spontaneous episodes where the calculation was made by Cameron Health/Boston Scientific from the electrogram stored in the device. Owing to lack of pre-defined criteria for induction testing, time to therapy was available from 195 inductions across a range of shock values up to 80J. Overall the mean (± SD) time to therapy was 15.1 (± 3.7) s which is less meaningful considering the range of shock energies.

Since the majority of shocks was delivered at 65J, mean time to therapy for that cohort was calculated independent of the others and found to be 15.1 ($\pm$3.8) s with a range of 7.0–37.0 s. Two patients had time to therapies $\geq$30 s. Time to therapy was recorded for 77 spontaneous VT/VF episodes, of which there were 81 shocks. The mean time to therapy for spontaneous episodes was 17.5 ($\pm$4.4) s with a range of 6.0 to 29.4 s reflecting a slightly longer charge time for the higher energy shock delivery in the ambulatory setting. The 95% CI for conversion efficacy of spontaneous episodes is 96.1% (90.8, 100%).

System-related complications

All clinical events were subclassified into observations (mitigation without the need for an invasive procedure) or complications (mitigation requiring an invasive procedure). In addition, sites were asked to classify whether a clinical event was related to the S-ICD system and/or the implant procedure. In the event that a clear relationship could not be documented but could not be ruled out, a conservative classification was adopted. At the time of analysis, a total of 129 clinical events (in 92 patients, 21%) were classified as being possibly related or definitely related to the S-ICD system or the implantation procedure. Of these, 35/456 (7.7%) were classified as complications in 29 patients giving a patient complication event rate of 6.4% (4.1, 8.6%) (*Table 3*).

There were no documented lead fractures or breakages. Four patients had a documented lead movement, two of which required no action and two required re-positioning. Fifteen system-related complications in 14 patients (3%) occurred in the first 30-day post-implant, which accounts for a peri-operative complication-free rate of 97%. *Figure 4* shows patients' complication-free system-related data for the first 360-day post-implant. At 180-day post-implant, 26 patients had 29 documented system- or implantation-related complications giving a complication-free rate of 94%. At 360-day post-implant 28 patients had 32 documented system or implantation-related complications and the complication-free rate was 94%.

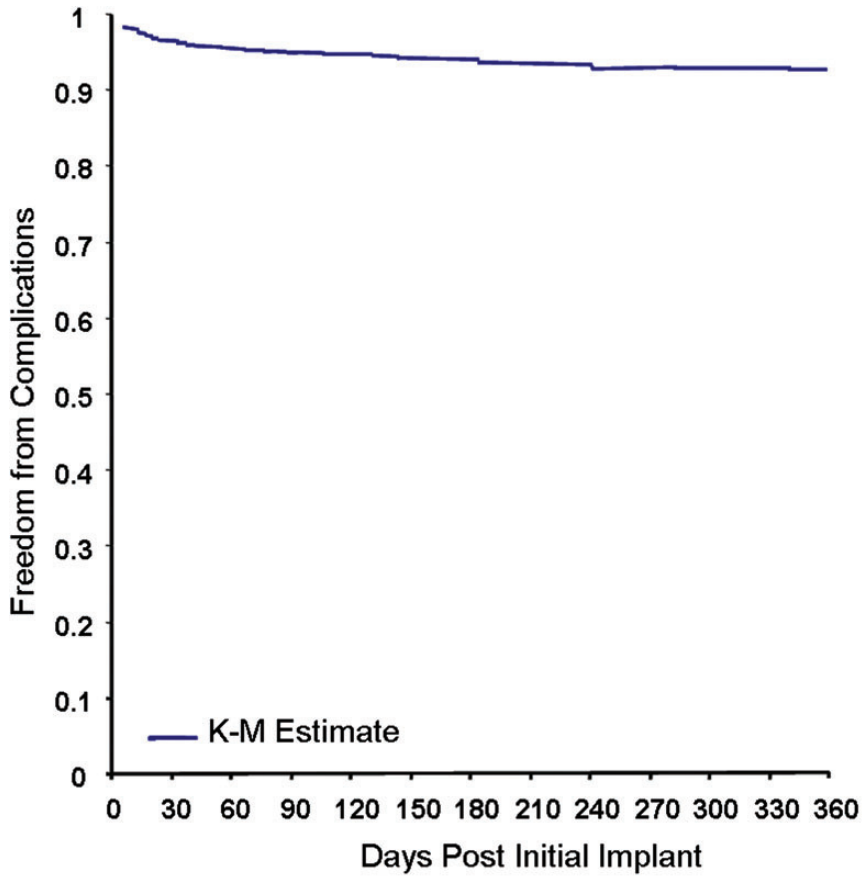
Infections

At the time of analysis, a total of 18 patients at 10 different sites had 20 documented infections or suspicions of infection related to the S-ICD procedure (4%). The 95% CI for total infection rate is 3.9% (2.2%, 5.7%). In one patient, this was due to a concomitant pacemaker implant, in one other secondary to capped leads of an explanted TV-ICD system. In both cases, the S-ICD system was unaffected. Serious infection leading to S-ICD removal was seen in 10 patients (explant rate 2.2%). Of note, only three sites had documented recurrent infections requiring explantation (in separate patients). For one site infections appeared to be linked to the timing of renovations of the surgical suite. For the other two sites, there is no clear relationship between experience and infection with explants occurring both at $<$6 months and $>$1 year after first implant.

Discussion

Although the TV-ICD system has served us well over the past 30 years, having been implanted in over 1 million patients worldwide, there remain significant concerns regarding the potential problems of long-term intravascular lead complications particularly in young primary prevention patients who may face over 40 years of generator and lead revisions.[8,17,23] This has spurred the endeavour to provide alternatives to combat what is often considered the 'Achille's heal' of the TV-ICD—the intravascular lead, at least in those patients not requiring permanent pacing or anti-tachycardia pacing (ATP). The EFFORTLESS S-ICD Registry was initiated in order to provide 'real-world' systematically collected system performance data over a suitably prolonged period beyond that normally collected in randomized controlled trials, since these are primarily interested in survival endpoints as opposed to the important details of system performance. The Registry currently demonstrates that the device is being successfully implanted in a broad spectrum of patients with 98% first procedure induced VF conversion efficacy. Furthermore, there has been 100% overall clinical conversion efficacy of discrete episodes of spontaneous VT/VF (88% first shock conversion efficacy) either immediately post-shock or within a few seconds of shock delivery. Overall, conversion efficacy of spontaneous episodes is 96.1% (90.8% CI, 100%). This is equivalent to the FDA Investigational Device Exemption (IDE) data where the conversion efficacy for spontaneous episodes was 92.1% on the first shock and 37 of 38 (97.4%) with one or more shocks.[24] Furthermore in the context of DFT testing, the Registry data show similar efficacy to IDE 99.7% (99.2, 100%) vs. 94.7% (with a 95% lower confidence limit of 91.7%). Five of the six VT/VF storm events were successfully converted by the device. The patient with Loeffler's syndrome who did not survive the cardiac arrest is an unusual indication. As this patient had an ongoing biopsy-proven inflammatory disease process requiring steroid therapy, this may have led to elevation of the DFT.

The first shock conversion efficacy of 88% is very much in line with rates published in TV-ICD and Cardiac Resynchronisation-Defibrillator (CRT-D) cohorts[25,26] which is particularly important considering the potential differences in the S-ICD patient population, including an overall average younger age and a high prevalence of non-ischaemic cardiomyopathies, congenital, and channelopathy patients—all of whom are historically more difficult to treat with the TV-ICD. The implant procedure has not been associated with the typical implant-related complications of haemo/pneumothorax and lead displacement seen in 2–6% of trial and Registry TV-ICD populations.[27–31] The only significant complication has been that of procedure-related infection affecting $\sim$4% of patients overall and resulting in explant in 2%. Infections are most probably related to procedural inexperience in terms of appropriate skin preparation, draping, and suturing associated with this new procedure which requires an unfamiliar, more surgical approach of left lateral thoracotomy skin incision and tunnelling of the lead. However, the learning curve and shared experience of optimal pre- and peri-operative technique should mean that this initial complication can be suitably addressed.[17] Indeed in the Cameron Health IDE study,[24] once optimal technique between centres was agreed upon there were no subsequent infections requiring explant after approximately the first 100 patients suggesting a problem related to inexperience of a new implantation technique. The relationship between infections and experience is less obvious in the EFFORTLESS Registry. It should also be recognized that infection remains a significant complication of TV-ICD implantation with acute infections in the first 30-day post-implant ranging between 2 and 4% (Entrust IDE, Canadian ICD Registry, Medicare, Canadian Advisory data) depending upon



	Day 30	Day 180	Day 360
KM Rate	97%	94%	94%
At Risk	453	381	290
Failed	14	26	28
Censored	3	62	148
Remaining	439	368	280

Figure 4 Kaplan–Meier analysis for freedom from subcutaneous implantable defibrillator system-related complications for the first 360-day post-implant.

the population of patients (age, co-morbidities) and experience of the implanting centres. Infections requiring system explantation range between 1 and 2% for TV-ICDs which is compatible with the early experience with the S-ICD.

The inappropriate shock rates (7%) are comparable with the standard TV-ICD registries and trials which range from 4 to 18%.[32–34] However, in contrast to TV systems, the main cause of inappropriate shocks with the S-ICD is T-wave oversensing. The S-ICD has several options for management of inappropriate shocks without the need for an invasive procedure including reprogramming of the sensing vector and exercise testing with template updates. Indeed, the more prolonged detection time and programming of a dual zone device with SVT discrimination algorithms and conditional shock zone for higher rates >220/min may have helped to minimize inappropriate shock therapy and allowed spontaneous VT episodes to self-terminate as has been recognized in recent studies of modifying VT detection criteria and delaying ATP therapies.[33–36] In the PREPARE trial which prolonged VT detection to 30/40 beats inappropriate shocks were reduced to 4% as opposed to 35% over 5 years in SCD-HeFT;[6,34] 35% of VT's self-terminated in PainFreeRx indicating that the strategy of prolonging detection time before committing to therapy is a reasonable approach supported by this recent TV-ICD data.[37]

Comparison with recent cohort studies

This is the largest series of S-ICD patients to be reported to date and reflects practice across multiple centres worldwide. Two recent single country series from the Netherlands[17] and UK[19] reported

upon 118 and 111 patients, respectively. The inappropriate shock rates were higher, occurring in 13 and 15% of patients and mainly due to T wave oversensing. This is double the rate observed in this larger cohort and probably is a reflection of several issues. Firstly, many of the reported patients were implanted with the device either prior to its CE mark, or immediately after. Subsequent updates to the noise detection algorithm occurred as a result of inappropriate therapy recorded in these early patients. Secondly, with continued experience there has been an increased recognition of appropriate patient management prior to device implant including ensuring there is ideally more than one acceptable sensing vector during screening; optimising heart rate thresholds for therapy as well as ECG screening in different postures and during increased heart rates. Similarly, the higher infection rates requiring explant of 5.8 and 4% vs. 2.2% in this series are most probably a reflection of increased physician experience and optimization of implant technique. In none of these series has there been a failure to deliver therapy in the programmed shock zone for ventricular arrhythmia although there was one arrhythmic death in the UK cohort. However, the use of the S-ICD as a first line therapy in all ICD patients without the need of pacing will require confirmation in clinical trials comparing the S-ICD to the TV-ICD which are currently ongoing.[38]

Limitations

This is a Registry designed to record the real world experience planning ultimately to recruit 1000 patients with 5 years of follow-up data. The initial results demonstrate the early outcomes in the first 12 months after system implantation. The issue of long-term device performance particularly appropriate and safe cardioversion of VF in daily life as opposed to the controlled confines of a DFT test will only become clearer with time. The fact that the system performs effectively at implant is supported by this and the IDE data.[24] It is recognized that controversies exist regarding whether DFT testing actually is appropriate for assessing ICD efficacy and most ICD cardioversion failures occur in the real-world under conditions of major metabolic derangement, hypoxia, and ischaemia which are beyond the normal ranges of standard DFT testing when the patient is in a well oxygenated, sedated state. Despite this, successful DFT at implant has been employed as an appropriate clinical safety endpoint particularly for a new technology and an indication of safe system performance as required by the FDA.

Conclusions

The first large cohort of real-world data from an International patient S-ICD system population demonstrates appropriate system performance with clinical event rates and inappropriate shock rates comparable with those reported for conventional ICDs.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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