The subcutaneous implantable cardioverter-defibrillator in review

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The subcutaneous implantable cardioverter defibrillator (S-ICD) is a completely extrathoracic device that has recently been FDA approved for the prevention of sudden cardiac death in select populations. Although the transvenous implantable cardioverter defibrillator (TV-ICD) has a proven mortality benefit in multiple patient populations, there are significant risks both with implantation and years after its placement. The S-ICD may help prevent some of these complications. Currently, the S-ICD is typically implanted in patients with prior device infection or at an increased risk for an infection, younger patients with difficult venous access related to either hemodialysis or difficult cardiac anatomy, patients who live active lifestyles, and those who may outlive the TV-ICD leads. There is an absolute contraindication for S-ICD implantations for patients who need pacing either for ventricular tachycardia or bradycardia because this device cannot perform these functions. To date, there are no randomized controlled trial (RCT) data evaluating the safety and efficacy of this relatively new device. Observational studies of both the S-ICD alone and in comparison with the TV-ICD have showed promising results, including a decrease in lead-related and periprocedural complications as well as a high level of effectiveness at terminating ventricular arrhythmias. These analyses over time may have contributed to the evolution and comfortability with the S-ICD system, as physicians are more often referring for and/or implanting this device for patients with appropriate indications. Furthermore, inappropriate shock rates with the S-ICD have decreased over time especially with dual zone programming. This review summarizes the results of a multitude of observational studies with respect to patient selection for the S-ICD, complication rates, appropriate and inappropriate shock rates, and programming. This review also tackles current ongoing randomized trials. Although the results of ongoing trials will be helpful, there is still a continued need to evaluate the efficacy of the S-ICD in broader patient populations including patients with several comorbidities and older patients so that more patients can be considered for this potentially lifesaving device. (Am Heart J 2019;217:131-9.)

According to recent statistics published in 2018 from the American Heart Association, cardiovascular disease constitutes >800,000 deaths in the United States yearly.[1] Of these deaths, approximately 50% are attributed to sudden cardiac death (SCD).[2,3] It is estimated that 50%-70% of sudden cardiac events are related to ventricular tachyarrhythmia.[3] There have been many strides over the years to circumvent deaths related to SCD, more specifically, the advent of the transvenous implantable cardioverter defibrillator (TV-ICD), which made its way to market in the early 1980s.

Several RCTs have shown survival benefit in select populations of patients who received a TV-ICD.[4,5] Although there are robust data supporting the use of the TV-ICD, there are also several challenges and drawbacks. Specifically, during implantation, there is a risk of pneumothorax, hemothorax, cardiac perforation with or without tamponade, and damage to the tricuspid valve.[6,7] These complications can lead to morbidity and mortality. Furthermore, there are long-term risks that include lead dislodgement and device infection that may result in systemic infection. The subcutaneous implantable cardioverter-defibrillator (S-ICD) was FDA approved in 2012 for use in the United States to address some of the complications of the TV-ICD.

The S-ICD is a completely extrathoracic device that is composed of a generator and 1 subcutaneous lead. The generator is implanted in the subcutaneous space in the left midaxillary line, typically between ribs 5 and 6. The subcutaneous lead runs parallel to the left of the sternum, terminating near the sternal notch.[8] The system is composed of 3 electrodes in total. One electrode is located in the device/generator itself. The other 2 are located at the terminal end of the subcutaneous lead and are separated by 8 cm. A visual example is displayed in Figure 1.

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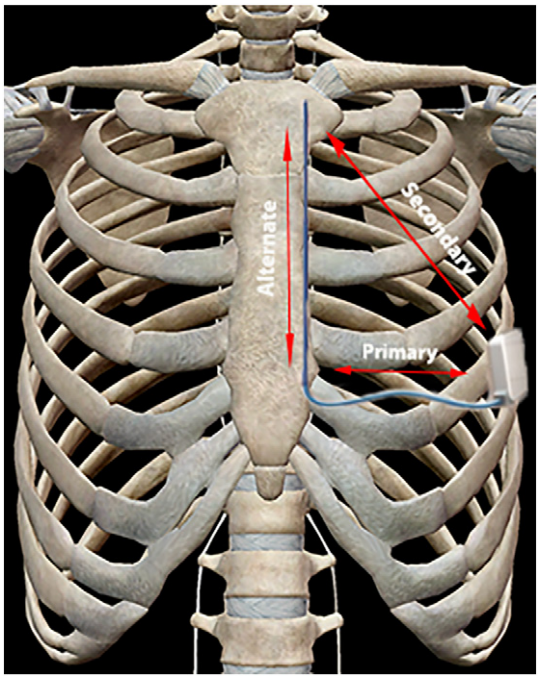
Figure 1



Graphic representation of the S-ICD and its 3 sensing vectors. The generator is placed between the fifth and sixth ribs near the left midaxillary line with a subcutaneous lead coursing just adjacent to the sternum.

The following review will describe the S-ICD system itself and include several observational studies that have analyzed multiple aspects of the system, including appropriate populations to consider for implantation, effectiveness, and complications.

Patient selection

Not all patients who have an indication for ICD placement are suitable candidates for an S-ICD. According to the American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines for ventricular arrhythmia and SCD, there is a Class I recommendation for an S-ICD in patients who are at a high risk for infection or are without appropriate venous access and have no indication for bradycardia or biventricular pacing and/or antitachycardia pacing (ATP).[2] Figure 2 demonstrates several factors physicians should consider when deciding between a TV-ICD and S-ICD.

Once a patient has been deemed an appropriate candidate for an S-ICD, a screening process should take place to avoid sensing issues such as undersensing of R waves and/or oversensing of T waves that may result in inappropriate ICD shocks. This screening process is carried out in 2 ways using either a Boston Scientific Zoom Programmer or a standard 12-lead ECG, and it involves assessing the QRS duration, QTc interval, and QRS:T-wave ratio.[9] These parameters must be evaluated in several different positions, including supine and standing, to gauge the ability of the system to detect appropriate cardiac electrical signals in various positions that patients may have in real life. It is estimated that 7%-15% of patients do not pass the screening test and are therefore not candidates for the S-ICD.[9]

Several different techniques have been used for implantation of a S-ICD over the years. The 3-incision technique utilizes a lateral incision at the midaxillary line for generator placement and 2 parasternal incisions, both inferiorly and superiorly, for lead placement.[10] Data on increasing infection risk with the superior parasternal incision[11] have led to the 2-incision technique,[12] eliminating the superior incision altogether. Cosmetically, there have also been studies analyzing implantation of the generator underneath the serratus anterior muscle itself as well as superficial to the serratus muscle but underneath the fascia.[12]

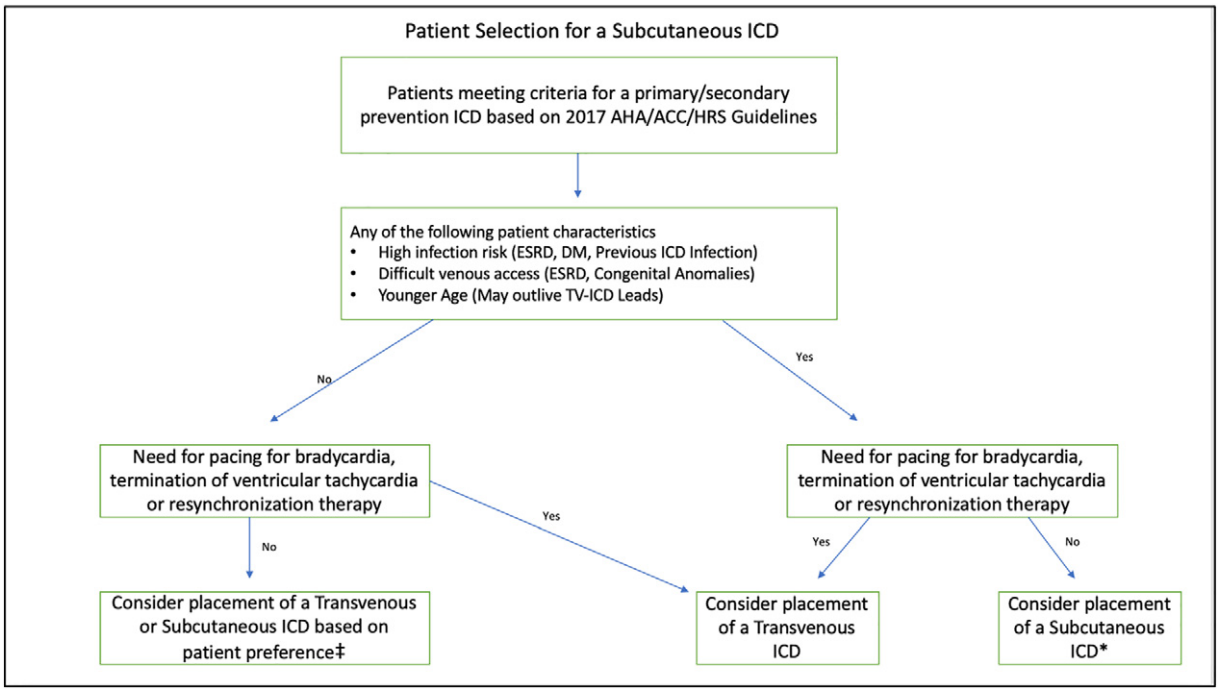
In a recent retrospective study published in 2017, Quast et al explored the clinical parameters that would aid in the selection of either an S-ICD or a TV-ICD by assessing incidence and predictors of ATP ventricular arrhythmias.[13] They evaluated 431 patients, median age 63 years, who were implanted with either a single- or dual-chamber TV-ICD. In total, 23% of the patient population experienced ATP; successful termination of ventricular arrhythmias was achieved in 67% of these patients. A prior history of nonsustained ventricular tachycardia or monomorphic ventricular tachycardia was the only predictor of ATP.[13] Patients with these features may not be good candidates for the S-ICD.

To better characterize patients who are receiving an S-ICD in clinical practice, Friedman et al performed a large retrospective analysis of the National Cardiovascular ICD Data Registry of patients implanted with ICDs over a 3-year period.[14] They found that of >390,000 ICD implantations, 3,717 were S-ICD and that patients who received an S-ICD were more likely to be black, have a history of nonischemic cardiomyopathy, be undergoing chronic dialysis, and have a history of cardiac arrest. Furthermore, this study revealed that patients with an S-ICD were less likely to have a history of atrial fibrillation or ventricular tachycardia and were less likely to have had a previous ICD.[14] With more widespread use of the S-ICD, future studies should reexamine the characteristics of patients receiving an S-ICD because these characteristics may evolve over time.

The evolving knowledge of the S-ICD

There have been several recent prospective studies that have provided helpful information on the S-ICD. These studies have included patients from the Investigation Device Exemption (IDE)[15] and the Evaluation of Factors

Figure 2



Factors to take into consideration when deciding between implantation of an S-ICD or TV-ICD. *Not all patients pass the screening for an S-ICD. ‡Please note that the S-ICD is not limited only to patients with the above characteristics.

Impacting Clinical Outcome and Cost Effectiveness of the S-ICD (EFFORTLESS)[16] registries. In 2015, a pooled analysis of both of these patient cohorts was published with approximately 3 years of postimplantation data.[17] In total, 882 patients were analyzed with >1,500 patient-years. The average age was 50.3 years, and 72.5% were male. Patient characteristics included a history of myocardial infarction (MI) (34.6%), atrial fibrillation (16.4%), congestive heart failure (42.3%), and previous TV-ICD (13.7%), and approximately 43% of the population had a left ventricular ejection fraction (LVEF) of ≤35% and received an S-ICD for primary prevention. The average LVEF of the patient cohort was 39.4%. The rate of complications was 4.5% within 30 days after device implantation and 11.1% at 3 years.[17] The most common complications were infection and suboptimal pulse generator or electrode position. Within 3 years, there were only 4 patients (0.4%) who needed the S-ICD removed due to the need for ventricular pacing. Of the 111 discrete ventricular tachycardia/ventricular fibrillation (VT/VF) events, 90.1% were terminated with the first shock and 98.2% were terminated with the 5 available shocks. Of the 51 episodes of pulseless VT/VF that occurred in 32 patients, 88.2% converted with the first shock.[17]

Shortly after the IDE and EFFORTLESS pooled study, Boersma et al stratified the combined patient cohort of 882 patients[17] into those with a primary versus secondary prevention indication for the S-ICD.[18] They analyzed 856 patients after excluding multiple patients for age less than 18 years and patients with insufficient data. Of the analyzed study population, 70.4% received the S-ICD for primary prevention. Of the patients implanted with a primary prevention S-ICD, 62.9% had an LVEF ≤35%, 24.7% had an LVEF >35%, and 12.4% did not have enough data. It is notable that of the patients implanted with a primary prevention S-ICD, 41% suffered from ischemic cardiomyopathy and 28% nonischemic. The other indications for a primary prevention S-ICD were hypertrophic cardiomyopathy and inherited arrhythmic disease. Patients in the primary prevention group with an LVEF ≤35% were older (57 vs 40 years) than patients in the LVEF >35% and had significantly more comorbidities. There was no difference in clinical complications related to the S-ICD between primary and secondary prevention patients, with a complication free rate of 88.7% and 88.5% at 3 years, respectively. This analysis showed a higher mortality rate among patients implanted with a primary prevention S-ICD versus those with a secondary prevention indication, at 3.3% and 2.3%, respectively. This

reportedly did not reach statistical significance. There was no difference between the primary and secondary prevention groups in the effectiveness of the S-ICD or the risk of inappropriate shocks, but there was a higher incidence of the need for appropriate therapy among patients with a primary prevention indication. Of the patients with a primary prevention indication, there was an all-cause mortality rate of 5.0% in patients with an LVEF ≤35% and 0% in those with an LVEF >35% over the mean follow-up of 644 days.

An updated analysis of data from the pooled IDE and EFFORTLESS registries was undertaken that focused on patients with a previously extracted TV-ICD who received an S-ICD.[19] This study included 747 patients with de novo S-ICD implantation, 75 with S-ICD implantation after TV-ICD extraction for infection, and 44 with S-ICD implantation after TV-ICD extraction for other reasons (transvenous lead failure and/or advisory alerts). The most notable result of this study was that, over the median follow-up period of 639 days, only 1.3% of the combined cohort that had a TV-ICD explanted because of an infection had a subsequent infection with the S-ICD that required intervention (ie, antibiotics and device removal). The incidence of infection was the same in patients who had de novo implantation of an S-ICD (no prior TV-ICD) and those who had a TV-ICD removed for reasons other than infection. There was also no difference in the complication rate in the TV-ICD explanted because of infection (10.7%) versus de novo S-ICD implantation (9.6%) and TV-ICD explanted for other reasons (6.8%) (P = .78).

The most recent data from the full EFFORTLESS study were published in August of 2017 and included nearly 1,000 patients (400 more patients than the study results published in 2014)[16] and >3,000 patient-years.[20] The mean age of the entire patient cohort was 48 years, and 72% of them were male. Of the total study population, 64.9% had an S-ICD placed for a primary prevention indication and 35.1% for secondary prevention. There were 57.7% of study participants who had an LVEF ≤35%. In total, patients in this study had multiple comorbidities, with 28.3% having hypertension, 28.1% with previous MI, 27.9% with a history of cardiac arrest, and 26.5% congestive heart failure. The 30- and 360-day overall complication rates were 4.1% and 8.4%, respectively. The most common complications noted were infection requiring device removal (2.4%), erosion (1.7%), and inappropriate shocks (1.1%).[20] Notably, the complication rates decreased over time, with a nearly 4.0% reduction in complications from time quartile 1 through 4. Over 3.1 years of the study period, 1.3% of patients had to have their S-ICD explanted because of a change in indication, including ATP, need for cardiac resynchronization therapy (CRT), and pacing for bradycardia. In total, 104 patients had 278 appropriate ICD discharges for VT/VF episodes and storm events.[20] Of the 192 episodes of discrete nonstorm VT/VF, 170 episodes (88.5%) were converted with the first shock and 187 episodes (97.4%) with the 5 available shocks. Overall, there were a 98% freedom from S-ICD complication rate, a 98.5% freedom from inappropriate shock rate, a 98.9% rate of no change to TV-ICD, and finally a 97.4% shock efficacy rate.[20] Table I summarizes the outcomes of the combined EFFORTLESS and IDE registries from 2015 and the up-to-date EFFORTLESS registry data in 2017. Figure 3 illustrates conversion rates for specific arrhythmic outcomes as well as inappropriate shock rates.

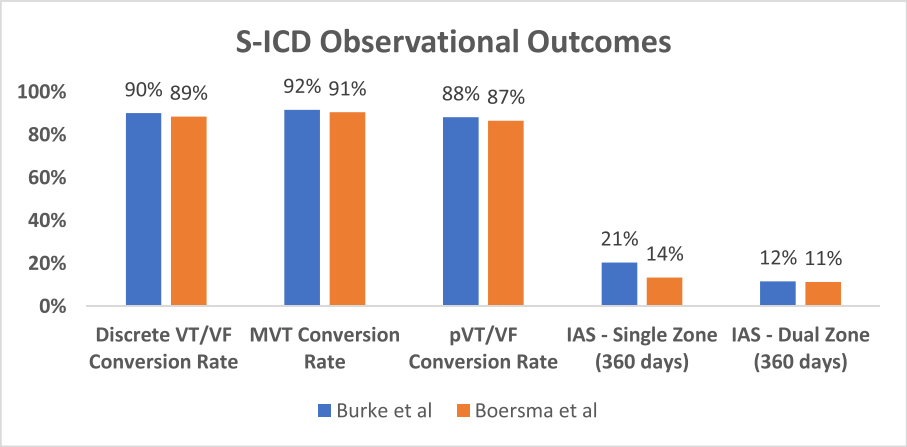
Lastly, the S-ICD System Post-Approval Study published the implantation and perioperative results of 1,637 patients in October of 2017.[21] When compared to other registries, including IDE and EFFORTLESS, this population had more patients with LVEF ≤35%, with >75% of patients falling into this category.[17] The overall mean age of the cohort was 53 years, with 68.6% being male. Of all study participants implanted with an S-ICD (1637), only 144 (8.8%) were implanted because this device was the only reasonable choice. Of these individuals, 93 (5.7%) were implanted because of their anatomy and/or lack of venous access, 22 (1.3%) due to infection risk, and 9 (0.5%) due to infection and/or malfunction of a prior TV-ICD. The rest of the patients (1493/1637 or 91.2%) were suitable candidates for both S-ICD and TV-ICD, but 858 patients (52.4%) preferred the S-ICD, 715 (43.7%) received S-ICD because of age, and 205 (12.5%) because of their activity level. There were a 99.0% freedom from complication rate caused by the S-ICD device itself and a 96.2% freedom from device- and procedure-related complications at 30 days. In total, 3.7% of the study population experienced complications in the perioperative period, with the most common device-related complication being failure to convert VF (0.4%) and the most common procedure-related complications being infection (1.2%) and hematoma (0.4%). Only 8 patients had to have their S-ICD extracted because of an S-ICD–related infection and 5 patients had theirs extracted because of failure to convert during defibrillation testing (DFT). An analysis of patients who experienced complications found that there was a positive correlation between infection and diabetes, younger age, and a higher body mass index (BMI).[21] Overall, comparing the EFFORTLESS registry[20] with the Post-Approval perioperative registry, patients included in the Post-Approval Study had a higher incidence of comorbidities, including more patients with

Table I. S-ICD observational studies and complication rates

Study	Year	n	Age* (y)	LVEF	Complication rate (30 d)	Complication rate (360 d)
Burke et al[17]	2015	882	50	39%	4.5%	11.1%
Boersma et al[20]	2017	985	48	43%	4.1%	8.4%

*Age is specified as a mean.

Figure 3



Shock-related outcomes.

heart failure (74.0% vs 26.5%), hypertension (61.6% vs 28.3%), diabetes (33.6% vs 11.3%), kidney disease (25.6% vs 8.2%), and MI (33.2% vs 28.1%). The Post-Approval Study in particular has some similar incidences of comorbidities as the TV-ICD studies such as the incidence of hypertension and diabetes, but the participants are on average younger and have a higher mean LVEF.[4,5]

S-ICD programming

There are typically 2 zones used for arrhythmia detection after the implantation of the S-ICD. Single-zone programming monitors rate alone, and dual-zone programming analyzes rate and also contains a rhythm monitoring algorithm to differentiate potentially lethal arrhythmias from more benign ones. Observational studies have found that the rate of inappropriate shocks is significantly lower with dual-zone programming, and this has prompted many physicians to use these settings.[17,20] In the pooled EFFORTLESS and IDE study, around 79.0% of patients had dual-zone programming, whereas in the Post-Approval Study, nearly 97% of the patients had dual-zone programming.[17,21] At 3 years, the incidence of inappropriate shock in the pooled study was 11.7% in patients with dual-zone programming versus 20.5% in patients with single-zone programming. The most recent EFFORTLESS results revealed the rate of inappropriate shocks in the first 3 years after implantation to be 11.4% for dual zone and 13.5% for single zone.[20] The most common reason for inappropriate shocks was T-wave oversensing. The S-ICD system uses a conditional discrimination zone for rates between 170 and 240 beats/min and will not treat arrhythmias lower than this cutoff point.[22] These settings play an important role in limiting inappropriate shock therapy by differentiating between supraventricular and ventricular tachycardia.

Importantly, the S-ICD also has the ability to detect atrial fibrillation and can differentiate it from potentially lethal arrhythmia. Detection of atrial fibrillation in patients who have otherwise not been known to have this arrhythmia may lead to early treatment and stroke prevention.

More experience leads to better outcomes

Given that the S-ICD system is relatively new, there has been a learning curve with its implantation. Currently, the S-ICD system is more commonly implanted at larger tertiary referral centers than other smaller centers across the United States. Several of the previously mentioned observational studies have shown that complication rates have had a decreasing trend with respect to time. Many have wondered about whether the decreasing risk of complications with the S-ICD is due to physicians becoming more comfortable and skilled with the implantation procedure. Knops et al analyzed the pooled EFFORTLESS and IDE data (882 patients) to ascertain the reason for the lower complication rates over time.[23] This subanalysis revealed that the median time from implantation of the S-ICD to a complication was 18 days. Quartiles were established based on experience. Quartile 1 included the first 4 implants per implanter, quartile 2 included implants 5 through 12, quartile 3 included implants 13 through 28, and finally quartile 4 included any implants >28. The results revealed that the complication rates decreased from 9.8% in quartile 1 to 5.4% in quartile 4, which were statistically significant. Between quartiles 1 through 4, there were an absolute risk reduction of 4.4% and a relative risk reduction of nearly 45%. Other results of this analysis showed that procedural time decreased through the experience quartiles, but when adjusting for confounders, including age, congenital heart disease, and prior ICD, this difference was no longer significant. There

was a statistically significant trend toward fewer inappropriate shocks over experience quartiles, but it was also found that the incidence of dual-zone programming increased over experience quartiles from 64% to 96%, which is more likely to be the reason for the decrease in inappropriate shock rate and less so based on physician experience. In conjunction with the recent sole update from the EFFORTLESS registry,[20] the consensus is that the more implantations a physician performs, the lower the risk of complications.[23]

Defibrillation testing

Previously, DFT was the standard of care after implantation of the TV-ICD.[24] There was a paradigm shift in DFT after TV-ICD implantation due to RCT data indicating an increased risk of perioperative complications and no difference in mortality and successful ICD therapy during follow-up.[25,26] Hence, DFT is generally not performed after implantation of a TV-ICD. The current recommendation for S-ICD implantation is that patients undergo DFT to establish the ability of the device at terminating a potentially lethal arrhythmia and the energy required to do so.[27] The class I recommendation for DFT in the S-ICD is due to the extrathoracic configuration of the device and the need for a higher energy requirement for successful termination of arrhythmias. Many of the previously mentioned studies reported results of the S-ICD terminating arrhythmia during DFT with promising numbers. More than 1,400 patients in the Post-Approval Study underwent DFT, with inducible VT/VF successfully converted in 98.7%.[21] Among patients undergoing DFT, prior TV-ICD extraction, height, and increased BMI predicted a higher risk of failed first shock conversion, whereas African American race predicted a lower risk. In the EFFORTLESS registry analysis, 861 patients underwent DFT, with 99.5% showing successful conversion.[20] Of the patients with successful conversion, 91.6% had success at ≤65 J. A recent retrospective study from Emory in 2018 analyzed 178 patients implanted with an S-ICD.[24] Of the 178 patients, 135 underwent DFT. Study participants were stratified into 2 groups: those who underwent DFT and those who did not. Overall, there was no difference in the rate of ventricular arrhythmia between the groups. There was also no difference in first shock effectiveness rates between the 2 groups either (88.4% vs 94.1%, $P = .97$).[24] In the Friedman et al analysis of the nationwide ICD registry, of >3,000 patients who were implanted with an S-ICD, nearly 2,800 underwent DFT.[14] A total of 2,588 (92.7%) patients were successfully defibrillated at 65 J or less, 2,629 patients (94.2%) at 70 J or less, 2,635 patients (94.4%) at 75 J or less, and 2,784 patients (99.7%) at 80 J or less. An interesting finding of this analysis was that over the 3-year period of observation, DFT decreased from 82.4% to 71.4% ($P < .001$).

Multiple studies have shown a correlation of a higher BMI and the rate of failed first shock conversion during DFT.[21,28] An analysis of the IDE registry indicated that the more obese the patients, the more likely they were to have a failed first shock conversion.[28] There may be some indication that patients who are obese should be considered for periodic DFT after S-ICD implantation to ensure effectiveness. The PRAETORIAN-DFT is a current RCT evaluating DFT in the S-ICD which should further elucidate the need for DFT in the S-ICD.[29]

Transvenous versus subcutaneous ICD

Several recent observational studies have compared the S-ICD to the TV-ICD. These studies have been pooled into 2 recent meta-analyses. The first, by Basu-Ray et al,[30] included 5 studies.[14,31-34] This meta-analysis included data on device complications and inappropriate shocks but did not present pooled outcomes for appropriate device therapy, as only 2 of the 5 studies reported these data. The prevalence of lead complications was significantly lower for the S-ICD than the TV-ICD (0.14% vs 1.02%; odds ratio [OR] 0.13, 95% CI 0.05-0.38). Data for non–lead-related complications were also reported. The prevalence of infection, system failure, and total inappropriate therapy was similar between the S-ICD and TV-ICD (0.34% vs 0.31%, OR 0.75, 95% CI 0.30-1.89; 0.32% vs 0.24%, OR 1.13, 95% CI 0.43-3.02; 8.3% vs 9.46%, OR 0.87, 95% CI 0.51-1.49, respectively). The reasons for inappropriate therapy in the TV-ICD groups were more related to sensing of SVT, whereas in the S-ICD, the most common reasons for inappropriate therapy were noise and T-wave oversensing. In July 2018, another meta-analysis of S-ICD versus TV-ICD was published,[35] including the studies in the 2017 meta-analysis[14,31-34] and 3 more studies.[36-38] In total, this meta-analysis included >1,800 patient-years in the S-ICD arm and >2,200 patient-years in the TV-ICD. Results were reported as pooled incidence rate ratios (IRRs). The IRR is a measure of the incidence rates that are occurring at any given point in time. For this study, incidence rates were pooled together from previous observational analyses. The IRR of all-cause complications was 0.90 (95% CI 0.58-1.42), which was nonsignificantly in favor of the S-ICD. Five of the 7 studies included in this meta-analysis provided data on lead-related complications with the resulting pooled IRR of 0.15 (95% CI 0.06-0.33), statistically significant and in favor of the S-ICD. All 7 studies analyzed the incidence of overall infection. The reported pooled IRR for infection was 2.00 (95% CI 0.95-4.22), which was nonsignificant but was in favor of less overall infections in the TV-ICD. Lastly, the pooled IRR ratio for inappropriate and appropriate shocks was 1.17 (95% CI 0.77-1.79) and 0.68 (95% CI 0.42-1.03), respectively; both did not reach statistical significance.

Overall, these meta-analyses have demonstrated equivocal results with respect to infection between the TV-ICD and S-ICD which may be due to lack of data and the need for more patients studied for longer intervals. It must be noted that although both the TV-ICD and S-ICD have risks of infection locally related to device implantation and pocket infection, S-ICD–related infections are generally less severe and less likely to be systemic when compared to the TV-ICD.[30,35] If a lead or device infection exists, whether it be the S-ICD or TV-ICD, extraction of the device and lead(s) is necessary. For leads with a dwell time of <1 year, extraction from both types of devices can be as easy as using simple traction and removal.[39,40] For leads with a dwell time >1 year, removal of TV-ICD can be more complex, often requiring laser.[39] Given the relatively recent use of the S-ICD, extraction techniques are still being studied. Current studies have shown that simple traction techniques work well for these devices. In more complex scenarios, extra incisions may be necessary for improved access to the device/lead as well as more effect traction.[40]

Current ongoing RCTs

More RCT data are needed to continue to understand the safety and efficacy of the S-ICD. There are currently several ongoing RCTs comparing the S-ICD to the TV-ICD. PRAETORIAN is a current multicenter, prospective, RCT comparing major adverse events between the S-ICD and the TV-ICD. The secondary end point of the trial is evaluation of whether the lack of ATP causes an increase in the incidence of appropriate shocks in the S-ICD arm.[41] The trial is expected to be completed in December 2019. The Avoid Transvenous Leads in Appropriate Subjects (ATLAS S-ICD) RCT started enrolling patients in February of 2017 and is to be completed in December of 2020.[42] This RCT is a head-to-head comparison of the S-ICD versus TV-ICD in patients younger than 60 years (older patients are allowed if they have an inherited arrhythmia syndrome, prior pacemaker or ICD removed for infection, need for hemodialysis, prior heart valve surgery, or chronic obstructive pulmonary disease). This RCT compares all aspects of the devices, including complications (perioperative and thereafter), inappropriate and appropriate shocks, shock efficacy, and an economic cost analysis. The Understanding Outcomes With the EMBLEM S-ICD in Primary Prevention Patients with Low Ejection Fraction (UNTOUCHED) is a single-arm clinical trial aimed to assess programmed zone cutoff similar to the MADIT RIT study.[43] The purpose is to compare the incidence of inappropriate shocks between the 2 devices. Finally, the PRAETORIAN-DFT trial is a study that will assess the ongoing need for DFT testing during the implantation of an S-ICD.

As the results of many of these randomized trials are revealed, there will be a continued need for further trials to assess the S-ICD in more patient populations. There are limited data in observational studies of patients with multiple comorbidities, and the RCTs that are under way are limited in their inclusion. Assessment of the S-ICD in the elderly and patients with end-stage renal disease is needed because these patient populations are unique in that they often have competing causes of death. The ATLAS S-ICD trial excludes patients older than 60 unless they have a specific indication as stated above, and the UNTOUCHED RCT excludes patients with an indication for a primary prevention ICD who have received hemodialysis within the last 180 days. It will be crucial for continued trials to understand the ideal populations in whom the S-ICD should be implanted.

Conclusions

The above-described observational studies have shown that the S-ICD can be both effective and safe. The rates of lead-related complications have significantly decreased with this device when compared to the TV-ICD with high rates of conversion of VT/VF after shock therapy. Rates of inappropriate shocks have improved over time as physicians have been able to optimize device settings to minimize oversensing of T-waves. Several studies have revealed that physicians are becoming more comfortable with this device as well with regard to its implantation and use. This finding is reflected with decreasing rates of complications as more devices are implanted per implanter, which are encouraging as the S-ICD becomes more ubiquitous. We are becoming more aware of populations in which the S-ICD would be optimal, but there are still several outstanding questions that need to be answered with respect to device use. Defibrillation testing is still the standard of care, but this practice has evolving evidence that it may not be needed, similar to the TV-ICD. An exception may potentially be patients with higher BMIs because there is evidence of higher energy requirements for effective defibrillation. Randomized controlled data will be helpful in informing future guidelines on ICDs. As we understand the S-ICD in more detail with pending RCTs, we can begin to extrapolate its use to broader and more comorbid populations to provide benefit to patients who otherwise would be poor candidates for the TV-ICD and improve the incidence of device-related morbidity and mortality.

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References

1. Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics—2018 Update: a report from the American Heart Association. Circulation Mar 20 2018;137:e67-e492.
2. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol Oct 2 2018;72:e91-e220.
3. Goldberger JJ, Buxton AE, Cain M, et al. Risk stratification for arrhythmic sudden cardiac death: identifying the roadblocks. Circulation May 31 2011;123:2423-30.
4. Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, Levine JH, Saksena 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. Multicenter Automatic Defibrillator Implantation Trial Investigators. The New England journal of medicine Dec 26 1996;335:1933–1940.
5. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med Mar 21 2002;346:877-83.
6. van Rees JB, de Bie MK, Thijssen J, et al. Implantation-related complications of implantable cardioverter-defibrillators and cardiac resynchronization therapy devices: a systematic review of randomized clinical trials. J Am Coll Cardiol Aug 30 2011;58:995-1000.
7. Kleemann T, Becker T, Doenges K, et al. Annual rate of transvenous defibrillation lead defects in implantable cardioverter-defibrillators over a period of >10 years. Circulation May 15 2007;115:2474-80.
8. Sponder M, Khazen C, Dichtl W, et al. Specific indications and clinical outcome in patients with subcutaneous implantable cardioverter-defibrillator (ICD) - A nationwide multicentre registry. Eur J Intern Med Feb 2018;48:64-8.
9. Chang SC, Patton KK, Robinson MR, et al. Subcutaneous ICD screening with the Boston Scientific ZOOM programmer versus a 12-lead ECG machine. Pacing and clinical electrophysiology : PACE May 2018;41:511-6.
10. Brouwer TF, Miller MA, Quast AB, et al. Implantation of the subcutaneous implantable cardioverter-defibrillator: an evaluation of 4 implantation techniques. Circulation Arrhythmia and electrophysiology Jan 2017;10, e004663.
11. Olde Nordkamp LR, Dabiri Abkenari L, Boersma LV, et al. The entirely subcutaneous implantable cardioverter-defibrillator: initial clinical experience in a large Dutch cohort. J Am Coll Cardiol Nov 6 2012;60:1933-9.
12. Knops RE, Olde Nordkamp LR, de Groot JR, et al. Two-incision technique for implantation of the subcutaneous implantable cardioverter-defibrillator. Heart rhythm Aug 2013;10:1240-3.
13. Quast ABE, Brouwer TF, Tjong FVY, Wilde AAM, Knops RE. Clinical parameters to optimize patient selection for subcutaneous and transvenous implantable defibrillator therapy. Pacing and clinical electrophysiology : PACE Jun 13 2018.
14. Friedman DJ, Parzynski CS, Varosy PD, et al. Trends and in-hospital outcomes associated with adoption of the subcutaneous implantable cardioverter defibrillator in the United States. JAMA Cardiol Nov 1 2016;1:900-11.
15. Weiss R, Knight BP, Gold MR, et al. Safety and efficacy of a totally subcutaneous implantable-cardioverter defibrillator. Circulation Aug 27 2013;128:944-53.
16. Lambiase PD, Barr C, Theuns DA, et al. Worldwide experience with a totally subcutaneous implantable defibrillator: early results from the EFFORTLESS S-ICD Registry. Eur Heart J Jul 1 2014;35:1657-65.
17. 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 Apr 28 2015;65:1605-15.
18. Boersma LV, Barr CS, Burke MC, et al. Performance of the subcutaneous implantable cardioverter-defibrillator in patients with a primary prevention indication with and without a reduced ejection fraction versus patients with a secondary prevention indication. Heart rhythm Mar 2017;14:367-75.
19. Boersma L, Burke MC, Neuzil P, et al. Infection and mortality after implantation of a subcutaneous ICD after transvenous ICD extraction. Heart rhythm Jan 2016;13:157-64.
20. Boersma L, Barr C, Knops R, et al. Implant and midterm outcomes of the subcutaneous implantable cardioverter-defibrillator registry: the EFFORTLESS study. J Am Coll Cardiol Aug 15 2017;70:830-41.
21. Gold MR, Aasbo JD, El-Chami MF, et al. Subcutaneous implantable cardioverter-defibrillator Post-Approval Study: clinical characteristics and perioperative results. Heart rhythm Oct 2017;14:1456-63.
22. Bardy GH, Smith WM, Hood MA, et al. An entirely subcutaneous implantable cardioverter-defibrillator. N Engl J Med Jul 1 2010;363:36-44.
23. Knops RE, Brouwer TF, Barr CS, et al. The learning curve associated with the introduction of the subcutaneous implantable defibrillator. Europace Jul 2016;18:1010-5.
24. Peddareddy L, Merchant FM, Leon AR, Smith P, Patel A, El-Chami MF. Effect of defibrillation threshold testing on effectiveness of the subcutaneous implantable cardioverter defibrillator. Pacing and clinical electrophysiology : PACE Jun 12 2018.
25. Healey JS, Hohnloser SH, Glikson M, et al. Cardioverter defibrillator implantation without induction of ventricular fibrillation: a single-blind, non-inferiority, randomised controlled trial (SIMPLE). Lancet Feb 28 2015;385:785-91.
26. Bansch D, Bonnemeier H, Brandt J, et al. Intra-operative defibrillation testing and clinical shock efficacy in patients with implantable cardioverter-defibrillators: the NORDIC ICD randomized clinical trial. Eur Heart J Oct 1 2015;36:2500-7.
27. Wilkoff BL, Fauchier L, Stiles MK, et al. 2015 HRS/EHRA/APHRS/SOLAECE expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. Heart rhythm Feb 2016;13:e50-86.
28. Frankel DS, Burke MC, Callans DJ, et al. Impact of body mass index on safety and efficacy of the subcutaneous implantable cardioverter-defibrillator. JACC Clin Electrophysiol May 2018;4:652-9.
29. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000 Feb 29–Identifier NCT03495297, a randomised trial of S-ICD implantation with and without defibrillation testing (PRAETORIAN-DFT) 2018 April 12 [cited 2018 October 5]; Available from: https://clinicaltrials.gov/ct2/show/NCT03495297.
30. Basu-Ray I, Liu J, Jia X, et al. Subcutaneous versus transvenous implantable defibrillator therapy: a meta-analysis of case-control studies. JACC Clin Electrophysiol Dec 26 2017;3:1475-83.
31. Brouwer TF, Knops RE, Kutyifa V, et al. Propensity score matched comparison of subcutaneous and transvenous implantable cardioverter-defibrillator therapy in the SIMPLE and EFFORTLESS studies. Europace Sep 1 2018;20:f240-8.
32. Lenarczyk R, Boveda S, Haugaa KH, et al. Peri-procedural routines, implantation techniques, and procedure-related complications in patients undergoing implantation of subcutaneous or transvenous automatic cardioverter-defibrillators: results of the

European Snapshot Survey on S-ICD Implantation (ESSS-SICDI). Europace Jul 1 2018;20:1218-24.
33. Brouwer TF, Yilmaz D, Lindeboom R, et al. Long-term clinical outcomes of subcutaneous versus transvenous implantable defibrillator therapy. J Am Coll Cardiol Nov 8 2016;68:2047-55.
34. Mithani A, Kath H, Eno E, Nathan K, Field J, Hunter K, Ortman M, Andriulli J, Russo A. Characteristics and clinical outcomes of patients undergoing subcutaneous versus transvenous single chamber ICD placement. Journal of the American College of Cardiology 2016/04/05/ 2016;67:860.
35. Baalman SWE, Quast ABE, Brouwer TF, Knops RE. An overview of clinical outcomes in transvenous and subcutaneous ICD patients. Curr Cardiol Rep Jul 10 2018;20:72.
36. Honarbakhsh S, Providencia R, Srinivasan N, et al. A propensity matched case-control study comparing efficacy, safety and costs of the subcutaneous vs. transvenous implantable cardioverter defibrillator. Int J Cardiol Feb 1 2017;228:280–285.
37. Kobe J, Reinke F, Meyer C, et al. Implantation and follow-up of totally subcutaneous versus conventional implantable cardioverter-defibrillators: a multicenter case-control study. Heart rhythm Jan 2013;10:29-36.
38. Mithani AA, Kath H, Hunter K, et al. Characteristics and early clinical outcomes of patients undergoing totally subcutaneous vs. transvenous single chamber implantable cardioverter defibrillator placement. Europace Feb 1 2018;20:308-14.
39. Wilkoff BL, Love CJ, Byrd CL, et al. Transvenous lead extraction: Heart Rhythm Society expert consensus on facilities, training, indications, and patient management: this document was endorsed by the American Heart Association (AHA). Heart rhythm Jul 2009;6:1085-104.
40. Nakhla S, Hussein AA, Brunner MP, et al. Removal of subcutaneous defibrillator shocking coils: lessons to learn for future extraction of subcutaneous defibrillator systems. Pacing and clinical electrophysiology : PACE Oct 2018;41:1341-4.
41. Olde Nordkamp LR, Knops RE, Bardy GH, et al. Rationale and design of the PRAETORIAN trial: a Prospective, RAndomizEd comparison of subcuTaneOus and tRansvenous ImplANtable cardioverter-defibrillator therapy. Am Heart J May 2012;163:753–760.e752.
42. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000 Feb 29–identifier NCT02881255, avoid transvenous leads in appropriate subjects (ATLAS S-ICD) 2016 Aug 6 [cited 2018 October 5] Available from: https://clinicaltrials.gov/ct2/show/study/NCT02881255.
43. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000 Feb 29–identifier NCT02433379, understanding outcomes with the EMBLEM™ S-ICD in primary prevention patients with low ejection fraction (UNTOUCHED) 2015 May 5 [cited 2018 October 5] Available from: https://clinicaltrials.gov/ct2/show/NCT02433379.