The Subcutaneous Implantable Cardioverter Defibrillator

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Abstract: The subcutaneous implantable cardioverter defibrillator (S-ICD) is a subcutaneous alternative to conventional transvenous ICD (TV-ICD) systems, which have previously been shown to treat life-threatening ventricular tachyarrhythmias in cardiac disease patients. A review of the literature reveals that S-ICDs have similar shock efficacy rates for both induced and spontaneous ventricular tachyarrhythmias when compared with TV-ICDs. Furthermore, S-ICDs seem to have a higher specificity for withholding therapy when supraventricular tachycardia is present compared with TV-ICDs. The advantages of the S-ICD system are numerous: fewer vascular complications including thrombosis and hemothorax, avoidance of fluoroscopy, and an easier means of lead replacement. These advantages make the S-ICD system most suitable for younger patients who may require replacements in later life, those with abnormal venous anatomy, and individuals prone to infection and/or central vein thrombosis. However, S-ICDs are not without their complications and are associated with a higher incidence of inappropriate shocks secondary to T wave oversensing. S-ICDs also lack antitachycardia pacing, making them a suboptimal device in patients with recurrent monomorphic ventricular tachycardia who would otherwise benefit from the antitachycardia pacing offered in TV-ICDs. Lastly, the limited number of long-term randomized, head-to-head studies involving direct comparison with TV-ICDs poses a challenge in the implementation of the S-ICD.

Key Words: subcutaneous implantable cardioverter defibrillators, subcutaneous ICD, transvenous ICDs, implantable cardioverter defibrillator, sudden cardiac death, ventricular arrhythmia

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Ventricular tachyarrhythmias leading to sudden cardiac death (SCD) are a well-known cause of mortality among cardiac disease patients.[1,2] It is estimated that the incidence of SCD in the United States ranges from 180,000 to >450,000 people per year.[3] Transvenous implantable cardioverter defibrillator (TV-ICD) devices have been shown in numerous clinical trials to prevent SCD by terminating fatal ventricular tachyarrhythmias in cardiac disease patients.[4–8] Initial TV-ICD systems utilized epicardial leads, but subsequent studies revealed that endocardial leads offer similar long-term stability with less perioperative mortality.[9–11] At present, TV-ICD systems consist of a pulse generator that is placed in a subcutaneous pocket along the left subclavicular line, and 3 or more TV leads situated within the heart chambers. According to the American Heart Association Expert Consensus released in 2014, TV-ICD systems are indicated for both primary and secondary prevention of SCD in patients with ischemic cardiomyopathy, nonischemic cardiomyopathy, sustained ventricular tachyarrhythmias, and a number of additional indications.[12] Despite their effectiveness in preventing SCD, TV-ICD systems are not without their complications.[13] Some of these complications include lead dislocation, lead fracture, sensing issues, infection, thrombosis, pneumothorax, hemothorax, and subclavian vein occlusion.[14–16] The largest contributing factor to these complications seems to be the invasive position of the endocardial leads.

In response to the growing concerns associated with endocardial leads, an alternative system that is placed subcutaneously has been developed.[17] Like TV-ICD systems, the subcutaneous ICD system (S-ICD; marketed as Emblem; Boston Scientific, Marlborough, MA) consists of a computer analyzer and battery pulse generator, which are placed subcutaneously in the lower left chest area at the axillary line but differs in that its leads are entirely subcutaneous along the sternum and do not come into contact with the endocardial walls. The S-ICD system was granted approval by the United States Food and Drug Administration in 2012 to be considered when conventional ICD may be disadvantageous.[18] Still, there is much uncertainty over the long-term complications of S-ICDs, and which patient populations would benefit the most compared to conventional TV-ICD systems.

THE S-ICD SYSTEM

The S-ICD system consists of an 8-cm shocking coil that sits parallel and 1–2 cm to the left of the sternum.[17] Figures 1 and 2 demonstrate the anatomical placement of the system.[17,19] Cardiac rhythms are sensed using vectors formed by a distal electrode near the manubriosternal junction, a proximal electrode near the xiphoid process, and the pulse generator, which sits over the sixth rib in the left midaxillary line. Because anatomic landmarks are used for implantation, fluoroscopy is not required. Sensing vectors are selected automatically using a software program from one of the following 3 combinations: proximal electrode-to-pulse generator, distal-to-proximal electrodes, or distal electrode-to-pulse generator. Vector selection favors the most appropriate QRS waveform with the least amount of double QRS counting and T wave oversensing. A template of the patient's baseline electrocardiogram rhythm is stored within the system to serve as comparison for morphology analysis in the event of an arrhythmia. "Shock Zones" are typically set to above 240 beats per minute (bpm) and there is also a "Conditional Shock Zone" that is programmable between 170 and 240 bpm for cases of supraventricular tachycardia. Intraoperative defibrillation testing is performed using 65-J shocks and spontaneous rhythms are terminated using up to five 80-J shocks. After shock delivery, the system offers up to 30 seconds of demand pacing for rhythms <50 bpm. In contrast to the TV-ICD systems, the S-ICD does not possess the capacity for antitachycardia pacing.

DEVELOPMENT OF THE S-ICD SYSTEM

The initial conception of an entirely S-ICD system evolved from the increasing concern over complications associated with TV leads. Early studies sought to determine the relationship between various subcutaneous electrode configurations and the shock energy needed to terminate an induced ventricular fibrillation (VF). Using canine subjects, Cappato et al[20] tested 11 different dual electrode configurations for their ability to terminate induced VF. All

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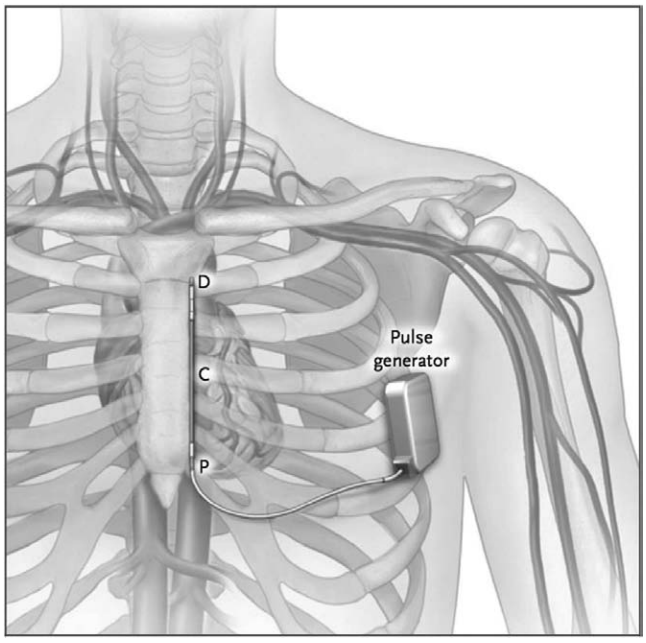

FIGURE 1. Subcutaneous implantable cardioverter-defibrillator (S-ICD) configuration. The pulse generator is shown near the 5th intercostal space at the mid-axillary line, with the proximal electrode (P), distal electrode (D), and 8-cm parasternal coil electrode (C). From Bardy et al.[17]

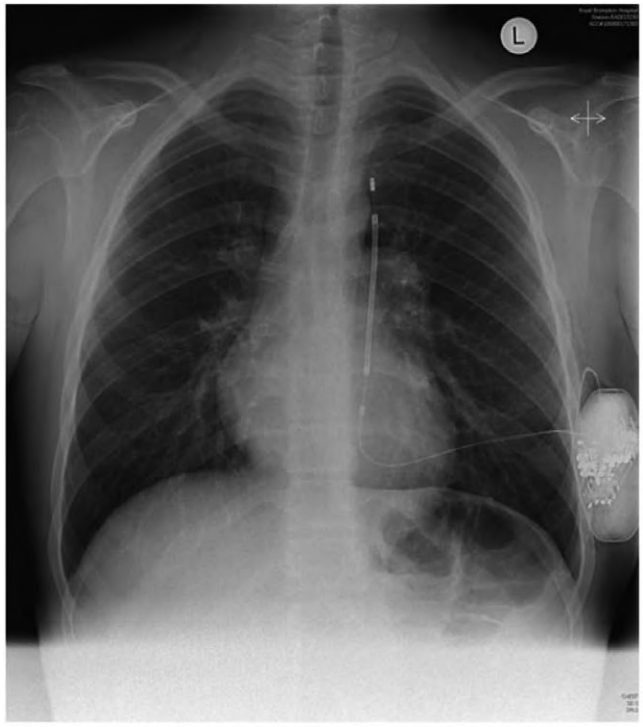

FIGURE 2. In situ placement of the Subcutaneous implantable cardioverter defibrillator (S-ICD). Posteroanterior chest x-ray demonstrating anatomical placement of the S-ICD system. From Jarman et al.[19]

TABLE 1. Shock Efficacy for Spontaneous Arrhythmias and Inappropriate Shock Rates Among Long-term Studies Involving S-ICD Patients

References	N	First-Shock Efficacy	Overall Shock Efficacy*	Inappropriate Shock Rate† (%)
Dabiri Abkenari et al[21]	31	57.9%	96.4%	16.1
Aydin et al[22]	40	57.9%	96.4%	5
Burke et al[26]	882	90.1%	98.2%	13.1
Galvão et al[24]	21	—	100%	23.8
Jarman et al[25]	16	—	—	25
Jarman et al[19]	111	—	100%	15
Olde Nordkamp et al[23]	118	98%	—	13

*Successful termination of rhythm within 5 shocks.
†Percent of patients who received inappropriate shocks.

configurations demonstrated a 100% termination rate for induced VF but required up to 80 J to do so, higher than the shock energy requirement for TV-ICDs to effectively terminate arrhythmias. Building on these results, Bardy et al[17] published a landmark study detailing the feasibility of the S-ICD in a series of human trials. The first phase of these trials focused on determining the optimal electrode configuration for effective defibrillation and found that a left lateral pulse generator with a parasternal coil electrode was superior to all others. The next phase then compared the defibrillation thresholds of the subcutaneous configuration with that of a TV-ICD system and confirmed that the S-ICD required significantly higher shock energy for effective defibrillation in humans. The last phase of their study involved the permanent implantation of the S-ICD system in 6 patients. During implantation, the system had a 100% termination efficacy for induced VF, but during follow-up, no spontaneous ventricular tachycardia (VT) or VF episodes occurred for the investigators to be able to assess the system's chronic conversion efficacy. A subsequent extension of this phase then followed 53 patients with the S-ICD over a mean of 10 months and found a 100% termination rate for all 12 spontaneous episodes of VT/VF that occurred. The promise of these initial studies led to larger human trials that aimed to further assess the efficacy and safety of S-ICDs relative to TV-ICDs.

ARRHYTHMIA DETECTION AND TERMINATION

Numerous single- and multicenter studies around Europe, and later the United States, have detailed their early experiences with the S-ICD system. Table 1 highlights studies yielding data related to spontaneous conversion rates and complication rates among patients who have received S-ICDs.[19,21–26] One of the first of these studies was a single center's experience in the Netherlands involving 31 patients who received the S-ICD.[21] During implantation, all 52 episodes of induced VF were successfully detected and terminated. However, 2 patients required a reversal in their lead polarity to achieve successful VF termination. During a median follow-up period of 286 days, 4 of the 31 patients experienced ventricular tachyarrhythmias and all episodes were successfully terminated. However, in 1 of these patients, it was found that multiple episodes of nonsustained VT had occurred, so the device was explanted in exchange for a TV-ICD system which could provide antitachycardia pacing.

A subsequent multicenter study in Germany found similar results in a cohort of 40 patients.[22] During a mean follow-up of 229 days, 10% of patients had experienced a total of 21 episodes of spontaneous ventricular tachyarrhythmia. The overall shock efficacy, defined as the ability to terminate a ventricular tachyarrhythmia with 5 shocks or less, was 96.4%. However, first-shock efficacy was lower

at 57.9%, which differs from TV-ICD studies that have reported up to 97% shock efficacy within the first 2 shocks.[27]

Olde Nordkamp et al[23] found a higher first-shock conversion efficacy at 98% in a group of 118 patients who were followed over a period of 18 months after receiving a S-ICD. The single patient who did not respond to initial shock therapy experienced a monomorphic VT that accelerated after shock therapy and later spontaneously terminated. In this patient, the S-ICD was explanted and exchanged for a TV-ICD system, which could provide antitachycardia pacing therapy. As in previous studies, all cases of intraoperatively induced VF were detected and terminated.

In another study by Galvão et al,[24] 5 of 21 patients who had received S-ICDs experienced a spontaneous arrhythmia and the overall shock conversion efficacy was 100%. However, an equal number of patients also received inappropriate shocks. Furthermore, 1 patient with arrhythmogenic right ventricular cardiomyopathy experienced a loss of telemetry, which prompted the investigators to replace the S-ICD with a TV-ICD.

Consistent with prior studies, Jarman et al[19,25] found a 100% detection and conversion rate for induced VF among 111 patients who received the S-ICD in the United Kingdom. During a mean follow-up of 12.7 months, roughly 12% of patient had experienced either VT or VF, all of which were successfully terminated, yielding an overall shock efficacy of 100%. However, 1 patient experienced a prolonged episode of monomorphic VT below the programmable Shock Zone rate, which at first did not elicit shock therapy. Later, this patient's VT degenerated into fine VF, which was then appropriately shocked into a ventricular escape rhythm and maintained with postshock pacing. In the subsequent seconds, the rhythm degenerated again into fine VF, which was again appropriately shocked. The patient later developed asystole and died shortly thereafter, presumably from subsequent arrhythmic events, which were not captured in the electrocardiogram storage. This unfortunate case demonstrates the utility of an appropriate Conditional Shock Zone and further suggests that the lack of antitachycardia pacing in S-ICD is a particularly prominent disadvantage for patients with monomorphic VT.

The most recent large-scale study on S-ICDs to date is a pooled analysis of 2 multicenter prospective studies, the Investigational Device Exemption (IDE) S-ICD System Clinical Investigation)[28] and Evaluation of Factors Impacting Clinical Outcome and Cost Effectiveness of the S-ICD (EFFORTLESS: Boston Scientific Post Market S-ICD Registry)[29] studies, which followed a combined 882 patients who underwent S-ICD implantation.[30] In both prospective studies used in the analysis, patients underwent S-ICD placement for both primary prevention and secondary prevention. A significant number of patients also underwent S-ICD placement after having experienced a TV-ICD complication, most commonly device-related infection. Over a follow-up period of 651 ± 345 days, 98.2% of spontaneous VT/VF events were terminated within 5 shocks, and 90.1% were terminated with the first shock alone. However, in patients who experienced spontaneous VT/VF storms, the overall conversion rate was 83.3%. The overall 2-year mortality rate in the pooled data was found to be 3.2%, which is lower that the reported 5% and 7% observed for the high rate and delayed therapy groups, respectively, in the Multicenter Automatic Defibrillator Implantation Trial-Reduce Inappropriate Therapy (MADIT-RIT) study.[31] The 2-year mortality rate of TV-ICDS was found to be even higher (11%) in another cohort followed in the SHockless IMPLant Evaluation (SIMPLE) trial.[32] It is important to note, however, that the study population in the pooled EFFORTLESS and IDE studies tended to involve patients who were younger males and with better preserved ejection fractions than the TV-ICD trials, which may have unfairly have yielded a lower mortality rate.

An attempt to directly compare TV-ICD leads with S-ICD leads was accomplished in the Subcutaneous versus Transvenous Arrhythmia Recognition Testing (START) study by Gold et al.[33] The START study used cutaneous leads (as surrogates for the S-ICD system) and endocardial leads (as surrogates for the TV-ICD systems) to compare conversion rates for induced VF in 64 patients. A total of 46 ventricular and 50 atrial arrhythmias (with a ventricular rate > 170 bpm) were induced. All leads were tested in a single-zone shock setting (ventricular tachyarrhythmia ≥ 170 bpm) and a dual-zone shock setting (VT ≥ 170 bpm; VF ≥ 240 bpm). In the single-zone shock setting, both S-ICDs and TV-ICDs detected induced ventricular tachyarrhythmias with 100% sensitivity. In the dual-zone shock setting, the S-ICD showed a sensitivity of 100% for induced ventricular tachyarrhythmias compared with 99.3% for the single-chamber TV-ICD systems. However, dual-chamber TV-ICD systems demonstrated a sensitivity of 100%. Overall, no statistical significance was found between TV-ICD systems and the S-ICD system in detecting induced ventricular tachyarrhythmias. The most striking finding of the START study was the significant difference in specificity between the S-ICD and TV-ICD systems. The S-ICD demonstrated a specificity of 98% for atrial arrhythmias compared with 68% seen in single-chamber TV-ICD systems and 67.3% seen in dual-chamber TV-ICD systems. Part of this difference may reflect the higher resolution analysis seen in S-ICD systems through the incorporation of up to 41 points on each ventricular complex. These results suggest promise in the ability of S-ICD to avoid inappropriate shocks secondary to supraventricular tachyarrhythmias.

Another study comparing S-ICDs with TV-ICDs, this time involving the entire devices themselves, looked at both induced and spontaneous conversion rates. In this multicenter case–control study, 69 patients who received the S-ICD were randomly age- and sex-matched matched with 69 patients who had received a single-chamber conventional TV-ICD.[34] During intraoperative defibrillation testing, S-ICDs achieved a conversion rate of 89.5% compared with 90.8% seen in TV-ICDs. However, when the shock polarity for unsuccessful S-ICDS was reversed and retested, conversion rates for the S-ICDs improved to 95.5%. Overall, the intraoperative conversion rates did not significantly differ between the 2 types of devices. During a mean follow-up of 217 days, both groups experienced spontaneous VT/VF episodes, all of which were all appropriately detected and terminated. In the S-ICD group, however, 1 patient with monomorphic VT who received 21 shocks had his device exchanged for TV-ICD, so that antitachycardia pacing could be achieved.

Time-to-Therapy

Time-to-therapy is an important clinical parameter in the setting of life-threatening ventricular tachyarrhythmias. One study found that the mean time to therapy for induced VF episodes with S-ICDs was 13.9 seconds (range, 11–21.6), which is consistent with several other studies.[21,24,28] Pooled results from the EFFORTLESS and IDE studies found a mean time to therapy of 19.2 seconds (±5.3) for all spontaneous VT/VF events.[30] It seems that significant delays in time-to-therapy beyond this may result in adverse clinical outcomes. For example, one study found that 2 episodes of VF failed to receive therapy until 24 and 27 seconds had passed, respectively, resulting in syncope.[25] However, in this same study, the investigators chose initially not to include an optional Conditional Shock Zone over concern for T wave oversensing. Given that the 2 patients with VF had only the single Shock Zone (median rates > 220 bpm) programmed, time-to-therapy may have improved had a Conditional Shock Zone > 200 bpm been utilized. Other studies suggest that a delay from the mean may not be associated with any adverse clinical outcomes. For example, the IDE study found that in the 13% of patient who

experienced spontaneous VT/VF episodes with a time-to-therapy >18 seconds, no clinical events such as syncope were observed.[28]

SAFETY AND COMPLICATIONS

The S-ICD system is a safe and well-tolerated device in the vast majority of patients who receive them. One of the more notable studies that looked at complication rates associated with S-ICDs is the IDE study. Over a follow-up period of 180 days, the type I complication-free rate, which measured complications directly attributable to the device, was determined to be 99% in 293 patients.[28] When type II (labeling-related) and type II (procedure-related) complications were also included in the analysis, the overall 180-day complication-free rate was 92.1%. Furthermore, there were no instances of lead failure, endocarditis, bacteremia, cardiac tamponade, cardiac perforation, pneumothorax, hemothorax, or subclavian vein occlusion during the observation period, all of which have been reported in TV-ICD systems.[11,13,14]

Surgical

The procedural advantages of the S-ICD system are numerous. First, the risk of vascular injury is significantly minimized during implantation compared with TV-ICDs due to the use of subcutaneous leads instead of endocardial leads. Intraoperative complications, such as hemothorax, pneumothorax, and thrombosis, are rarely reported during S-ICD implantation.[21,25] Contrastingly, TV-ICD systems have been associated with venous thrombosis, pericardial effusion, pneumothorax, tension pneumothorax, hydropneumothorax, and hemothorax.[13–16] The use of subcutaneous leads significantly reduces the risk of significant vascular injury, perforation, or clotting. However, pocket hematomas have been observed in patients receiving S-ICDs while on anticoagulation.[34] Another unique advantage of S-ICD implantation is the avoidance of fluoroscopy during implantation. Because TV-ICD implantation requires fluoroscopic visualization, patients are at an increased health risk from radiation exposure. Contrastingly, implantation of the S-ICD utilizes anatomic landmarks and resides entirely within the subcutaneous space, which enables practitioners to confidently implant the device without fluoroscopic guidance. Lastly, S-ICD implantation typically requires only a combination of local anesthesia and conscious sedation, sparing the need for general anesthesia, which is occasionally used for TV-ICD placement.[23]

One potential area for concern with S-ICD implantation is the need for the defibrillation testing protocol, which is an assessment of the device's ability to terminate induced episodes of VF with a 65-J shock; TV-ICD implantation does not require intraoperative defibrillation testing. In fact, the Safety of Two Strategies of ICD Management at Implantation (SAFE-ICD) trial, which assessed the complication rate, 2-year mortality and incidence of SCD in 2120 patients undergoing TV-ICD implantation either with or without intraoperative defibrillation testing found there was no statistical differences between either 2 groups.[35] The SIMPLE trial found similar results in a population of 2500 patient randomized to either defibrillation testing or no defibrillation testing.[32] Thus, as opposed to the S-ICD implantation protocol, TV-ICD implantation rarely requires intraoperative defibrillation testing. Nonetheless, defibrillation testing is largely successful and nonharmful in S-ICD patients. In cases in which initial termination is not successful, reversing the lead polarity often results in a successful defibrillation test outcome.

Inappropriate Shocks

Perhaps, the greatest concern with the S-ICD system is the relatively high rate of inappropriate shocks, which ranges from 5% to 25% of patients.[19,23,28–30] The largest study involving pooled data on 882 patients from the EFFORTLESS registry and IDE trial found an inappropriate shock rate of 13.1%.[30] In TV-ICD systems, it is well known that inappropriate shocks are associated with an overall increase in all-cause mortality.[36] Using data from the Multicenter Automatic Defibrillator Implantation Trial (MADIT) II study, Daubert et al[36] found that one or more inappropriate shocks occurred in 11.5% of 719 patients who had received a TV-ICD. In another large-scale study involving TV-ICD patients, the cumulative incidence of inappropriate shocks was 18% after 5 years of follow-up.[37] Though these rates do not drastically differ from those reported in S-ICDs, there are limited long-term studies available on S-ICDs to assess the chronic risk of inappropriate shocks compared with TV-ICDs.

The most common cause of inappropriate shocks in TV-ICDs is atrial fibrillation or flutter, followed by others forms of supraventricular tachycardia, and lastly, abnormal sensing such as T wave oversensing. Predicators of inappropriate shocks included atrial fibrillation, smoking, and a diastolic blood pressure ≥80 mm Hg. Contrastingly, the most common cause of inappropriate shocks in S-ICDs is T wave oversensing.[21,30] Importantly, T wave oversensing seems to be more common in younger patients. Jarman et al[25] found that younger patients were significantly more likely to experience an inappropriate shock due to T wave oversensing than older patients (24 vs 37 years). In the TV-ICD population, there is also a relatively high rate of inappropriate shocks in younger patients, but the overwhelming factor is lead failure rather than oversensing.[38] Roughly 21% of pediatric patients (mean age, 16 years old) with a TV-ICD experience inappropriate shocks.

Strategies to correct for this high rate of T wave oversensing in S-ICD patients are currently being developed. In a study by Kooiman et al,[39] it was found that the annual incidence of inappropriate shocks in S-ICD patient was 10.8%, and of these cases, 73% were attributed to T wave oversensing. However, in this study, it was also determined that template reprogramming during exercise is associated with a significant reductions in the incidence of T wave oversensing and subsequent inappropriate shocks. To accomplish this, patients who had received inappropriate shocks due to T wave oversensing were asked to exercise to achieve heart rates above the threshold in which their initial inappropriate shock had originally occurred. All 3 sensing vectors were then assessed for the frequency of T wave oversensing while the patient remained tachycardic. The most suitable vector with the least episodes of T wave oversensing was selected, and a new template of the patient's cardiac rhythm morphology was obtained during maximal exercise. If T wave oversensing occurred in all 3 vectors, then the rate threshold for shock therapy was simply increased. Of the 8 patients who underwent this exercise reprogramming strategy, only 1 patient continued to receive inappropriate shocks over a follow-up period of 14.1 months. Another study examining this exercise protocol found similar results in 8 of 11 patients who had previously experienced inappropriate shocks secondary to T wave oversensing.[23] Thus, exercise reprogramming may be a useful means of preventing subsequent T wave oversensing and inappropriate shocks in high-risk patients.

Another cause of inappropriate shocks in S-ICDs is supraventricular tachycardia.[21] In the IDE study, more than one-third of the inappropriate shocks that occurred were due to supraventricular tachycardia with rapid ventricular response.[28] In analysis, however, the investigators found that the use of the programmable conditional shock zone, as opposed to a therapeutic shock zone alone, was associated with a 70% relative reduction in inappropriate shocks secondary to supraventricular tachycardia. Alterations in rate settings have previously already been known to be beneficial in TV-ICD patients. Moss et al[30] found that careful rate programming in TV-ICDs can have a substantial impact on the number of inappropriate shocks. In their study, 1500 patients were randomly assigned to 1 of 3 shock

programming modes: high-rate therapy (2.5-second delay before the initiation of therapy at a heart rate of ≥200 bpm), delayed therapy (with a 60-second delay at 170–199 bpm, a 12-second delay at 200–249 bpm, and a 2.5-second delay at ≥250 bpm), or conventional rate therapy (with a 2.5-second delay at 170–199 bpm and a 1.0-second delay at ≥200 bpm). During a follow-up of 1.4 years, both high-rate therapy and delayed therapy were associated with reductions in a first occurrence of inappropriate therapy and all-cause mortality. Additionally, in the pooled analysis of the EFFORTLESS and IDE studies, single-zone programming correlated to a Kaplan–Meier incidence of inappropriate shocks at 3 years of 20.5% compared with double-zone programming of 11.7%.[30] These results highlight the potential value of programming an appropriate shock zone rate and utilizing the optional Conditional Shock Zone rate in S-ICD patients.

Pacing

A clear disadvantage of the S-ICD system is its lack of significant pacing capabilities. Though the system offered up to 30 seconds of postshock pacing for bradycardia, it does not provide long-standing bradycardia or antitachycardia pacing. Monomorphic VT is a particularly challenging arrhythmia with respect to S-ICDs as it has been shown that antitachycardia pacing is just as effective as shocks in rhythm termination.[40] One S-ICD cohort found that a patient with hypertrophic cardiomyopathy and repetitive monomorphic VT had received 21 shocks over the follow-up period of 217 days.[34] The investigators of this study chose to switch the S-ICD with a TV-ICD system to provide painless overdrive antitachycardia pacing. Numerous other reports have surfaced citing recurrent monomorphic VT as a primary reason in S-ICD explantation.[22,23] As such, in instances of recurrent monomorphic VT, S-ICD may be a poor choice due to its lack of antitachycardia pacing, which has previously been shown to be highly effective in treating monomorphic VT. Furthermore, antitachycardia pacing in TV-ICD systems has been shown to limit the occurrence of first shocks without adversely affecting mortality.[41]

Device Size and Battery Life

The S-ICD system is larger than that of most conventional TV-ICD systems.[42–44] Current specifications for the S-ICD system state that the generator is 83.1 × 69.1 × 12.7 mm, whereas some conventional TV-ICDs, such as the Evera XT (Medtronic, Fridley, MN) are as small as 64 × 51 × 13 mm.[45,46] Larger sized devices may in turn play a role in patient discomfort and surgical implantation challenges. Furthermore, there is insufficient evidence to suggest whether or not the current S-ICD can reduce its overall size due to limitations in the surface area required for defibrillation. Additionally, the battery life of S-ICD systems is significantly shorter compared with TV-ICDs. With an average battery span of 7.3 years, this poses a concern for congenital heart disease patient who would need frequent battery replacement over their lifetime. Many TV-ICD devices, such as the Inogen by Boston Scientific report battery lives as long as 11.7 years.[47]

Lead Complications

One of the greatest motivators for the development of the S-ICD system was undoubtedly issues associated with TV-ICD leads. In a cohort of 990 patients who received a TV-ICD, the annual lead failure rate reached 20% after a 10-year follow-up period.[48] The most common lead defects were insulation defects (56%), lead fractures (12%), loss of ventricular capture (11%), abnormal impedance (10%), and abnormal sensing (10%). Interestingly, lead defects were found more commonly in younger patients and females. Another cohort of 74 patients with TV-ICDs found that the cumulative failure probability of TV leads was 37% at 68.6 months, the most common indicator being postshock oversensing.[16]

There are limited data on the long-term performance of subcutaneous leads. To assess the long-term defibrillation potential of subcutaneous leads, Kettering et al[49] performed defibrillation testing on 132 TV-ICD patients who had also received subcutaneous electrodes at time of implantation. Subcutaneous electrodes consistently delivered appropriate arrhythmia detection during a median follow-up of 1419 days. Furthermore, only 8 patients experienced major complications associated with their subcutaneous leads. Though these subcutaneous leads differed from the type implanted with the S-ICD system, they suggest that successful long-term defibrillation testing can be achieved with a relatively low complication rate.

Investigators have also previously reported that lead dislocation with S-ICDs are amenable to suture sleeve techniques. One cohort involving 15 patients who had received a S-ICD found that 13.3% experienced migration of their proximal/xiphoid electrode.[21] Additionally, 1 of these patients subsequently experienced inappropriate shocks due to aberrant detection of myopotentials. However, in this same study, the addition of a xiphoid suture sleeve during implantation in an additional 16 patients was successful in preventing subsequent lead migration issues. In another study, lead dislocation, usually caudal migration of the xiphoid lead, was observed in 3 of 118 patients.[23] After the addition of a suture sleeve as part of the implantation protocol, no additional incidences of lead dislocations were observed.

Infection Risk

Cardiac devices pose a threat of infection for an already vulnerable patient population. The most common type of infections associated with cardiac devices, including pacemakers and ICDs, are pocket infections and device-related endocarditis.[15,50] However, more serious complications can also occur, including septic arthritis, vertebral osteomyelitis, and lung abscesses. With TV-ICDs, there is an inherent risk of introducing pathogens into the vascular system with TV-ICD implantation.[51] The vast majority of ICD infections are caused by coagulase-negative staphylococci and *Staphylococcus aureus*. The overall risk of infections associated with TV-ICDs has been reported to range from 0.13% to 19.9%.[15] According to one of the largest studies, which followed 4.2 million patients who had received an implantable cardiac electrophysiological device, including pacemakers and TV-ICDs, the incidence of infection was 1.61% over a follow-up period of 16 years.[52]

Earlier and smaller studies involving S-ICD implantation have previously reported relatively high rates of device-related infections. For example, Jarman et al[19] found a 10% rate of infection in their study population, half of which required explanation. In another study, 7 out of 118 (5.9%) patients with an S-ICD experienced an infection.[23] However, in the much-larger pooled analysis of the EFFORTLESS and IDE studies, the overall infection rate associated with S-ICDs in the first 2 years was 1.7%, which was the major cause of device-related complications.[30] This incidence does not significantly differ from the overall incidence of infections in other ICDs previously reported. Additionally, it was observed that with S-ICD implantation, the incidence of device-related complications is inversely correlated with practitioner experience. The majority of S-ICD infections tend to be localized to the superficial tissue surrounding the device components rather than systemic infections such as endocarditis or sepsis. Furthermore, superficial wound infections can be effectively managed in S-ICD patients with antibiotics rather than device explantation. In certain cases, sternal wound revisions or device explanations have been necessary when antibiotics fail or when there is a high index of suspicion for a looming systemic infection.[28]

Structural Damage

Given the larger distance and subsequently higher voltage required for effective shocks in S-ICDs compared with TV-ICDS, a question has been raised concerning the extent of shock-induced myocardial and skeletal muscle damage. With the S-ICD system,

the larger distance needed to travel requires a voltage of 80 J, much higher than the standard 35-J shocks delivered by TV-ICDs. A swine study comparing the levels of troponin and creatine kinase released after shock delivery revealed that S-ICDs yielded more skeletal muscle injury than TV-ICD leads.[53] At 4 hours postshock therapy, pigs who received the S-ICD systems had a far greater release of creatine kinase-MM (CK-MM) than those who received a TV-ICD, reflecting more skeletal muscle and subcutaneous damage. However, pigs that received a TV-ICD had 188 times the level of troponin I compared with pigs that received an S-ICD, suggesting that S-ICDs are associated with less myocardial damage. Case reports have also surfaced suggesting larger skeletomuscular damage induced by S-ICD systems, one reporting an anterior shoulder dislocation after defibrillation threshold testing.[54] Despite the higher structural damage to skeletal muscle, the apparent lower risk of myocardial injury seen with S-ICD devices suggests a possible benefit over the TV-ICD system. The extent to which a given rise in troponin after shock application is an indication of true myocardial injury, or simply a benign release of cytoplasmic enzymes, is unclear.[55]

PATIENT SELECTION

Certain subpopulations have been shown to both tolerate and benefit favorably from S-ICD implantation over TV-ICD implantation. One crucial population includes those with prior TV-ICD infections, whom when placed with an S-ICD, may have a decreased incidence of subsequent infection. Dialysis patients who are also at an increased risk of infection, may also benefit from S-ICD placement over a TV-ICD. In a retrospective study by El-Chami et al,[56] 27 patients on dialysis and 52 patients without dialysis were fitted with S-ICDs and followed for a period of 7 months. Although the dialysis population was older and more likely to be diabetic, there were no statistically significant differences in device-related complications, infections, inappropriate shocks (including T wave oversensing), heart failure hospitalizations, or mortality. Furthermore, despite a relatively similar rate of infections, it would theoretically be easier to replace a subcutaneous system when deciding to remove the infectious nidus. Dialysis patient may also benefit from S-ICD placement if there is concern over central vein stenosis, which has previously been reported to occur with TV-ICDs.[57] In the dialysis population, TV leads pose a risk of central venous stenosis which, in the setting of arteriovenous access in an ipsilateral upper extremity, can lead to considerable significant upper extremity and facial edema. In fact, the prevalence of central vein occlusion in patients with chronic defibrillator leads is as high as 7%.[58] The pathophysiology of this stenosis is hypothesized to be due to intravascular endothelial damage and thrombus formation, eventually resulting in occlusive fibrosis.[59] Thus, dialysis patients may benefit from S-ICD placement if there is considerable concern over infection or central vein stenosis.

S-ICDs may also be favorable in the pediatric population, in those with congenital heart disease or patients with abnormal vasculature. The pediatric population poses a significant challenge for TV-ICD placement, as the smaller anatomy and future growth may not only impede device placement, but also predispose to device dislodging or lead dislocations over time.[60] In fact, in a study by Link et al,[61] which retrospectively examined 11 patients who had received either an epicardial system or TV-ICD (mean age 16), there was a significantly higher complication rate seen when compared with adult recipients. Specifically, the pediatric population experienced more infections and lead malfunctions requiring lead replacements. The authors hypothesize that the frequent need for lead replacement in the younger population is due to the continued growth of the thorax and a relatively more active lifestyle. Similarly, Von Bergen et al[62] found that in 210 pediatric patients who underwent TV-ICD placement (median age, 15.4 years), there was a high rate of inappropriate discharges (25% in 5 years) among congenital heart disease patients. Although inappropriate shocks secondary to T wave oversensing is indeed more common in younger patients who have received S-ICDs, it is unclear how the overall rate of inappropriate shock rates compare with TV-ICDs in randomized head-to-head trials.

There has also been a deisire to develop a means of screening for individuals who may be particularly susceptible to T wave oversensing. Perhaps, most crucial to identifying these individuals is the Boston Scientific QRS-T morphology screening (TMS) assessment, which is a transparent plastic tool used to assess electrocardiogram morphology before S-ICD placement. To accomplish this, surface electrocardiograms are obtained from electrodes placed on a patient in a manner similar to the S-ICD system orientation. A patient "passes" the TMS assessment if at least one sensing vector demonstrated appropriate QRS-T wave morphology against standardized measurements. In a study by Groh et al,[63] 100 patients underwent electrocardiographic analysis using the TMS assessment before S-ICD placement. It was determined that 8% of these patients failed the TMS assessment and were, thus, at a high risk of T wave oversensing.[63] Additionally, the authors found that those with inverted T waves on a standard 12-lead electrocardiogram in leads most analogous to the S-ICD vectors (leads I, II, and aVF), were at the highest risk of failing the TMS. In fact, when T wave inversions were present in all 3 of the S-ICD congruent leads, nearly 50% of those patients failed the subsequent electrocardiographic screening tool. Another study by Olde Nordkamp et al[64] found a similar rate of 7.4% in 230 patients screened using the TMS assessment. The authors also found that independent predictors of TMS failure included R:T ratio <3 in the lead with the largest T wave (odds ratio [OR], 14.6), hypertrophic cardiomyopathy (OR, 12.6), heavy weight (OR, 1.5), and prolonged QRS (OR, 1.5). Similarly, Randles et al[65] found that prolonged QRS duration was an independent predictor of S-ICD ineligibility in their population of 196 patients who underwent TMS assessments.

OTHER TV-ICD ALTERNATIVES

It should be noted that there already exists a relatively well-studied alternative to the TV-ICD and S-ICD systems, namely the wearable cardioverter defibrillator (WCD) system, or the LifeVest (Zoll Medical Corporation; Chelmsford, MA). Numerous studies have demonstrated that WCDs reduce morality and have shock efficacy rates comparable to TV-ICDs.[66–68] In fact, one of the largest studies to date which involved 3569 patients, showed that the first-shock efficacy rate for VT/VF episodes was 99%.[67] The advantages of WCDs include a lack of need for any surgical intervention and an easier means of removal or replacement. However, the problems with WCDs mostly lay in the lack of randomized, controlled studies to compare them to conventional TV-ICDs. Furthermore, the effectiveness of WCDs is contingent on patient compliance and appropriate use.

ONGOING CLINICAL TRIALS

There are 2 major ongoing clinical trials that seek to elucidate more data on S-ICD and their role in the prevention of SCD. The Prospective, RAndomizEd comparison of subcuTaneOus and tRansvenous ImplANtable cardioverter defibrillator therapy (PRAETORIAN) study is an ongoing randomized 2-arm trial comparing S-ICD and TV-ICD in 700 patients.[69] The primary endpoint is to assess noninferiority of the S-ICD in the rate of inappropriate shocks and ICD-related complications. This study will also evaluate efficacy and mortality rates. The second study, the S-ICD System Post Approval Study, is a long-term trial assessing the Type I complication-free rate and the overall shock effectiveness of the S-ICD system over a 60-month follow-up period.[70] The study has a target sample size of 1025 subjects and is estimated to be complete by 2020.

CONCLUSIONS

TV-ICDs have been shown to treat life-threatening ventricular tachyarrhythmias and reduce mortality in cardiac disease patients. The S-ICD system is a novel alternative to the conventional TV-ICD system. A review of the current literature reveals that there is similar shock efficacy between the 2 systems in terminating both induced and spontaneous ventricular tachyarrhythmias. However, there are few randomized, head-to-head studies directly comparing S-ICDs with TV-ICDs, so their comparative performance and safety profiles still remain elusive. The advantages of the S-ICD system are numerous: fewer intraoperative complications, fewer vascular complications, fewer infections, and an easier means of replacement. These advantages make the S-ICD system particularly useful for younger patients, those with abnormal venous access, and individuals prone to central vein stenosis/thrombosis and infection. Though S-ICDs seem to have a similar rate of inappropriate shocks compared with TV-ICDS, and arguably a greater specificity for withholding therapy in supraventricular tachycardias, there are limited data on the long-term performance of S-ICDs. Furthermore, the S-ICD system is an inappropriate device for the treatment of recurrent monomorphic VT or symptomatic bradycardia due to its lack of significant pacing abilities. Lastly, there is clearly a higher percentage of inappropriate shocks, which are attributed to T wave oversensing, and this phenomenon should prompt future investigators to examine if screening, algorithm adjustments or device design can reduce these occurrences. At present, data from ongoing trials are accumulating and will hopefully shine light on the long-term shock efficacy and complication rates of S-ICDs.

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