Infection and mortality after implantation of a subcutaneous ICD after transvenous ICD extraction

Lucas Boersma, MD, PhD,[*] Martin C. Burke, DO,[†] Petr Neuzil, MD, PhD,[‡] Pier Lambiase, MD, PhD,[§] Ted Friehling, MD,[‖] Dominic A. Theuns, PhD,[¶] Fermin Garcia, MD,[#] Nathan Carter,[**] Timothy Stivland,[**] Raul Weiss, MD,[††] on behalf of the EFFORTLESS and IDE Study Investigators

From the [*]St Antonius Ziekenhuis, Nieuwegein, The Netherlands, [†]Heart Rhythm Center, University of Chicago, Chicago, Illinois, [‡]Homolka Hospital, Prague, Czech Republic, [§]The Heart Hospital, Institute of Cardiovascular Science, University College London, London, United Kingdom, [‖]Inova Fairfax Hospital, Falls Church, Virginia, [¶]Erasmus Medical Center, Rotterdam, The Netherlands, [#]Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, [**]Boston Scientific Corporation, St. Paul, Minnesota; and [††]Ohio State University, Columbus, Ohio.

BACKGROUND The subcutaneous implantable cardioverter-defibrillator (S-ICD) provides an alternative to the transvenous implantable cardioverter-defibrillator (TV-ICD). Patients undergoing TV-ICD explantation may be eligible for reimplantation with an S-ICD; however, information on safety outcomes in this complex population is limited.

OBJECTIVE This analysis was designed to provide outcome and safety data from S-ICD patients who received their device after TV-ICD explantation.

METHODS Patients in the S-ICD IDE Study and EFFORTLESS Registry with a prior TV-ICD explantation, as well as those with no prior implantable cardioverter-defibrillator (ICD), were included. Patients were divided into 3 groups: those implanted with the S-ICD after TV-ICD extraction for system-related infection (n = 75); those implanted after TV-ICD extraction for reasons other than system-related infection (n = 44); and patients with no prior ICD (de novo implantations, n = 747).

RESULTS Mean follow-up duration was 651 days, and all-cause mortality was low (3.2%). Patients previously explanted for TV-ICD infection were older (55.5 ± 14.6, 47.8 ± 14.3 and 49.9 ± 17.3 years in the infection, noninfection, and de novo cohorts, respectively; $P = .01$), were more likely to have received the ICD for secondary prevention (42.7%, 37.2% and 25.6%; $P < 0.0001$) and had higher percentages of comorbidities, including atrial fibrillation, congestive heart failure, diabetes mellitus, and hypertension, in line with the highest mortality rate (6.7%). Major infection after S-ICD implantation was low in all groups, with no evidence that patients implanted with the S-ICD after TV-ICD explantation for infection were more likely to experience a subsequent reinfection.

CONCLUSION The S-ICD is a suitable alternative for TV-ICD patients whose devices are explanted for any reason. Postimplantation risk of infection remains low even in patients whose devices were explanted for prior TV-ICD infection.

KEYWORDS Death; sudden; Subcutaneous ICD; Infection; Safety

ABBREVIATIONS **ICD** = implantable cardioverter-defibrillator; **NCDR** = National Cardiovascular Data Registry; **S-ICD** = subcutaneous implantable cardioverter defibrillator; **TV-ICD** = transvenous implantable cardioverter defibrillator

(Heart Rhythm 2016;13:157–164)

Introduction

The number of patients implanted with an implantable cardioverter-defibrillator (ICD) for either a secondary[1,2] or a primary prevention indication[3,4] has increased substantially over the past 2 decades.[5] As implantation numbers continue to increase because of the recognized mortality benefit of

The S-ICD System IDE Clinical Investigation (S-ICD IDE study) and the EFFORTLESS S-ICD (Evaluation of Factors Impacting Clinical Outcome and Cost-Effectiveness of the S-ICD) Registry are sponsored in their entirety by Cameron Health, Inc, a subsidiary of Boston Scientific Corporation. Dr. Boersma has received consulting fees from Medtronic and Boston Scientific and speaking fees from Medtronic, Boston Scientific, and Biotronik. Dr. Burke has reported receiving consulting fees, research grants, and honoraria from Boston Scientific and research grants from Medtronic and St. Jude Medical, as well as consulting fees from and equity in AtaCor Medical. Dr. Lambiase has reported receiving speaker fees and research grants from Boston Scientific, Medtronic, St. Jude Medical, and the University College London Hospitals Biomedicine Research Centre, National Institute for Health Research. Dr. Theuns has reported receiving research grants from Biotronik and Boston Scientific and consulting fees from Boston Scientific. Nathan Carter and Tim Stivland are employees of Boston Scientific. Dr. Weiss has reported receiving consulting fees, speaking fees, and research grants from Biosense Webster, Biotronik, Boston Scientific, Medtronic, and St. Jude Medical. **Address reprint requests and correspondence:** Dr Lucas Boersma, Cardiology Department, St Antonius Hospital, Nieuwegein, The Netherlands.. E-mail address: l.boersma@antoniusziekenhuis.nl.

1547-5271 http://dx.doi.org/10.1016/j.hrthm.2015.08.039

these devices, so does the incidence of both device and lead extraction for reasons such as end of life,[6] infection,[7,8] and device malfunction or manufacturer advisory.[9,10] Data from the National Cardiovascular Data Registry (NCDR) ICD Registry show that between April 2010 and June 30, 2011, of 174,499 hospital visits, 47% were repeat procedures for reasons such as device upgrade, battery end of life, and systemic infection,[11] and it is known that complication rates are higher with reimplantations, particularly if a lead implantation or revision is involved.[11,12] In addition, morbidity and mortality are particularly high in patients with an infected transvenous ICD (TV-ICD) system, especially when a systemic infection or endocarditis is present,[13] and the risk of reinfection after system reimplantation is also of concern.[14]

The subcutaneous ICD (S-ICD) was developed to provide an alternative to the TV-ICD, because it is implanted without any transvenous or epicardial leads. Studies demonstrating the safety and effectiveness of the S-ICD have been published,[15,16] and the S-ICD appears to be a good alternative for a variety of patients eligible for a TV-ICD system.[17] In this retrospective analysis, we evaluated the outcomes of patients undergoing S-ICD implantation after extraction of a TV-ICD system for any reason. Mortality rates and intraoperative and postoperative complication rates were examined and compared with those of patients receiving an S-ICD as their initial ICD implant (de novo implants).

Methods

Patient population

Patients included in the pivotal safety and efficacy study (S-ICD System IDE Clinical Investigation) and the EFFORTLESS S-ICD Registry (Evaluation of Factors Impacting Clinical Outcome and Cost-Effectiveness of the S-ICD) were assessed for this analysis. The design and methodology for each study have been published in detail elsewhere.[15,18] The main trial results of the IDE were published in 2013,[15] whereas a preliminary report on overall performance of the S-ICD system in EFFORTLESS was published in 2014.[16] Recently, the initial safety and efficacy results from the pooled dataset with 2-year follow-up were also reported.[19] Briefly, the IDE study was a prospective, nonrandomized study designed to evaluate the safety and efficacy of the S-ICD system for US Food and Drug Administration approval. A total of 330 patients were enrolled, of whom 314 received an S-ICD implantation. Mean follow-up duration was 661 days, with a range of 17 to 1012 days. In contrast, the ongoing EFFORTLESS Registry has enrolled 1000 patients and is a standard-of-care post-market evaluation documenting the long-term clinical outcome of S-ICD patients followed up for 5 years in 9 countries. At the time of the present analysis, data were available from the first 581 patients who received S-ICDs. Thirteen patients were common between the 2 studies. Sixteen patients available at the time of analysis were not included because of lack of information on prior TV-ICD implantation status, which left an analysis cohort of 866 patients. The poolability of study data, event definitions, and event adjudications have been described previously.[15,16,19] Ethical approval was obtained at all centers for the purpose of each study, and all patients provided informed consent according to national and institutional regulations.

Three separate groups were analyzed, which consisted of (1) repeat procedures in which the S-ICD implant was to replace a previous TV-ICD extracted for infection; (2) repeat procedures in which the S-ICD implant was to replace a previous TV-ICD extracted for reasons other than infection; and (3) S-ICD patients whose devices were implanted as an initial procedure, or de novo implants. All groups were evaluated for all-cause mortality; infection rates after S-ICD implantation, and other procedural and device-related complications.

Clinical complications

All clinical events collected in both studies were independently monitored. Events were documented and then subclassified into complications or observations. Complications were those that required a prolonged hospitalization or a need for reintervention. All deaths were automatically classified as complications independent of underlying cause. Complications were additionally classified as to whether there was a relation to the S-ICD system or the implantation procedure. An implantation-related complication was defined as any complication that was directly or indirectly caused by the implantation procedure. A device-related complication was defined as any event related to the implanted S-ICD system, including lead-, tunneling tool–, and generator-related complications. In the event that a clear relationship could not be documented but could not be ruled out, a conservative classification of the complication as being related to the S-ICD system or procedure was adopted.

Statistical and data analysis

Baseline demographics and clinical variables, including medical history, risk factors, comorbidities, and New York Heart Association functional class for heart failure, are presented as available. Continuous variables are summarized as means with standard deviations or as medians and ranges where appropriate. Continuous data were compared by the Student t test. Categorical variables are summarized as frequencies and percentages and were compared with χ^2 test. Complication-free rates were analyzed with the Kaplan-Meier methodology. All statistical analyses were performed with SAS Enterprise Guide, version 5.1 (SAS 9.3).

Results

A total of 866 patients from 31 clinical centers were included in the analysis. Follow-up data for complications and mortality were available for all patients. For the ongoing EFFORTLESS Registry, the data reflect information available as of November 18, 2013; for the IDE Study, the data

Table 1 Reasons for TV-ICD explantation

Primary indication for TV-ICD explantation	S-ICD reimplantation after TV-ICD extraction
Infection	75 (63.0)
End of battery life	5 (4.2)
Lead fracture/failure/advisory	30 (25.2)
Device malfunction	1 (0.8)
Thrombus on lead	8 (6.7)
Total	119 (100)

Values are n (%).

reflect information from all implanted patients. Of the 866 patients, 747 had de novo implants (86.3%), whereas 75 (8.7%) had reimplantation procedures after extraction of a TV-ICD for system-related infection and 44 (5.1%) after extraction of a TV-ICD for reasons other than infection. The indications for TV-ICD explantation are shown in Table 1. In patients whose TV-ICD was explanted for reasons other than infection, the majority of explantations (68.2%) were because of transvenous lead failure or advisory alerts. Whether infection was the reason for the TV-ICD explantation was captured for all patients. The nature of the infection was not specifically collected, although there were sufficient data collected on the case report form to identify that at least 11 of 75 patients (14.7%) were suffering from a systemic infection at the time of TV-ICD explantation. In 7 of these patients (63.6%), endocarditis was specifically documented. Mean follow-up duration for all S-ICD patients was 651 days, with a range of 2 to 1542 days (median 639 days). There were no significant differences in the mean follow-up duration for each cohort. Demographic and clinical characteristics of the 3 cohorts are shown in Table 2. The patients whose devices were explanted for infection were significantly older than both the cohort of patients whose TV-ICD was explanted for non–infection-related events and the de novo implantation cohort, (55.5 ± 14.6, 47.8 ± 14.3, and 49.9 ± 17.3 years, respectively; $P = .01$); were more likely to have the device implanted for secondary prevention (42.7%, 37.2%, and 25.6%, respectively; $P < .0001$); and had a higher incidence of comorbidities, including atrial fibrillation, congestive heart failure, diabetes mellitus, hypertension, prior myocardial infarction, and stroke. In contrast, those who received de novo implants had a significantly lower mean ejection fraction than either of the cohorts undergoing TV-ICD extraction and S-ICD replacement (38.7 ± 17.5% and 46.3 ± 19.3% for the non–infection-related cohort and 41.8 ± 17.0% for the infection-related cohort; $P = .05$).

Table 2 Baseline demographics and clinical characteristics divided by cohort

Demographic	Reimplantation: Prior TV-ICD infection	Reimplantation: Prior TV-ICD, no infection	No previous TV-ICD explantation (de novo)	*P* value
Age (y)				.0146
Mean ± SD	55.5 ± 14.6	47.8 ± 14.3	49.9 ± 17.3	
Range	19.0–86.0	18.6–73.0	7.0–88.0	
Sex				.3901
Male	56 (74.7)	28 (63.6)	542 (72.6)	
Female	19 (25.3)	16 (36.4)	205 (27.4)	
Height (cm)	173.7 ± 9.8	175.2 ± 9.2	174.5 ± 10.4	.7257
Weight (kg)	85.8 ± 21.4	79.1 ± 15.6	86.2 ± 23.1	.1620
BMI (kg/m^2)				.0470
Mean ± SD (median)	28.3 ± 6.1 (26.8)	25.6 ± 4.1 (25.1)	28.3 ± 6.7 (27.2)	
Range	16.4–51.7	17.4–35.7	15.2–69.0	
Indication				<.0001
Primary prevention	43 (57.3)	27 (62.8)	554 (74.4)	
Secondary prevention	32 (42.7)	16 (37.2)	191 (25.6)	
Ejection fraction (%)	41.8 ± 17.0	46.3 ± 19.3	38.7 ± 17.5	.0314
Medical history				
NYHA class II to IV at enrollment	31 (41.3)	9 (20.5)	284 (38.1)	.0495
Atrial fibrillation	19 (25.3)	5 (11.4)	119 (15.9)	.0720
COPD	6 (8.0)	2 (4.5)	47 (6.3)	.7458
Congestive heart failure	36 (48.0)	11 (25.0)	310 (42.7)	.0399
Diabetes mellitus	22 (29.3)	2 (4.5)	130 (17.4)	.0023
Hypertension	37 (49.3)	7 (15.9)	284 (38.1)	.0014
Myocardial infarction	39 (52.0)	10 (22.7)	252 (33.8)	.0015
Stroke	6 (8.0)	0 (0)	38 (5.1)	.1591
Valve disease	10 (13.3)	5 (11.4)	98 (13.1)	.9416
Ablation	5 (6.7)	7 (15.9)	28 (3.8)	.0006
CABG	14 (18.7)	4 (9.1)	83 (11.1)	.1315
Pacemaker	3 (4.0)	2 (4.5)	17 (2.3)	.4559
Percutaneous revascularization	24 (32.0)	10 (22.7)	160 (21.4)	.1112
Valve surgery	9 (12.0)	3 (6.8)	41 (5.5)	.0800

Values are n (%), mean ± SD, or mean ± SD (median).

BMI = body mass index; CABG = coronary artery bypass graft surgery; COPD = chronic obstructive pulmonary disease; NYHA = New York Heart Association; SD = standard deviation.

Table 3 Complication rates according to patient cohort

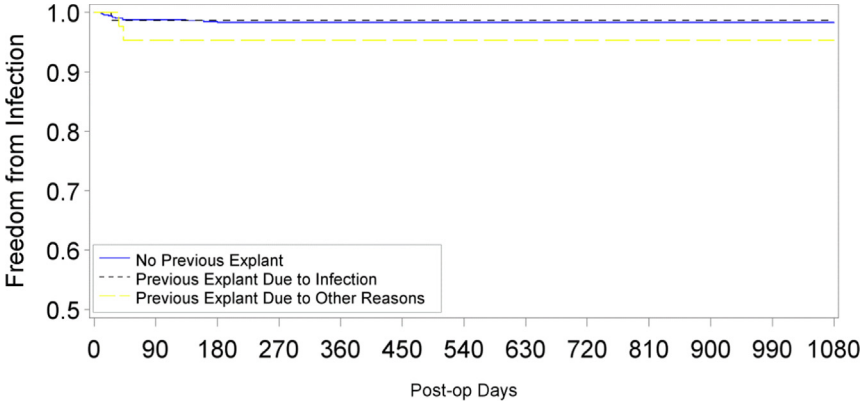
	Reimplantation: Prior TV-ICD infection (n = 75)		Reimplantation: Prior TV-ICD, no infection (n = 44)		No prior TV-ICD explantation (de novo) (n = 747)		
Complication description	Events	Patients	Events	Patients	Events	Patients	*P* value
All complications	12	8 (10.7)	4	3 (6.8)	90	72 (9.6)	0.78
Device system infection	1	1 (1.3)	2	2 (4.5)	14	12 (1.6)	0.34
Erosion	1	1 (1.3)	1	1 (2.3)	10	9 (1.2)	0.83
Incision/superficial infection	0	0 (0.0)	0	0 (0.0)	3	3 (0.4)	0.79

Values are number of events or n (%).
TV-ICD = transvenous implantable cardioverter-defibrillator.

Clinical complications

The total number of patients with system- or procedure-related complications was not significantly higher ($P = .78$) in the cohort whose TV-ICD explantation was for infection (10.7%) than in either the cohort for whom TV-ICD explantation was not related to infection (6.8%) or the de novo S-ICD patient group (9.6%). Complication rates were not driven by a high incidence of any specific event but rather an accumulation of individual events (Table 3). Because the risk of reinfection after system reimplantation is of concern, the patient cohorts were also specifically evaluated for reinfection rates after implantation with the S-ICD. Figure 1 presents the Kaplan-Meier survival curves for the incidence of infection up to 3 years after the S-ICD implantation procedure for all 3 cohorts. During this period, only 1 S-ICD patient (1.3%) from the cohort of patients whose TV-ICDs were explanted because of infection developed a subsequent infection that required intervention, specifically intravenous antibiotic drugs followed by explantation. This rate was similar to the infection rate seen in the de novo S-ICD implantation cohort, in which 12 patients (1.6%) developed an infection that required intervention. In the cohort of patients whose TV-ICDs were explanted for reasons other than infection, the rate of infection after S-ICD implantation was 4.5% (n = 2 patients; P = NS).

During follow-up, a total of 28 deaths were observed in the entire study population (3.2%). None of the deaths were related to either the S-ICD implantation procedure itself, S-ICD infection, S-ICD therapy (appropriate or inappropriate), or other S-ICD–related events but rather to worsening of heart failure or other comorbidity (Table 4). Only 1 death occurred within 30 days of implantation.[19] The median time between S-ICD implantation and death was 304 days. Among the TV-ICD extraction cohorts, no patient deaths were observed in the cohort reimplanted with an S-ICD after extraction of a TV-ICD for reasons unrelated to infection, whereas 5 deaths (6.7%) occurred in the cohort of 75 patients whose TV-ICDs were extracted for infection, and 23 (3.1%) occurred in the cohort of 747 patients without a prior TV-ICD (P = NS). In the patients with prior TV-ICD extraction for infection, death was most often predominantly caused by progression of heart failure and was never caused by infection or reinfection (Table 4). The 3-year Kaplan-Meier survival curves for each cohort are shown in Figure 2.



No Previous Explant	100	98.8	98.3	98.3	98.3	98.3	98.3	98.3	98.3	98.3	98.3	98.3	98.3
Prior TV Explant - Infection	100	98.7	98.7	98.7	98.7	98.7	98.7	98.7	98.7	98.7	98.7	98.7	98.7
Prior TV Explant - other reasons	100	95.3	95.3	95.3	95.3	95.3	95.3	95.3	95.3	95.3	95.3	95.3	95.3

Figure 1 Kaplan-Meier survival curves for freedom from infection. Survival curves documenting freedom from device-related infections that required intervention after implantation of a subcutaneous implantable cardioverter-defibrillator, according to status of prior device implantation: previous transvenous (TV) device explantation because of infection; previous explantation for other reasons; no previous explantation. Post-op = postoperative.

Table 4 Causes of out-of-hospital mortality and corresponding time between S-ICD procedure and death according to cohort*

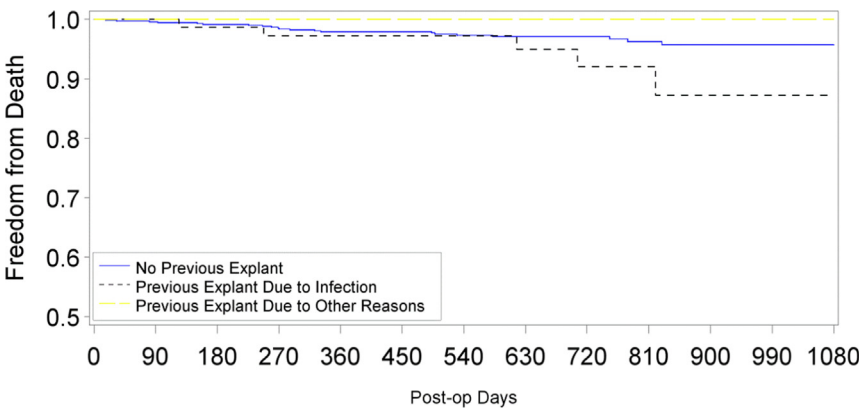
Death classification	No. of patients	Days after S-ICD implantation
Reimplantation: Prior TV-ICD infection		
Cardiac: Pump failure	3	124, 248, 820
Cardiac: Arrhythmic	1	617
Noncardiac (unspecified)	1	706
Total (% of population)	5 (6.7)	Average = 503 ± 301 days
No prior TV-ICD explantation (de novo)		
Cardiac: Pump failure	7	33, 246, 259, 331, 498, 530, 776
Cardiac: Arrhythmic	0	
Noncardiac (unspecified)	6	81, 286, 582, 829, 1176, 1215
Pneumonia; respiratory failure	4	93, 151, 159, 493
Unknown	6	17, 226, 269, 270, 322, 753,
Total (% of population)	23 (3.1%)	Average = 417 ± 338 days

S-ICD = subcutaneous implantable cardioverter-defibrillator; TV-ICD = transvenous implantable cardioverter-defibrillator.
*There were no deaths among the reimplantation cohort with prior TV-ICD and no infection.

Discussion

Because complication rates, including mortality, have been shown to be higher in patients undergoing repeat ICD implantation procedures, particularly when a device is explanted for infection, the current analysis was designed to compare complication rates between patients who received the S-ICD as a de novo implantation and those whose devices were implanted after TV-ICD explanation for any reason.

Over the past few years, expanding indications for ICD implantation,[2,3] including a younger primary prevention population, coupled with more recent challenges related to device and lead advisories and recalls[20–22] have resulted in increasing rates of reoperations and lead and full system explantations, often with the need for reimplantation. Complications associated with ICD explantations have been well documented and, depending on the type of lead and its length of time in the venous system, have been quite high.[10–12] There are fewer prospective data, however, available that are specifically related to the outcomes of patients who have undergone reimplantation after extraction. The current study provides insight into the long-term complication rates associated with receiving an S-ICD as a replacement device after TV-ICD extraction instead of a new transvenous lead system, as well as providing reference data from a de novo S-ICD cohort. The majority of patients included in the post–TV-ICD extraction cohorts were explanted because of infection (63%), of which 14.7% had a documented systemic infection. Although this percentage is lower than previously reported,[23,24] this is likely a result of underreporting in both the US IDE study and the EFFORTLESS Registry, because there was no specific question in the case report form that related to the type or severity of infection that resulted in TV-ICD explantation. The second largest cohort of patients included in the TV-ICD extraction population included those whose system had been extracted because of lead failure,



No Previous Explant	100	99.6	99.6	99.6	97.9	97.9	97.3	97.1	97.1	96.3	96.3	95.8	95.8
Prior TV Explant - Infection	100	100	100	100	97.2	97.2	97.2	95.0	92.1	92.1	92.1	87.2	87.2
Prior TV Explant - other reasons	100	100	100	100	100	100	100	100	100	100	100	100	100

Figure 2 Kaplan-Meier survival curves. Survival curves documenting mortality over 3 years according to status of prior device implant: previous transvenous (TV) device explantation because of infection; previous explantation for other reasons; no previous explantation. Post-op = postoperative.

fracture, or as a result of a device advisory. Five patients received the S-ICD after the extraction of a TV-ICD as a result of battery end-of-life behavior, of whom 3 patients also had documentation that at the time of extraction, there was also a suspected or actual lead failure. Recent data from the US NCDR ICD registry showed that more than 28% of ICD reoperations that occurred for reasons of battery end-of-life behavior also included a lead revision.[11] In addition, Kramer et al[6] documented that 2.5% of patients (or 2759 patients) having a TV-ICD replacement for battery end-of-life behavior between January 2005 and March 2010 also had concomitant device malfunction, recall, or infection. Because the S-ICD system was not available during the period of these 2 analyses, it remains to be determined whether in such cases switching to the S-ICD will become a common alternative to replace a TV-ICD system, particularly in situations in which a lead also has to be revised.

The overall incidence of reported clinical complications (approximately 11%) within the total patient population was within the same range as other reports from the general TV-ICD literature.[11,25,26] Because each study used its own limited definition of which clinical events would be reported, it is difficult to make a direct comparison of complication rates within the S-ICD versus TV-ICD patient populations. Both the S-ICD IDE study and EFFORTLESS Registry collected data on all reported clinical events, which could tend to result in overreporting. However, the key event rates that could be compared between different studies (eg, incidence of stroke, lead dislodgement, cardiac perforation) appeared to be similar or even lower in the S-ICD patients. The overall complication rate for TV-ICD patients whose devices were explanted for infection was not significantly higher than for either of the other 2 S-ICD cohorts, and there were no procedural or device-related events that were documented to occur more frequently in any of the cohorts.

The incidence of S-ICD infection that results in explantation or revision in the overall cohort was 1.7%, which was slightly higher than reported in the NCDR ICD Registry[11] but in line with rates from the Ontario ICD database[12] and a recent meta-analysis of 6433 patients included in 18 ICD trials.[27] It should also be emphasized that none of the documented S-ICD infections were systemic. Infection in the IDE Study[15] and the Dutch S-ICD cohort report[28] followed a temporal pattern, with a peak observed early in the trial related to inexperience with the new implantation technique. In the IDE Study, once the optimal technique had been agreed on between centers, there were no subsequent infections that required explantation in the latter two-thirds of the study.[15]

The lack of an elevated infection rate in the cohort of patients implanted with an S-ICD after TV-ICD explantation for infection is notable. Maytin et al,[29] whose data set included outcomes of 520 transvenous lead extraction procedures for an infectious indication, documented that 48% of patients who required a repeat extraction within the course of the study (21.4 ± 22.6 months) required this procedure for another infectious cause. Although these patients must have, by definition, received a replacement TV-ICD system, no details were given concerning the exact time between the initial extraction and the subsequent replacement procedure. In a smaller study by Deharo et al,[23] the time window from infected TV-ICD extraction to reimplantation ranged from 10 to 1192 days, yet they found no evidence that time to reimplantation was a predictor of reinfection or subsequent mortality. Therefore, the observation that patients in whom an S-ICD is implanted after a TV-ICD extraction because of infection are at no higher risk of developing either a subsequent reinfection or requiring a subsequent lead or system extraction is one of the most important findings of the present study and suggests the S-ICD may be ideal as a reimplantation device in endocarditis-related ICD patients without a pacing indication.

During follow-up, there were no procedural or S-ICD device-related deaths, and the overall mortality rate of 3.2% was lower than reported in other prospective clinical evaluations of ICD patient outcomes.[30] This may reflect the fact that in general, patients included in the S-ICD trials were younger and had a higher ejection fraction on average than traditional TV-ICD clinical trial populations. Annual mortality rates are reported to be higher among patients who have undergone a transvenous device explantation than among TV-ICD patients who have not. Importantly, the rate is still higher in patients treated for infection. Maytin et al[29] reported an 8.4% annual mortality rate in their population of transvenous lead extraction patients, which increased to 25% in the subgroup with systemic infection. Although it was not specifically reported in their paper, it can be assumed that the majority if not all of these patients would have been reimplanted with a transvenous device. In the single-center experience from Deharo et al,[23] there was an 11.2% mortality rate reported for patients who had undergone transvenous system extraction for infection and subsequent reimplantation. In contrast, although S-ICD patients whose TV-ICD was explanted for infection still had the highest mortality of any of the S-ICD cohorts, the 6.7% rate was substantially lower than the transvenous system cohorts described above. The higher mortality rate for the S-ICD patients who underwent TV-ICD explantation for infection does not appear to be correlated with the presence of a prior infection, as has been documented in TV-ICD studies,[13] but appears to reflect the morbidity demographics of this subgroup, which had a higher percentage of secondary prevention indications and incidence of significant comorbidities than the other cohorts presented here. Clearly, for all ICD patients, reducing the potential for an initial infection and in particular a systemic infection is likely to improve long-term outcomes. For this reason, future data may demonstrate that the S-ICD provides additional advantages over TV-ICDs as a de novo implantation, because the risk of systemic infection should be substantially lower.

Study limitations

The current study is retrospective, with the intrinsic shortcomings of such a study, and the follow-up periods differed

between the IDE Study and EFFORTLESS Registry. Specific information on the history of the TV-ICD systems that were replaced by an S-ICD, including number of prior leads or generators and the nature of primary infections, is limited. Time to S-ICD implantation after TV-ICD extraction was also not prospectively gathered; however, time to implantation was also not identified in the largest comparative transvenous extraction study,[29] and in smaller comparative studies has not shown to be a predictor of outcomes.[13,23] The patients included inherently had a higher likelihood of survival, because they had survived their TV-ICD explantation and had been reimplanted with the S-ICD; therefore, there was no true control group with which to specifically compare outcomes. The sample size of the 2 TV-ICD extraction cohorts is relatively small and may not allow any definitive conclusions.

Conclusions

Patients reimplanted with an S-ICD after explantation of a TV-ICD experienced low rates of major complications and mortality compared with published data for transvenous devices, which suggests that the S-ICD is a suitable alternative for TV-ICD replacement. In particular, the current data provide evidence that patients implanted with an S-ICD after explantation of a TV-ICD for infection do not experience elevated rates of reinfection.

Acknowledgments

The authors acknowledge the large contribution of investigators and institutions participating in the EFFORTLESS S-ICD Registry and IDE study. The authors also would like to thank Helen Reeve, PhD, for writing assistance.

References

1. The Antiarrhythmics Versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. N Engl J Med 1997;337:1576–1583.
2. Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, Levine JH, Sakensa S, Waldo AL, Wilber D, Brown MW, Heo M. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. N Engl J Med 1996;335:1933–1940.
3. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, Daubert JP, Higgins SL, Brown MW, Andrews ML. Multicenter Automatic Defibrillator Implantation Trial II Investigators. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med 2002;346:877–883.
4. Bardy GH, Lee KL, Mark DB, et al. Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure [published correction appears in N Engl J Med 2005;352:2146]. N Engl J Med 2005;352:225–237.
5. Hammill SC, Kremers MS, Stevenson LW, et al. Review of the registry's fourth year, incorporating lead data and pediatric ICD procedures, and use as a national performance measure. Heart Rhythm 2010;7:1340–1345.
6. Kramer DB, Kennedy KF, Spertus JA, Normand S-L, Noseworthy PA, Buxton AE, Josephson ME, Zimetbaum PJ, Mitchell SL, Reynolds MR. Mortality risk following replacement implantable cardioverter-defibrillator implantation at end of battery life: results from the NCDR. Heart Rhythm 2014;11:216–221.
7. Baddour LM, Epstein AE, Erickson CC, et al. American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee; Council on Cardiovascular Disease in Young; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Nursing; Council on Clinical Cardiology; Interdisciplinary Council on Quality of Care; American Heart Association. Update on cardiovascular implantable electronic device infections and their management: a scientific statement from the American Heart Association. Circulation 2010;121:458–477.
8. Prutkin JM, Bao H, Curtis JP, Al-Khatib SM, Aggarwal S, Uslan DZ. Factors associated with infection in 200,909 Medicare implantable cardioverter defibrillator implants: results from the National Cardiovascular Registry. Circulation 2014;130:1037–1043.
9. Kleeman T, Becker T, Doenges K, Vater M, Senges J, Schneider S, Saggau W, Weisse U, Seidl K. Annual rate of transvenous defibrillation lead defects in implantable cardioverter-defibrillators over a period of >10 years. Circulation 2007;115:2474–2480.
10. Maytin M, Wilkoff BL, Brunner M, et al. Multicenter experience with extraction of the Riata/Riata ST ICD lead. Heart Rhythm 2014;11:1613–1618.
11. Steckman DA, Varosy PD, Parzynski CS, Masoudi FA, Curtis JP, Sauer WH, Nguyen DT. In-hospital complications associated with reoperations of implantable cardioverter defibrillators. Am J Cardiol 2014;114:419–426.
12. Krahn AD, Lee DS, Birnie D, Healey JS, Crystal E, Dorian P, Simpson CS. Ontario ICD Database Investigators. Predictors of short-term complications after implantable cardioverter-defibrillator replacement: results from the Ontario ICD Database. Circ Arrhythm Electrophysiol 2011;2:136–142.
13. Sohail MR, Henrikson CA, Braid-Forbes MJ, Forbes KF, Lerner DJ. Increased long-term mortality in patients with cardiovascular implantable electronic device infections. Pacing Clin Electrophysiol 2015;38:231–239.
14. Tarakji KG, Chan EJ, Cantillon DJ, Doonan AL, Hu T, Schmitt S, Fraser TG, Kim A, Gordon SM, Wilkoff BL. Cardiac implantable electronic device infections: presentation, management and patient outcomes. Heart Rhythm 2010;7:1043–1047.
15. Weiss R, Knight BP, Gold MR, Leon AR, Herre JM, Hood M, Rashtian M, Kremers M, Crozier I, Lee KL, Smith W, Burke MC. Safety and efficacy of a totally subcutaneous implantable-cardioverter defibrillator. Circulation 2013;128:944–953.
16. Lambiase PD, Barr C, Theuns DA, et al. EFFORTLESS Investigators. Worldwide experience with a totally subcutaneous implantable defibrillator: early results from the EFFORTLESS S-ICD Registry. Eur Heart J 2014;35:1657–1665.
17. Akerström F, Arias MS, Pachón M, Puchol A. Jesús Jiménez-López. Subcutaneous implantable defibrillator: state-of-the-art 2013. World J Cardiol 2013;5:347–354.
18. Pedersen SS, Lambiase P, Boersma LV, Murgatroyd, Johansen JB, Reeve H, Stuart AG, Adragao P, Theuns DA. Evaluation of factors impacting clinical outcome and cost effectiveness of the S-ICD: design and rationale of the EFFORTLESS S-ICD Registry. Pacing Clin Electrophysiol 2012;35:574–579.
19. Burke MC, Gold MR, Knight BP, et al. Safety and efficacy of the totally subcutaneous implantable defibrillator: 2 year results from a pooled analysis of the IDE Study and EFFORTLESS Registry. J Am Coll Cardiol 2015;65:1605–1615.
20. Bruner MP, Cronin EM, Duarte VE, et al. Clinical predictors of adverse patient outcomes in an experience of more than 5000 chronic endovascular pacemaker and defibrillator lead extractions. Heart Rhythm 2014;11:799–805.
21. Brunner MP, Cronin EM, Jacob J, et al. Transvenous extraction of implantable cardioverter-defibrillator leads under advisory: a comparison of Riata, Sprint Fidelis, and non-recalled implantable cardioverter-defibrillator leads. Heart Rhythm 2013;10:1444–1450.
22. Fazal IA, Shepherd EJ, Tynan M, Plummer CJ, McComb JM. Comparison of Sprint Fidelis and Riata defibrillator lead failure rates. Int J Cardiol 2013;168:848–852.
23. Deharo J-C, Quatre A, Mancini J, et al. Long-term outcomes following infection of cardiac implantable electronic devices: a prospective matched cohort study. Heart 2012;98:724–731.
24. Sohail MR, Uslan DZ, Khan AH, Friedman PA, Hayes DL, Wilson WR, Steckelberg JM, Stoner S, Baddour LM. Management and outcomes of permanent pacemaker and implantable cardioverter defibrillator infections. J Am Coll Cardiol 2007;49:1851–1859.
25. Gould PA, Gula LJ, Champagne J, et al. Outcome of advisory implantable cardioverter defibrillator replacement: one year follow-up. Heart Rhythm 2008;5:1675–1681.
26. Poole JE, Gleva MJ, Mela T, et al. for the REPLACE Registry Investigators. Complication rates associated with pacemaker or implantable cardioverter-defibrillator generator replacements and upgrade procedures: results from the REPLACE Registry. Circulation 2010;122:1553–1561.
27. Ezzat VA, Lee V, Ahsan S, Chow AW, Segal O, Rowland E, Lowe ME, Lambiase PD. A systematic review of ICD complications in randomized control trials versus registries: is our "real-world" data an underestimation? Open Heart 2015;2:e000198.
28. Olde Nordkamp LRA, Dabiri Abkenari L, Boersma LVA, Maas AH, de Groot JR, van Oostrom AJ, Theuns DA, Jordaens L, Wilde AA, Knops RE. The entirely

subcutaneous implantable cardioverter-defibrillator: initial clinical experience in a large Dutch cohort. J Am Coll Cardiol 2012;19:1933–1939.
29. Maytin M, Jones SO, Epstein LM. Long-term mortality after transvenous lead extraction. Circ Arrhythm Electrophysiol 2012;5:252–257.
30. Kutyifa V, Huth Ruwald AC, Aktas MK, Jons C, McNitt S, Polonsky B, Geller L, Merkely B, Moss AJ, Zareba W, Bloch Thomsen PE. Clinical impact, safety, and efficacy of single- versus dual-coil ICD leads in MADIT-CRT. J Cardiovasc Electrophysiol 2013;24:1246–1252.

CLINICAL PERSPECTIVES

Because of expanding indications for implantable cardioverter-defibrillators (ICDs) over the past 2 decades, the number of patients in whom an ICD has been implanted has increased substantially. As implantation numbers increase, so inherently does the incidence of both device and lead extraction procedures, particularly in light of a recent series of device malfunctions and advisories. Coupled with a primary prevention population that is typically younger than the historic secondary prevention patient, it is clinically essential that the risks associated with reimplantation are fully understood, particularly if the patient's device is being explanted for reasons of infection, which is often associated with a higher risk of morbidity and mortality. The entirely subcutaneous ICD (S-ICD) was developed specifically to provide an alternative to the transvenous ICD (TV-ICD), and although data are now available that in general support that the S-ICD is both safe and effective, its performance in the more complex patient populations, such as those being reimplanted after explantation of a TV-ICD system (whether for infection-related reasons or not), has not been established. The analysis presented here addresses those concerns by demonstrating that overall morbidity and mortality rates associated with implantation of an S-ICD after explantation of a TV-ICD are low, and in addition, that there is no increased risk of reinfection should a patient have been explanted initially for transvenous device- or system-related infection. Practically, these data support that the S-ICD may be ideal as a reimplantation device, particularly in endocarditis-related ICD patients without the need for pacing.