Longevity of the Subcutaneous Implantable Defibrillator
Long-Term Follow-Up of the European Regulatory Trial Cohort

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Background—The recent advent of subcutaneous implantable cardioverter defibrillators (S-ICDs) has provided investigators with a safe and effective new therapy in patients at risk of sudden cardiac death. At present, no data are available with regard to the longevity of these new devices. This study evaluated the longevity of the S-ICD system.

Methods and Results—All patients enrolled in the European Regulatory Trial were included in the analysis. During follow-up, time and causes of device replacement or explantation were assessed and categorized. Device longevity was estimated using Kaplan–Meier analysis. Fifty-five patients were followed for a median of 5.8 years. During follow-up, 26 (47%) patients underwent device replacement and 5 (9%) underwent device explantation. Median time to replacement was 5.0 years (Q1–Q3, 4.4–5.6 years). Replacement was caused by battery depletion in 25 patients (92%), of which 5 within 1.5 years because of premature battery depletion, and by infection in 1 patient (2%). Replacement for a transvenous ICD system was required in 4 patients (7%) because of ineffective defibrillation in 1 (0.003 per patient-year), need for resynchronization therapy in 2 (0.01 per patient-year), and for antidibrady pacing in 1 (0.003 per patient-year). At 5 years follow-up, 71% of devices were still in service.

Conclusions—This study provides the first estimate of S-ICD system longevity since its introduction in clinical practice. Median longevity of the first generation S-ICD system was 5.0 years. The majority of devices were replaced because of battery depletion.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01117792.

(Circ Arrhythm Electrophysiol. 2015;8:1159-1163. DOI: 10.1161/CIRCEP.115.002953.)

Key Words: arrhythmias, cardiac ◼ bradycardia ◼ death, sudden, cardiac ◼ defibrillators, implantable ◼ longevity

Several large randomized trials have shown the efficacy of the implantable cardioverter defibrillator (ICD) in reducing mortality in selected patients at high risk of arrhythmic death from ventricular arrhythmias.1-4 Despite the proven mortality benefit, the ICD has been associated with morbidity because of short-term and long-term complications with transvenous leads.5-7 These complications include pneumothorax, cardiac perforation, systemic infections, acute and chronic lead displacement, insulation breaches, and conductor breaks. Removal of infected or failed transvenous leads is associated with considerable morbidity and mortality.6,9 These complications are part of the rationale to develop an entirely subcutaneous ICD (S-ICD) system with no leads within or on the heart and preservation of the central venous circulation.10 The feasibility and safety of the S-ICD system were established in early human studies.11-13 The safety and effectiveness of the S-ICD system for the treatment of ventricular arrhythmias were proven in the investigational device exemption (IDE) trial.14 Recently, an interim analysis of the EFFORTLESS registry presenting real-world data of patients implanted with the S-ICD system regarding clinical data has been published.15 However to date, there are no data present about the longevity of the S-ICD. The aim of this study was to analyze longevity of the S-ICD.

Methods

Study Population
The study cohort of the European Regulatory Trial consisted of 55 patients who underwent implantation in Europe and New Zealand between December 2008 and February 2009. All patients were eligible candidates for S-ICD implantation among the patients referred for ICD implantation at each participating center. The inclusion criterion of the trial was a class I, II-a, or II-b indication for ICD therapy.
None of the patients had an indication for bradycardia pacing, cardiac resynchronization therapy, ventricular tachycardias with rates <170 beats per minute, or documented monomorphic ventricular tachycardias which could be terminated by antitachycardia pacing. The study protocol of the European Regulatory Trial was approved by the ethics committee at each participating institution. All study participants provided written informed consent.

**Device Description**

The S-ICD system consists of a pulse generator, which is implant placed 1 to 2 cm parallel to the left midsternal line. The device weighs 145 g and has a volume of 69 mL. The device delivers nonprogrammed single- and dual-chamber ICDs.

**WHAT IS KNOWN**

- The subcutaneous implantable cardioverter defibrillator (ICD) is a viable and safe alternative to contemporary transvenous ICD systems in patients without an indication for bradycardia therapy, cardiac resynchronization therapy, or need for antitachycardia pacing therapy.

**WHAT THE STUDY ADDS**

- The longevity of the first generation subcutaneous ICD systems is slightly less compared to single- and dual-chamber ICDs.
- Longevity of the subcutaneous ICD is not affected by delivered shock therapy.
- The need for a transvenous ICD system replacement due to the development of an indication for bradycardia therapy, cardiac resynchronization therapy, or antitachycardia pacing therapy is low.

The indications for device replacement and explantation were ERI, premature ERI because of excessive battery drainage, malfunction of device, or infection. Permanent removal of the implanted S-ICD system was defined as explantation. Reasons for explantation were, for example, a change to a transvenous ICD system because of development of an indication for bradycardia pacing, cardiac resynchronization therapy, or antitachycardia pacing. Premature ERI was defined as ERI within 36 months after implantation, which is based on the value given in the warranty. All other replacements based on battery depletion after >36 months service time were defined as normal ERI. End of follow-up with administrative censoring of longevity of devices still in service was set on December 1, 2014.

**Data Analysis**

Continuous variables are presented as mean±SD or as median with 25th and 75th percentiles, where appropriate. Categorical data are presented as counts and percentages. Event-free rates from device replacement were calculated with the Kaplan–Meier method. Event-free rates were expressed with a 2-sided 95% confidence interval (CI). Patients who reached the end of follow-up without ERI were censored for administrative reasons. Patients who died before ERI were treated as censored observations. To evaluate the relation between ICD shocks and elective device replacement, Cox regression analysis was applied with number of delivered shocks as time-varying covariate. Statistical analysis was performed using SPSS version 21 (IBM Corp, Somers, NY). Statistical significance was defined as \( P<0.05 \) (2-tailed).

**Results**

Clinical characteristics of the patients enrolled in the European Regulatory Trial are presented in Table. Among the patients, 44 (80%) were men, and 37 (67%) had ischemic heart disease. Primary prevention was the indication for ICD placement in 43 (78%) patients. The number of patients who died before ICD replacement was 8 (15%); 3 cardiac and 5 noncardiac deaths. None of the deaths were related to the S-ICD system or implant procedure.

During a median follow-up of 5.8 years (5.7–5.9 years), 26 (47%) devices were replaced and 5 (9%) were explanted. The indications for device replacement and explantation are presented in Figure 1. Of the total cohort, 4 (7%) patients had the S-ICD explanted and received a transvenous ICD system. Two of them developed an indication for cardiac resynchronization therapy (CRT) because of symptomatic heart failure (New York Heart Association class III; 0.01 per patient-year), 1 patient had an indication for bradycardia pacing because of symptomatic bradycardia (0.003 per patient-year), and 1 patient received a transvenous ICD system as specified by protocol of the European Regulatory Trial in case of ineffective defibrillation testing. One device was explanted because of infection.

The majority of devices (81%) were replaced based on ERI. Overall, the median time for device replacement was 5.0 years (4.4–5.6 years). Event-free rates for device replacement were 94% (95% CI, 83%–98%) after 2 years, 89% (95% CI,
Device longevity is an important factor to improve the cost-effective application of ICD therapy. According to several device registries, no association between number of shocks and elective device replacement was found (hazard ratio, 1.01; 95% CI, 0.98–1.04; \( P = 0.29 \)).

Discussion

This is the first study to analyze the longevity of the subcutaneous ICD since its clinical introduction. The primary results of this analysis indicate that the median longevity of the S-ICD is 5 years as projected by the manufacturer. The majority of devices were replaced because of battery depletion, and ≈7% of the devices were explanted because of a nonbattery-related indication.

Nowadays, the majority of ICDs are implanted on account of primary prevention of sudden death. The majority of these primary prevention patients are expected to survive their first ICD and will probably need 1 or more device replacements.\(^{16} \) Device longevity is an important factor to improve the cost-effective application of ICD therapy. According to several studies, device longevity increased from a mean of 19 months in the late 1980s to ≈60 months at present.\(^{17–20} \) When analyzed per type of contemporary transvenous ICD, single-chamber ICDs have a mean longevity of 5.5 years and dual-chamber ICDs 5.8 years.\(^{20} \) Compared with contemporary transvenous ICD systems, longevity of the first generation S-ICD is slightly shorter with a median longevity of 5.0 years. During follow-up of the first implanted S-ICD cohort, premature ERI because of rapid battery depletion was observed in 5 devices (9%). Analysis identified a battery manufacturing issue and led to a field safety notification issued at the time of the IDE trial. No adverse clinical outcomes were reported as a result of premature battery ERI, and the replacements were uneventful. In subsequent S-ICD studies, premature battery depletion was observed in 2 cases (0.6%) in the IDE trial and in 1 case (0.2%) in the EFFORTLESS registry.\(^{14,15} \) When considering transvenous ICD systems, premature ERI has been reported in 9% of transvenous devices.\(^{21} \) Battery malfunctions were the most common cause of device failure in a meta-analysis of device registries.\(^{22} \)

A concern with the S-ICD system may be the inability to pace. Obviously, the S-ICD system is not indicated for patients with bradycardia or need for cardiac resynchronization. The number of ICD recipients who require bradycardia pacing during their follow-up is low, 3% of patients in the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) and 4% in the Dual Chamber and VVI Implantable Defibrillator (DAVID) study.\(^{1,23} \) Heart failure is usually a progressive condition and patients initially implanted with an ICD might later on develop an indication for CRT. The upgrade rate of ICD recipients to CRT varies among studies. In a retrospective single-center study, 3.8% of patients had their device upgraded to CRT during a follow-up of 4 years.\(^{24} \) Although in the European Cardiac Resynchronization Therapy Survey on CRT implant procedures, 28.2% were identified as upgrade from ICD to CRT-D.\(^{25} \) In a recent sub study of the Resynchronization-defibrillation for Ambulatory Heart Failure Trial (RAFT) study, 12.3% of ICD patients had an attempted upgrade to CRT.\(^{26} \) In our analysis, ≈7% of the S-ICD systems were explanted and replaced by a transvenous ICD system because of the need for bradycardia pacing or CRT. The interim analysis of the EFFORTLESS registry reported a low explant rate of the S-ICD, occurring in 3.7% of patients mainly because of infection.\(^{15} \) In 1% of patients, the S-ICD was replaced for a transvenous ICD system because of recurrent ventricular arrhythmias or patient decision.

Limitations

There are several limitations to this study. The number of patients is low compared with the IDE trial and the EFFORTLESS registry. However, the median follow-up

![Figure 1. Proportions of the indications for device replacement and explantation. ERI indicates elective replacement indication; and TV-ICD system, transvenous ICD system.](Image 69x70 to 257x191)

![Figure 2. Event-free rates for device replacement because of normal and premature battery depletion. Regarding the curves, devices were censored in case of explantation for reasons other than battery depletion.](Image 306x562 to 536x717)
of the first implanted S-ICD cohort is >5 years warranting an analysis of longevity of the subcutaneous defibrillator. Device longevity was defined as the time from implantation to replacement and thus not the day of detection of ERI. Overestimation of longevity can be neglected because replacement is performed within 1 to 2 weeks after detection of ERI.

Conclusions

The longevity of the first generation S-ICD systems is slightly less compared with single- and dual-chamber ICDs. The majority of devices were replaced because of battery depletion. During a median of 5-year follow-up, the need for a transvenous ICD system replacement was rather low.

Disclosures

Dr Theuns has received institutional grant and consulting fee from Boston Scientific. Dr Hood has received lecture honoraria, institutional grant, and consulting fees from Boston Scientific. Dr Cappato has equity and intellectual property rights from Cameron Health, a subsidiary of Boston Scientific, and lecture honoraria, institutional grant, and consulting fees from Boston Scientific. Dr Knops has institutional grant from Boston Scientific. Dr Maass receives lecture honoraria from Boston Scientific. Dr Boersma receives lecture honoraria and consulting fees from Boston Scientific. The other authors report no conflicts.

References


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Circ Arrhythm Electrophysiol. 2015;8:1159-1163; originally published online July 6, 2015; doi: 10.1161/CIRCEP.115.002953

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