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REVIEW TOPIC OF THE WEEK

Safety and Efficacy of the Subcutaneous Implantable Defibrillator

Geoffrey F. Lewis, MD, Michael R. Gold, MD, PhD

ABSTRACT

Multiple randomized, multicenter trials have established the role of the implantable cardioverter-defibrillator (ICD) in the treatment and prevention of sudden cardiac death. However, transvenous ICD leads have significant short- and long-term complications, offsetting some of the benefit of this therapy. This has led to the development of the entirely subcutaneous ICD. This system is safe and effective, avoiding the need for intravascular leads. It is best suited for patients at low risk for pacing and increased risk for transvenous lead complications. Ongoing randomized and long-term registries will help identify the optimal role of this device in clinical practice. (J Am Coll Cardiol 2016;67:445–54)

Despite advances in medical therapy, sudden cardiac death (SCD) remains a leading cause of cardiovascular mortality worldwide. The implantable cardioverter-defibrillator (ICD) is the most effective treatment to date for either primary or secondary prevention of SCD when utilized in concert with appropriate medical therapy. ICDs reduce mortality and are cost-effective in specific patient populations that are at increased risk (1–5). Contemporary ICD systems typically consist of transvenous intracardiac leads and a subcutaneous, pectoral pulse generator to provide defibrillation and pacemaker capabilities.

Despite their proven efficacy and relative safety, potential short- and long-term complications are associated with these devices, including infection, pneumothorax, venous thrombosis, lead dislodgement, lead malfunction, and lead perforation (6). A recent meta-analysis of randomized clinical trials finds the following complication rates related to device implant: pneumothorax, 1.1%; hematoma, 1.2%; lead dislodgement, 3.1%; and infection, 1.5% (7). Other studies of real-world implants have found complication rates of 0.16% and 0.12% for lead perforation and pericardial tamponade, respectively (8). The 10-year transvenous lead failure rate is as high as 20% (9). Moreover, due to anatomic or structural abnormalities (e.g., congenital heart diseases, mechanical heart valves, or other rare situations), certain patients are unable to have a traditional ICD placed (10,11). Although complication rates with transvenous ICD implantation are generally low, they contribute to the morbidity and, possibly, mortality of the procedure and may reduce its utilization.

Alternative implantable device options for prevention of SCD have been developed. Epicardial or pericardial patches do not require intravascular access, but are infrequently used because of the need for thoracotomy for placement and high failure rates (12). Until recently, no other permanent substitute for the traditional ICD was available. Beginning more than a decade ago, an entirely subcutaneous implantable cardioverter-defibrillator (S-ICD) was developed and later became commercially available. The S-ICD (Boston Scientific, Marlborough, Massachusetts) consists of a pulse generator and single lead with a shock coil. The pulse generator is implanted in the left lateral position, between the anterior and mid-axillary lines near the apex of the left ventricle. A single lead for sensing and defibrillation is tunneled

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From the Division of Cardiology, Medical University of South Carolina, Charleston, South Carolina. Dr. Gold has received consulting fees from and performed clinical trials with Boston Scientific, Medtronic, and St. Jude. Dr. Lewis has reported that he has no relationships relevant to the contents of this paper to disclose.

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ABBREVIATIONS AND ACRONYMS

ATP = antitachycardia pacing

CRT = cardiac resynchronization therapy

DFT = defibrillation threshold

ICD = implantable cardioverter-defibrillator

SCD = sudden cardiac death

S-ICD = subcutaneous implantable cardioverter-defibrillator

SVT = supraventricular tachycardia

VF = ventricular fibrillation

VT = ventricular tachycardia

from the lateral pocket medially to the xiphoid process and subsequently cephalad and is usually positioned 1 to 2 cm to the left of and parallel to the sternum, with the distal tip near the manubriosternal junction (13). The lead consists of sensing electrodes at the subxiphoid (proximal) and manubriosternal junction (distal) positions, separated by an 8-cm shocking coil (**Figure 1**). Using the pulse generator as a third electrode provides 3 potential sensing vectors (pulse generator to proximal or distal electrode and distal to proximal electrode). The shock vector is from pulse generator to coil and is reversed if more than 1 shock is needed to terminate an arrhythmia. The S-ICD lacks functionality for bradycardia or antitachycardia pacing, but can provide up to 30 s of post-shock transthoracic pacing (14).

When considering the results of S-ICD clinical trials, it is notable that the patient populations were typically younger, with less advanced heart disease, and often with "niche" indications, including channelopathies, previous ICD infection, or congenital heart disease. In early trials, the mean age ranged from 33 to 56 years (15–21). In trials reporting any channelopathy patients, rates ranged from 10% to 28% (15,17,20,22–24). Although these important groups are often viewed as the primary target population for the S-ICD, they may not provide an accurate basis for comparison with the common primary and secondary prevention ICD populations.

The largest cohort for comparison to real-world ICD patients is the pooled data from the IDE (Investigational Device Exemption) study and the EFFORTLESS (Evaluation oF FactORs ImpacTing CLinical Outcome and Cost EffectiveneSS of the S-ICD) registry (23). This diverse population includes 882 patients receiving ICDs. Primary prevention patients made up 69.9% of the study, and overall mean ejection fraction (EF), including secondary prevention patients, was 39.4 ± 17.6%. Mean age was 50.3 ± 16.9 years. Overall, even this patient population is younger and consists of more patients with preserved EF than most transvenous ICD trials. On the basis of these experiences, a recent paper proposes that excellent candidates for the S-ICD include young patients and those with limited vascular access, channelopathies, congenital heart disease, and prior infection of transvenous ICD; whereas poor candidates include those with indications for pacing, with monomorphic ventricular tachycardia (VT) amenable to antitachycardia pacing (ATP), who are cardiac resynchronization therapy (CRT)-eligible, and those failing pre-implant screening (25). Recently published case series have shown the S-ICD to be a safe and effective alternative in dialysis patients, a prototypical population with limited vascular access (26,27).

The S-ICD received CE Mark approval in Europe in 2008, largely on the basis of small early trials (15). As a result of the IDE trial (21), U.S. Food and Drug Administration approval followed in 2012. Worldwide, >3,000 S-ICD systems were implanted in 2013 (28) and with >10 years of aggregate experience, larger patient cohorts are now being examined.

SAFETY

Avoidance of risks associated with the procedure and long-term presence of intravascular leads was a major driving force in development of the S-ICD. The structure of the S-ICD lead differs significantly from a transvenous ICD lead. Finally, development of advanced discrimination algorithms in the S-ICD has decreased the inappropriate shock rate for supraventricular arrhythmias significantly.

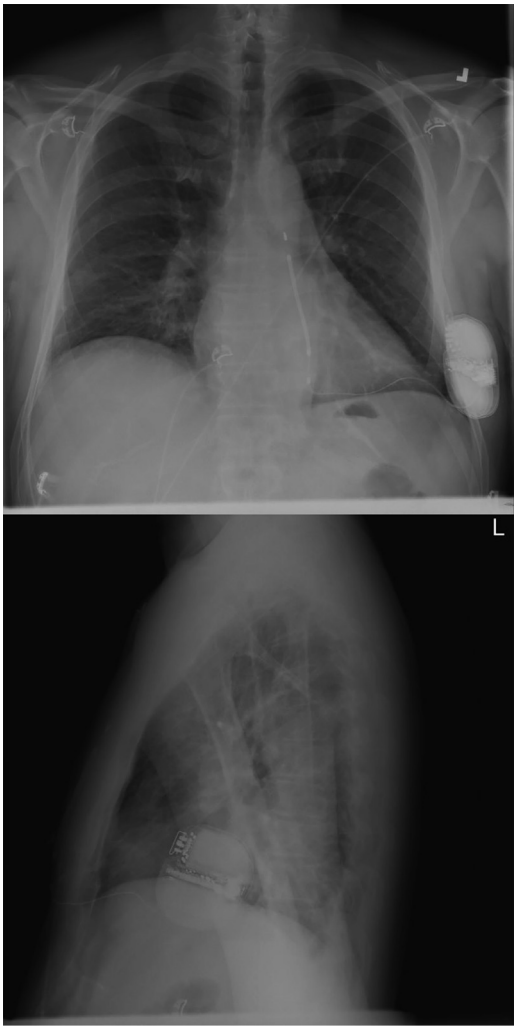
INFECTION. Significant problems associated with early S-ICD implants included device infection, lead migration, and, to a lesser extent, implant-site hematoma and device erosion. In the trial culminating in European CE Mark approval, only 2 of 55 (3.6%) devices became infected (15). Subsequent descriptions of real-world clinical experience demonstrated significantly higher infection rates. In 2012, Jarman et al. (19) and Olde Nordkamp et al. (17) reported device infection in 11 of 111 (9.9%) and in 7 of 118 implants (5.9%), respectively. Others reported lower device infection rates, ranging from 0% to 3.2%, with the highest reported percentage being a single device infection among only 31 patients (16,18,20). The U.S. IDE trial reported 18 suspected or confirmed infections among 330 implants (5.5%) (**Table 1**) (21). Only 4 of these patients required device explant, and the others were deemed to be only superficial infections. There was a decreasing incidence with greater operator and institutional experience, consistent with a "learning curve," resulting in an infection rate comparable to that of transvenous ICDs, reported as 0.13% to 1.9% (29,30). Early results of the EFFORTLESS S-ICD registry are similar: 18 of 472 (3.8%) patients had documented or suspicion of infection related to the S-ICD procedure (24); 10 patients (2.1%) required device explant; and only 3 institutions had multiple cases of infection requiring device removal. Over 5.8 years of follow-up, the European Regulatory Trial cohort had 1 device infection necessitating removal (31). Although all hardware-related infections have the potential to

become systemic and life threatening, an important distinction between transvenous and subcutaneous ICD infections is their association with endocarditis and bacteremia, which were reported in 22% to 54% of transvenous ICD infections (32,33). None of the S-ICD infections reported in the IDE trial and EFFORTLESS registry were associated with endocarditis or bacteremia (21,24). As with transvenous ICDs, S-ICD-related infections require individualization of care to determine in which circumstances device explant or other invasive management is necessary.

IMPLANT SITE COMPLICATIONS. Less common complications related to S-ICD implant include hematoma and device erosion. Reports of hematoma at the device implant site are rare in published case series. Köbe et al. (20) report a single hematoma among 69 S-ICD implants (20). Early results of the EFFORTLESS S-ICD registry report only a single hematoma in 472 patients (0.2%) evaluated over a mean of 558 days of follow-up (24). Multiple other cohorts, including the large IDE trial, report no implant-related hematomas (15–19,21). Hematoma formation rates with the S-ICD compare favorably with traditional ICD hematoma rates of 0.86%, as reported in the National Cardiovascular Data Registry, and 1.2% to 2.4% in randomized clinical trials (7,34,35). Device erosion, a feared complication due to the associated risk of infection and potential need for additional invasive procedures, has also been reported with S-ICD implantation. This is suggested to result from the large size of the pulse generator and/or the implant location in the axilla. An early experience by Jarman et al. (22) reported an alarming 18.8% (3 of 16) rate of device erosion. However, other cohorts have not reproduced this high device erosion rate. Among the minority of trials reporting any cases of pulse generator erosion, rates ranged from 1.7% to 1.8% (17,19). Nonetheless, the size of the first-generation S-ICD's pulse generator has clearly been an issue. The generator has a volume of 69.9 cc, weighs 165 g, and measures 78.2 × 65.5 × 15.7 mm. Each of these measurements is larger than a comparable transvenous ICD. This large size, particularly the thickness, has been problematic for some patients, primarily those of smaller body habitus. The second-generation S-ICD pulse generator has a smaller volume (59.5 cc), and weight (130 g); it measures 83.1 × 69.1 × 12.7 mm (36) (**Figure 2**). Although the reduced pulse generator size may result in decreased incidence of pulse generator erosion, there is, as yet, no published data on this topic.

Recently published data from the combined IDE and EFFORTLESS registries demonstrate the learning curve associated with S-ICD implants (37).

FIGURE 1 Postero-Anterior and Lateral Chest Radiographs of an Implanted S-ICD



S-ICD = subcutaneous implantable cardioverter-defibrillator.

Complication rates decreased significantly between operators with the least (9.8%) and most (5.4%) experience, and seem asymptotic after 13 implants.

S-ICD LEAD. The requirement for transvenous leads has been described as the "Achilles' heel" of traditional ICDs; thus, its avoidance is a major advantage of the S-ICD (38). Utilization of a subcutaneous lead circumvents difficulties with transvenous lead implantation in patients with altered vascular or cardiac anatomy, such as those with obstructed venous systems or congenital heart disease. Lead migration was identified as an early and repetitive difficulty with the S-ICD, often requiring lead revision, thus exposing the patient to additional risk and causing

TABLE 1 Summary of S-ICD Trials

	Bardy et al. (15) (n = 55)	Dabiri Abkenari et al. (16) (n = 31)	Aydin et al. (18) (n = 40)	Jarman et al. (22) (n = 111)	Olde Nordkamp et al. (17) (n = 118)	Köbe et al. (20) (n = 69)	Weiss et al. (21) (n = 330)	Lambiase et al. (24) (n = 472)	Burke et al. (23) (n = 883)
Age, yrs	56 ± 13	53 ± 4	42 ± 15	33	NA	46 ± 16	52 ± 16	49 ± 18	50 ± 17
Male	80	77	70	NA	75	72	74	72	72.5
Follow-up	10 ± 1 months	286 days	229 days	12.7 ± 7.1 months	18 ± 7 months	217 ± 138 days	330 days	558 days	651 ± 345 days
Ischemic cardiomyopathy	37 (67.0)	18 (58.0)	9 (22.5)	15 (14.0)	45 (38.0)	11 (15.9)	137 (41.4)	166 (37.0)	330 (37.8)
LVEF	35 ± 14	38 ± 15	47 ± 15	NA	41 ± 15	46 ± 16	36 ± 16	42 ± 19	39 ± 18
Primary prevention	43 (78.0)	21 (67.0)	17 (42.5)	55 (50.0)	71 (60.0)	41 (59.4)	262 (79.0)	282 (63.0)	610 (69.9)
Inappropriate shocks	5 (9.0)	5 (16.0)	2 (5.0)	17 (15.0)	15 (13.0)	3 (4.0)	41 (13.0)	32 (7.0)	14 (2.5)
Appropriate therapy (% successful)	3 (100.0)	4 (100.0)	4 (96.4)	13 (100.0)	8 (100.0)	3 (100.0)	21 (95.2)	33 (100.0)	111 (98.2)
Complications									
Infection	2 (3.6)	1 (3.2)	0	11 (9.9)	7 (5.9)	1 (1.4)	18 (5.6)	11 (2.3)	14 (1.5)
Lead migration	6 (10.9)	2 (6.4)	0	0	3 (2.5)	0	0	4 (0.8)	7 (0.8)
Device erosion	0	0	0	2 (1.8)	2 (1.7)	0	0	4 (0.8)	12 (1.4)
Hematoma	0	0	0	0	0	1 (1.4)	0	1 (0.2)	4 (0.4)
Patient characteristics									
Ischemic cardiomyopathy	37 (67.0)	18 (58.0)	9 (22.5)	15 (14.0)	45 (38.0)	11 (15.9)	137 (41.4)	166 (37.0)	330 (37.8)
Dilated cardiomyopathy	10 (18.0)	4 (13.0)	9 (22.5)	5 (5.0)	30 (25.4)	25 (36.2)	NA	43 (9.1)	277 (31.8)
HOCM	NA	NA	5 (12.5)	22 (20.0)	NA	10 (14.5)	NA	58 (12.2)	
Congenital heart disease	2 (4.0)	NA	NA	13 (12.0)	1 (0.8)	3 (4.4)	NA	33 (7.0)	
Brugada syndrome	NA	2 (6.5)	NA	14 (13.0)	NA	NA	NA		
Idiopathic VT/VF	NA	5 (16.1)	12 (30.0)	17 (15.0)	15 (13.0)	NA	NA	34 (8.0)	40 (4.6)
Ventricular noncompaction	NA	1 (3.0)	NA	NA	NA	NA	NA		
Valvular heart disease	NA	1 (3.0)	1 (2.5)	NA	NA	NA	NA		
Long QT	NA	NA	NA	10 (9.0)	NA	NA	NA		
CPVT	NA	NA	NA	7 (6.0)	NA	NA	NA		
Inherited channelopathy		5 (16.1)		31 (27.9)	27 (23.0)	14 (20.3)		60 (13.0)	90 (10.3)
Other	6 (11.0)	NA	13 (32.5)	13 (12.0)	57 (48.0)	NA	NA	14 (2.9)	

Values are mean ± SD, %, or n (%).

CPVT = catecholaminergic polymorphic ventricular tachycardia; HOCM = hypertrophic obstructive cardiomyopathy; LVEF = left ventricular ejection fraction; NA = not available; S-ICD = subcutaneous implantable cardioverter-defibrillator. VF = ventricular fibrillation; VT = ventricular tachycardia.

inappropriate ICD shocks due to myopotentials and T-wave oversensing (15-22). In response to lead migration issues, the manufacturer introduced a suture sleeve to secure the lead at the xiphoid incision that has essentially eliminated the incidence of this complication. The EFFORTLESS registry found only 4 episodes of lead migration among 472 patients (0.85%) (24).

S-ICD lead structure differs from traditional leads in ways that confer advantages in durability and lead failure. The 10-year transvenous ICD lead failure rate is approximately 20% (9). Previous extravascular ICD leads, such as epicardial patches, also have high failure rates, but are structurally unique (12). Because the S-ICD lead does not require a stylet for placement, it has no central lumen, which provides greater tensile strength. Furthermore, due to its subcutaneous location, the S-ICD lead is less exposed to environmental stress. Given that lead failures typically do not appear for several years after implant, real-world experience of long-term survival of the S-ICD lead is needed. The longest follow-up reported to date is 5.8 years in the European Regulatory Trial, during which there were no reported lead malfunctions or failures (31). If the S-ICD lead proves more durable, repeat invasive procedures and other complications associated with lead failure (e.g., inappropriate shocks and malfunctions in pacing or sensing function) could be reduced. Clearly, even longer-term follow-up is necessary before firm conclusions regarding S-ICD lead durability can be drawn, although the short and intermediate follow-up data are very encouraging.

INAPPROPRIATE SHOCKS. Delivery of inappropriate shocks due to errors in arrhythmia discrimination or oversensing was observed repeatedly in early S-ICD studies. The first trials and patient cohorts reported inappropriate shock rates of 5% to 25% (15-22). Traditional ICDs have inappropriate shock rates <5% (39). Inappropriate shocks in early trials were often due to T-wave oversensing, lead migration, or supraventricular tachycardias (SVTs). Introduction of the suture sleeve effectively eliminated lead migration, as

discussed earlier. A software update with improved SVT discrimination and device reprogramming has reduced the incidence of inappropriate shocks due to SVT and T-wave oversensing. Early versions of the S-ICD were programmed with a shock-only zone at a relatively low rate (180 beats/min). Current nominal device settings include a conditional zone, which applies SVT discriminators, and a shock zone for rates >220 beats/min. These changes reflect the findings of the prospective, multicenter START (Subcutaneous versus Transvenous Arrhythmia Recognition Testing) trial, which compared discrimination algorithms of the S-ICD with traditional transvenous ICD systems (14). In the START trial, patients undergoing dual- or tri-chamber transvenous ICD implant had both cutaneous (corresponding with S-ICD sensing vectors) and transvenous electrograms recorded during induced supraventricular and ventricular arrhythmias. Signals were interpreted offline by the S-ICD and traditional ICDs. The S-ICD discrimination algorithm includes 3 double-detection algorithms to prevent double counting, morphology comparison to stored sinus rhythm template, analysis of beat-to-beat morphology changes, and comparison of QRS width to a sinus template. The S-ICD was found to have 100% sensitivity for appropriate detection of VT and ventricular fibrillation (VF). Additionally, using dual-zone programming, the S-ICD had 98% specificity for appropriately withholding therapy for SVT. Usage of dual-zone programming has been found to increase with operator experience, thus resulting in a reduction in inappropriate shock rate (37). The specificity of transvenous ICDs was inferior to that of the S-ICD (13,14). Despite the very low incidence of inappropriate shocks from supraventricular arrhythmias, T-wave oversensing leading to inappropriate therapy remains problematic with the S-ICD. The incidence has been reduced with the use of pre-implant electrocardiographic screening, although this screening makes approximately 8% of patients ineligible to receive an S-ICD (40). Use of the S-ICD sensing algorithm has been proposed as a pre-implant screening device to increase specificity, thus reducing inappropriate shocks (41). Exercise testing during pre-implant screening has been suggested for all patients (42) and is effective in establishing the preferred sensing vector and lead placement in hypertrophic cardiomyopathy patients (43). T-wave inversions resulting from ischemia or left ventricular hypertrophy make a patient 23× more likely to fail screening. Very large or very small QRS complexes can also lead to screening failure. Patients who experience T-wave oversensing after implant can most often be managed noninvasively through device programming (20,24).

FIGURE 2 Photograph of Lateral Views of First-Generation S-ICD, Second-Generation (Emblem) S-ICD, and Single-Chamber ICD Pulse Generators Demonstrating Device Thickness

ICD = implantable cardioverter-defibrillator; S-ICD = subcutaneous implantable cardioverter-defibrillator.

A recent revision of the discrimination algorithm should further reduce such inappropriate shocks (44). A less common cause of inappropriate shocks is change in QRS morphology after the sinus rhythm template is acquired at implant, such as development of right bundle branch block. This can typically be managed noninvasively by acquiring a new QRS morphology template that the device uses for comparison during arrhythmia episodes. With the software and programming updates in recent versions of the S-ICD, inappropriate shock rates appear comparable to that of transvenous ICDs, although there has been no head-to-head comparison in equivalent patient populations. The EFFORTLESS registry, primarily using dual-zone programming and higher shock cutoff rates, reports inappropriate shock rates of 7% (24). Traditional ICD registries report inappropriate shock rates of 4% to 18% (45–47). However, newer transvenous device algorithms have shown lower inappropriate shock rates. The ADVANCE III (Avoid Delivering Therapies for Nonsustained Arrhythmias in ICD Patients III) trial, for example, randomized ICD patients to standard (18 of 24) or prolonged (24 of 30)

intervals for detection of ventricular arrhythmia prior to delivery of therapy (48). The prolonged interval strategy resulted in less therapy (ATP or shock), equivalent mortality, and reduced the inappropriate shock rate from 11.6 to 5.1 per 100 patient-years.

LACK OF PACEMAKER/ATP FUNCTIONALITY. Modern ICDs are implanted not only for prevention of SCD, but also, at times, for pacemaker and CRT functions. A major limitation of the S-ICD is its lack of pacemaker functionality, which eliminates it as an option for patients with a requirement or high likelihood for demand pacing. As CRT is an important component of therapy for advanced heart failure, CRT-eligible patients should not receive an S-ICD. In the European Regulatory Trial cohort, followed for 5.8 years, 1 of 55 patients (1.8%) developed an indication for bradycardia pacing and had the S-ICD explanted (31). In the same cohort, 2 of 55 patients (3.6%) developed symptomatic heart failure and underwent S-ICD explant in favor of a transvenous CRT device (31). In such situations, consideration can be given to concurrent use of the S-ICD with a transvenous pacemaker in lieu of S-ICD explant. This approach was successfully used in small case series, although careful assessment for "cross-talk" between the devices is required (49,50). As there have been no large studies of the safety and feasibility of this approach, it should be used cautiously at this time. A related issue is the inability to deliver ATP, when indicated, in lieu of painful shocks. Both inappropriate and appropriate shocks increase mortality among ICD patients (6,39). Clinicians may be apt to consider a device incapable of ATP to be inferior. However, previous trials may have overestimated the incidence of ATP. An analysis of SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial) patients suggests that approximately 15% of patients with New York Heart Association functional class II to III heart failure will experience monomorphic VT necessitating ATP therapy over almost 45.5 months of follow-up (51). This analysis also found that only 7% of the total patient population received more than 1 shock for high-rate monomorphic VT, a 1.8% per year risk. Additionally, studies such as MADIT-RIT (Multicenter Automatic Defibrillator Implantation Trial–Reduce Inappropriate Therapy) and ADVANCE III have shown reduction in need for therapies with prolonged detection intervals, due to spontaneous termination of arrhythmia (39,48). Although this data suggests that chances of requiring ATP therapy are generally low, a significant number of ICD patients may avoid shock therapy via ATP, and this possibility should be considered at time of implant.

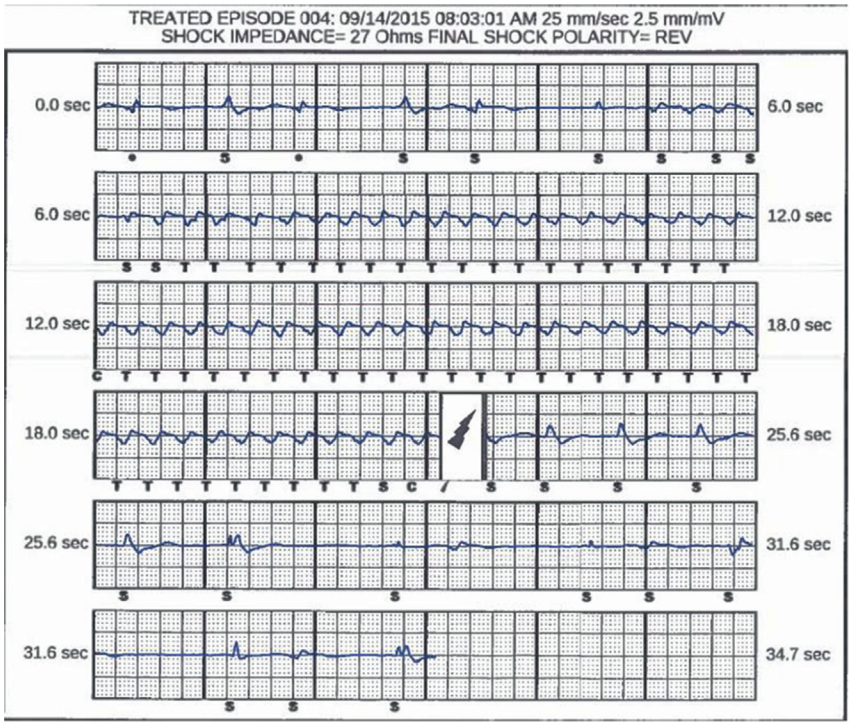
DEVICE LONGEVITY. Longevity is a concern with all implantable devices, as device replacement exposes the patient to risks related to infection and procedural complications. All ICDs have limited battery life and require pulse generator replacement once the battery becomes depleted below a critical point. Manufacturer estimates of first-generation S-ICD battery life were approximately 5 years (52). Recently published data from the European Regulatory Trial found a median time to replacement of 5.0 years (31), with 71% of S-ICD devices in service 5 years after implant. This calculation included patients who had devices removed for issues unrelated to battery life, including replacement with transvenous ICD in 4 patients. However, during the 5.8 years of follow-up, 5 of 55 patients (9%) required replacement within 1.5 years due to premature battery depletion. The latest single-chamber transvenous ICDs are predicted to have a >10-year battery life (53); in this respect, the S-ICD does not compare favorably. The second-generation S-ICD is predicted to have a 7.3-year battery life (36); however, this manufacturer claim has not been substantiated by real-world experience. Until battery life is equivalent to contemporaneous transvenous ICDs, the S-ICD will require more frequent generator changes for battery depletion.

EFFICACY

Although the best measure of ICD efficacy is the number of lives saved from SCD, obtaining this information requires long-term follow-up studies that are not yet available for a relatively new device such as the S-ICD. Large, multicenter cohorts of patients with S-ICDs are now underway that will provide initial information regarding real-world device efficacy.

Defibrillation threshold (DFT) testing, performed at the time of device implant, is used to predict shock efficacy in the event of ventricular tachyarrhythmia. The S-ICD delivers all shocks at 80 J and can reverse polarity with each successive shock if more than 1 is needed to terminate the arrhythmia (14). **Figure 3** shows an example of successful detection and termination of a VF episode. Because of the pulse generator's location in the lateral (as opposed to the pectoral) position, the S-ICD has a more horizontal shock vector than that of transvenous ICDs. A comparison of DFT testing in 49 patients undergoing S-ICD versus transvenous ICD implant found a mean DFT of 11.1 J in transvenous ICDs versus 36.6 J in S-ICDs (15). Despite the larger absolute energy requirement, because the S-ICD delivers an 80 J shock, the absolute DFT safety margin was slightly greater in the S-ICD. In the initial European clinical

FIGURE 3 S-ICD Stored Electrogram Showing Appropriately Detected and Treated Ventricular Fibrillation



The **arrow** at the discontinuity in the tracing represents the delivered shock. S-ICD = subcutaneous implantable cardioverter-defibrillator.

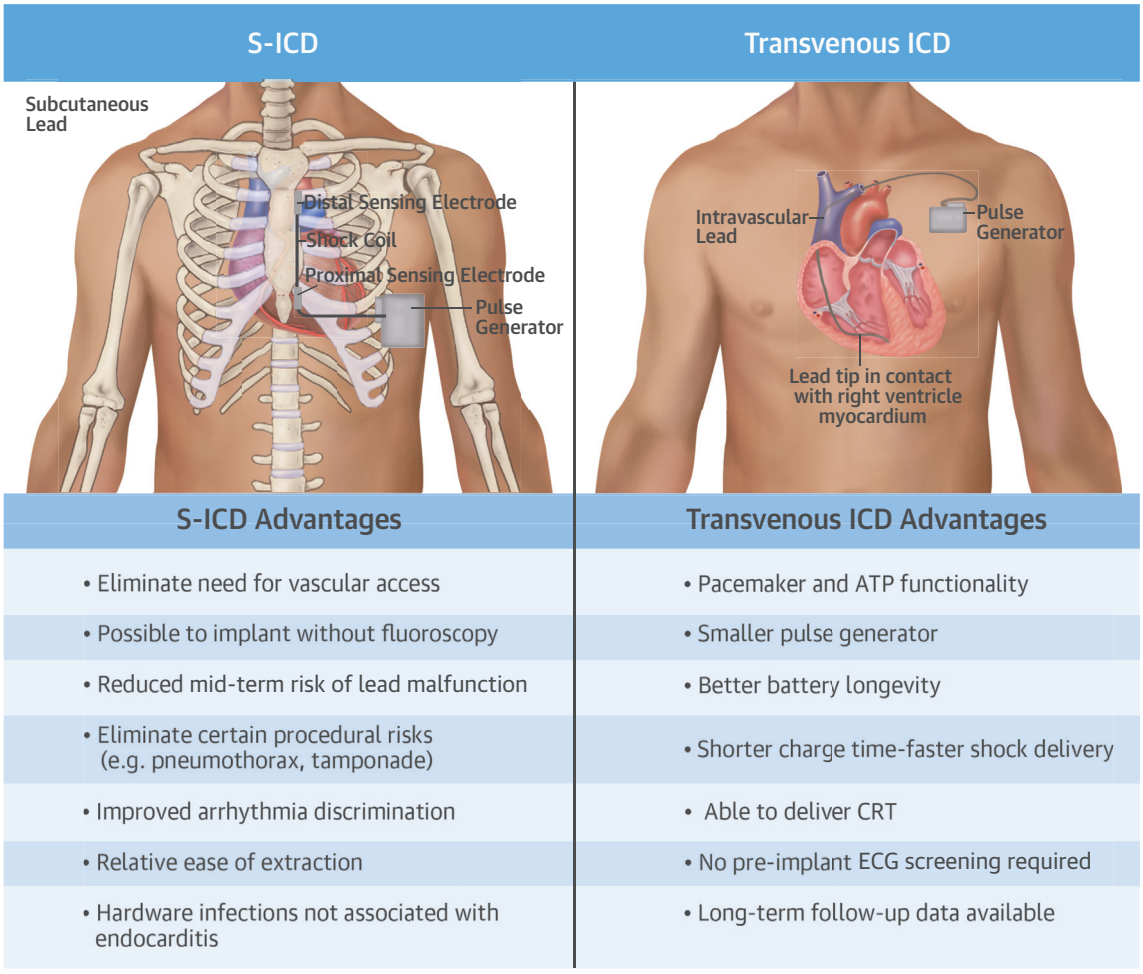
trial, the authors report 100% sensitivity for detection of induced VF and 98% shock efficacy (15). Similarly, high efficacy was noted in the IDE trial (21). If studies continue to show such high efficacy, it seems likely that routine defibrillation testing will not be needed at implant.

Although these findings suggest that the S-ICD may be as clinically effective at terminating arrhythmias as traditional ICDs, DFT testing does not necessarily correlate to real-world efficacy. The PRAETORIAN (Prospective, RAndomizEd comparison of subcuTaneOus and tRansvenous ImplANtable cardioverter-defibrillator therapy) randomized clinical trial will provide a head-to-head comparison of traditional ICDs and S-ICDs to establish their relative efficacy (54).

Arrhythmia discrimination and resultant reduction in the inappropriate shock rate is another important measure of S-ICD efficacy. Programming and discrimination algorithms have evolved significantly since the introduction of the S-ICD. Early versions were programmed with a shock-only zone at 180 beats/min, which led to unacceptably high rates of shocks for sinus tachycardia and other SVTs. With publication of the MADIT-RIT trial, there has been a general move toward longer detection intervals and higher cutoff rates (39). The START trial (discussed earlier) showed the S-ICD to be equivalent or superior to transvenous ICDs in arrhythmia detection and discrimination (14). The publication of START led to widespread use of dual-zone programming, arrhythmia discriminators, and higher cutoff rates with the S-ICD. Inappropriate shock rates markedly decreased with these changes. Pooled data from the IDE and EFFORTLESS trials shows an increase in dual-zone programming from 51% to 95% and a concurrent 34% reduction in inappropriate shocks after publication of START (24). Overall, with the adoption of programming changes, the ability of the S-ICD to avoid inappropriate shocks is equivalent to that of a transvenous ICD.

Perhaps the most meaningful evaluation of S-ICD efficacy lies in its ability to convert spontaneous episodes of VT and VF. Early trials, although having low rates of spontaneous arrhythmia, reported S-ICD shock efficacies between 95.2% and 100% (15–21). Concerns have been raised regarding utility of the S-ICD in certain channelopathy patients who, due to typically younger age and lack of need for pacemaker support, otherwise seem to be good candidates. A specific example is Brugada syndrome patients, who

CENTRAL ILLUSTRATION **A Comparison of Safety and Efficacy of the S-ICD With Transvenous ICD**



Lewis, G.F. et al. J Am Coll Cardiol. 2016; 67(4):445-54.

ATP = antitachycardia pacing; CRT = cardiac resynchronization therapy; ECG = electrocardiogram; ICD = implantable cardioverter-defibrillator; S-ICD = subcutaneous implantable cardioverter-defibrillator.

might experience T-wave oversensing due to dynamic morphology changes (25). Although large group data for this specific patient population are not available, case reports found the S-ICD to effectively terminate spontaneous arrhythmias and did not find inappropriate shocks (55). The largest study available to date incorporates pooled data from the IDE trial and early results from the EFFORTLESS S-ICD database. This dataset includes 882 patients and a mean of 651 days of follow-up (23). Spontaneous VT/VF occurred in 59 patients, with a total of 111 events. Shock efficacy for these events was 90.1% and 98.2% for 1 and multiple shocks (up to 5), respectively. These conversion rates are comparable to those observed with transvenous ICDs. Various trials have reported first-shock efficacy of 83% to 90% with transvenous ICDs and overall shock efficacy of 97.3% to 99.6% (4,52,56). The pooled data from IDE and EFFORTLESS showed an S-ICD annual mortality rate of 1.6% and a 2-year mortality rate of 3.2% (24). Mortality data are difficult to compare in light of the younger patients, higher EF (mean 39%), and less advanced heart failure in the IDE and EFFORTLESS population. Additionally, as with all ICD trials, mortality is not only related to SCD. Taken as a whole, the findings in this large patient population suggest that S-ICDs and transvenous ICDs are equally safe and clinically efficacious in terminating spontaneous episodes of VT/VF.

CONCLUSIONS

With the first S-ICD implants occurring >10 years ago, there is a growing, although still incomplete, worldwide body of evidence (in the absence of head-to-head randomized trials) suggesting its non-inferiority to traditional ICD systems with regard to safety and efficacy, with certain advantages of each device type (**Central Illustration**). Although the earliest implants were complicated by higher-than-expected rates of infection, lead dislodgement, and inappropriate shocks, the incidence of these events has been markedly reduced by increased operator experience and advances in implant technique and device programming. The learning curve for individual operators was clearly demonstrated by the combined IDE trial and EFFORTLESS registry results (37). Patient populations in these early trials were unique, due to the preponderance of young patients with channelopathies, congenital heart disease, and other rare conditions. In real-world clinical situations, the S-ICD has >98% overall shock efficacy for acute conversion of VT/VF, equivalent to transvenous ICDs. DFT testing has been highly successful with the S-ICD and the absolute DFT margin is actually slightly greater than with transvenous ICDs. Although available safety and efficacy data for the S-ICD are very encouraging, clinical trials including large numbers are not yet available. In the coming years, data from the complete EFFORTLESS ICD registry, the U.S. post-marketing registry, and head-to-head performance versus transvenous ICDs in the PRAETORIAN trial will provide a great deal of additional information (24,54). The UNTOUCHED (Understanding Outcomes With the S-ICD in Primary Prevention Patients with Depressed Ejection Fraction) study is a prospective registry of primary prevention patients with reduced EF (57), which will provide valuable data on this device in the most common cohorts receiving ICDs. The second-generation S-ICD has improvements, including smaller generator size, longer battery life, and capabilities for remote monitoring (36). With currently available information, the S-ICD is an appealing alternative to traditional ICDs for specific patient populations in whom traditional ICD implant would have greater risk or difficulty and, arguably, may be considered for any patient undergoing ICD implantation.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Michael R. Gold, Division of Cardiology, Medical University of South Carolina, 114 Doughty Street, MSC 592, Charleston, South Carolina 29425-5920. E-mail: goldmr@musc.edu.

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