The Subcutaneous Implantable Cardioverter-Defibrillator: New Insights and Expanding Populations

Thomas A Turnage, MD, John A Kpaeyeh Jr, MD, and Michael R Gold, MD, PhD

Division of Cardiology, Medical University of South Carolina, Charleston, SC

Abstract

Implantable cardioverter defibrillators (ICDs) have become a mainstay of treatment in patients at risk for sudden cardiac death. The majority of contemporary ICDs are implanted transvenously; however, this approach carries acute procedural and long-term risks. The subcutaneous ICD (S-ICD) was developed, in part, to circumvent some of these adverse events or as an alternative option in patients unable to undergo transvenous implantation. Early promising trials evaluating the S-ICD were small and focused on niche populations. More recently, larger trials included broader populations with worse heart failure and co-morbidities that may be more representative of typical ICD recipients. These studies have consistently demonstrated positive results. This review describes the S-ICD system, implantation, and the safety and efficacy of the device.

Introduction

Implantable cardioverter-defibrillators (ICD) demonstrate a mortality reduction in patients at risk for sudden cardiac death.[1–4] Transvenous lead placement with a subcutaneous, pectoral pulse generator has been the standard approach for ICD implantation for the past two decades,[5] and have a high rate of successful implantation and a very low risk of in-hospital mortality.[6] Despite increased operator experience, improvements in technology and surgical technique, there are risks inherent in the surgical procedure and transvenous ICDs. Recent data from the US National Cardiovascular Data Registry (NCDR) demonstrate an adverse event rate of 2.2 % and a 1.56 % major adverse event rate (defined as death, cardiac arrest, lead dislodgment, hemothorax, pneumothorax, tamponade, urgent cardiac surgery, myocardial infarction, cerebral vascular accident, and set screw problem).[7]

Although there is a low overall risk of periprocedural complications, additional long-term risks are associated with transvenous ICDs. Rates of infection are reported near 1.5 %,[7,8] and may include cardiac and non-cardiac sites. Lead complication rates approach 10 % in randomized controlled trials[8] and the annual failure rate increases proportionally with time after implantation.[9] Reasons for failure include dislodgment, insulation defects, fracture, loss of capture, inability to sense appropriately, or abnormal impendence. In an effort to address these concerns, an entirely subcutaneous ICD (Cameron Health/Boston Scientific) was developed gaining Conformité Européene (CE) approval in Europe in 2008 and Food and Drug Administration (FDA) approval in 2012.[5]

Subcutaneous Implantable Cardioverter-defibrillator System, Screening, and Implantation

The subcutaneous ICD system consists of a pulse generator that is connected to a lead containing a single high-voltage, low-impedance shock coil and two sensing electrodes. The device senses from one of three different vectors: proximal ring to generator (primary); distal tip electrode to generator (secondary); and distal tip to proximal ring electrode (alternate). The volume of the first generation of the device is 69 ml, with a mass of 145 g.[10] The second generation is slightly smaller, with a volume of 59.5 mL and mass of 130 g.[11]

Preliminary short-term trials beginning in 2001 sought to identify the most effective electrode position for the subcutaneous ICD (S-ICD) on the basis of anatomical landmarks. Four different electrode positions were tested and the most effective location was a left lateral pulse generator with an 8-cm coil electrode positioned to the left of the sternum.[12] Patients under consideration for S-ICD implantation should undergo a preimplant ECG to assess for QRS-T wave morphology to reduce double counting of T-waves resulting in inappropriate defibrillations.[13] ECG screening is necessary to ensure patient compatibility with one of the three vectors utilized with the S-ICD device. In the largest registry to date, patients were required to pass the screening in at least one vector in the supine and standing position. Of the 1637 patients evaluated, full data on all three vectors were available for review in 1622 patients. ECG vector screening was acceptable in two and all three vectors in 93.8 % and 51.4 % of patients, respectively. Lower BMI or higher left ventricular

ejection fraction (LVEF) were predictive characteristics of patients only passing one vector.[14]

The generator is implanted between the mid-axillary and anterior axillary lines connected to the electrode, which is tunneled typically 1 to 2 cm to the left of and parallel to the sternum.[15] *Figure 1* illustrates the anatomic location as well as the sensing vectors of the S-ICD system. In early implantations, the lead was tunneled via an inferior and superior parasternal incision (three-incision technique). In a recent trial, however, the majority of implantations were via the two-incision technique, requiring only an inferior sternal incision.[14] A study of 69 patients implanted with an S-ICD at three German centers demonstrated a mean implantation time of 70.8 ± 27.9 min, which did not differ significantly from conventional ICD implantation times.[16] Sedation strategies have varied widely across trials, with the rates of general anesthesia use ranging from 47 %[17] to 100 %.[18] In the recently published US S-ICD post-market approval study (S-ICD PAS), general anesthesia was utilized in 64.1 % of implantations.[14] Arrhythmia termination is typically tested using 65 J shocks at the conclusion of the procedure. Once implanted, the device output is a non-programmable 80 J shock. The device automatically reverses the polarity of the shock if the initial attempt is unsuccessful. Maximum therapy consists of five defibrillations.[18] Aside from 30 sec of post-shock asystole demand pacing, the device has no anti-bradycardic or anti-tachycardia (ATP) functions.[15]

The 2017 American Heart Association/American College of Cardiology/ Heart Rhythm Society guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death recommend S-ICD implantation in patients meeting criteria for ICD whom:

- have inadequate vascular access or an unacceptable risk of infection (Class I, level of evidence [LOE] B- non-randomized [NR]); or
- pacing for bradycardia, termination of ventricular tachycardia, or CRT is neither needed nor anticipated (Class IIa, LOE B-NR).

S-ICD implantation is not recommended in patients in whom pacing for bradycardia, ATP, or CRT is necessary or envisioned (Class III, LOE B-NR).[13]

Populations Studied

Evaluation of the clinical trials investigating the S-ICD system requires knowledge of the population analyzed. Early studies commonly included a high proportion of niche populations who were younger with little or no structural heart disease and fewer co-morbidities than most series of patients receiving transvenous ICDs. Mean age ranged from 42 to 53 years.[16–22] Two publications reported median ages of 20 and 33 years.[23,24] The majority of early cohorts consisted of fewer than 120 patients.[16–19,23,24] Subsequently, the results from the EFFORTLESS (Evaluation oF FactORs ImpacTing Clinical Outcome and Cost EffectiveneSS of the S-ICD) registry were reported on a population of 985 S-ICD recipients.[25] Within these studies, the prevalence of primary electrical heart disease ranged from 20 %[16] to 75 %.[23] When reported, mean LVEF was greater than 35 % in all cases[16–22,25] and greater than 40 % in five studies.[16–18,21,25] Primary prevention was the initial indication for implantation in 42 %[18] to 79 %[20] of cases. Men represented at least 70 % of each cohort[16–22,25] in all but one trial, where men accounted for 9 out of 16 patients.[23] Although these studies provided valuable information regarding the S-ICD system, as

Figure 1: S-ICD System
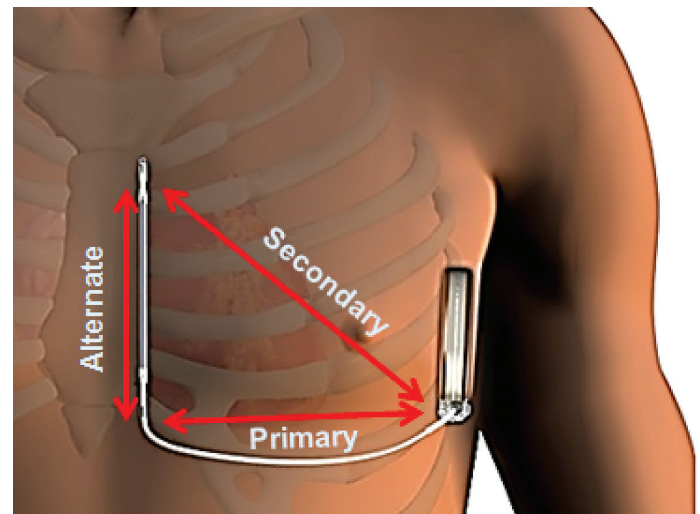
Anatomic location and sensing vectors of the subcutaneous implantable cardioverter-defibrillator system.

noted above the cohorts studied are not entirely representative of typical ICD patients. Accordingly, these differences should be considered when extrapolating the results to broader populations.

Two recent publications have analyzed S-ICD implantation in larger populations with higher prevalence of concomitant co-morbidities. Friedman et al retrospectively analyzed NCDR ICD data from 2012 to 2015 and performed a propensity matched analysis of 5760 patients in a 1:1:1 fashion to compare outcomes among patients implanted with S-ICD, single-chamber, and dual chamber ICD. Patients implanted with S-ICD were found to be more often younger, female, African American, and dialysis dependent, and were more likely to have experienced prior cardiac arrest when compared with more traditional ICD counterparts. Mean LVEF was 32 % and the prevalence of dialysis dependence was 20 % in the S-ICD cohort.[26] A second study, mandated following FDA approval (PAS study), prospectively enrolled and followed patients who received an S-ICD. This population consisted of 1637 S-ICD recipients, 13.4 % of whom were on dialysis. Mean LVEF (32 %) was also lower than other prior S-ICD studies and patients within this study had more co-morbidities than prior publications. The majority of patients had both heart failure and hypertension and over one-third had diabetes. Patients with an LVEF < 35 % and heart disease constituted approximately 75 % of all patients. Additionally, a lower number of patients with inherited channelopathies were enrolled.[14] The PAS study demonstrated that in contemporary clinical practice, the S-ICD population has shifted more from selected niche population to typical ICD cohorts. *Table 1* compares the populations studied from the S-ICD Clinical Investigation (IDE), EFFORTLESS, and S-ICD PAS trials.

Safety

As with any medical procedure, there are risks inherent in the implantation of ICDs. However, these risks differ among the types of ICDs implanted. Complications associated with the implantation of transvenous ICDs include pneumothorax, hemothorax, nerve or vascular damage, hematoma, infection, lead dislodgment or malfunction, cardiac perforation, and tamponade. A meta-analysis of traditional ICD

Table 1: Baseline Patient Characteristics: S-ICD IDE, EFFORTLESS, and S-ICD PAS

	S-ICD IDE	EFFORTLESS	S-ICD PAS
Patients	314	985	1637
Age (years)	51.9 ± 15.5	48.0 ± 17.0	52.0 ± 15.0
Male	74.1 %	72.0 %	68.6 %
Mean LVEF	36.1 ± 15.9 %	43.0 ± 18.0 %	32.0 ± 14.6 %
LVEF ≤ 35 %	NR	57.7 %	75.4 %
Primary prevention	79.0 %	64.9 %	76.7 %
CHF	61.4 %	26.5 %	74.0 %
HTN	15.3 %	28.3 %	61.6 %
Diabetes	NR	11.3 %	33.6 %
Kidney disease	NR	8.2 %	25.6 %

Baseline patient characteristics in three large trials. CHF = congestive heart failure; HTN = hypertension; LVEF = left ventricular ejection fraction; NR = not reported.

randomized controlled trials demonstrated a complication rate of 9.1 %, though a few studies included devices implanted via a thoracotomy. This was compared with a 'real-world' complication rate of 3.08 % for ICD implantation derived from NCDR between 2006 to 2010.[8] Discrepancy between the two rates may be, at least somewhat, accounted for by the intrinsic nature of a comparison between randomized controlled trials and registry data. It is likely that the NCDR registry underestimates long-term complications given the nature of the data collection post implant. A second publication also corroborated the reported complication rate from the NCDR data during that same time period.[27] The rates of the most common adverse events were as follows: lead dislodgement 1.02 %, hematoma 0.86 %, pneumothorax 0.44 %, and cardiac arrest 0.29 %.[27] Other studies quote slightly higher rates of pneumothorax and hematoma.[6,8] NCDR data from 2010 to 2011 demonstrate an even lower adverse event rate.[7]

Although ICD periprocedure adverse event rates are acceptably low, the complications associated with a chronic indwelling transvenous ICD, if present, often lead to significant comorbidity and reoperation. Infection has been reported in 1.5 % of transvenous devices.[7,8] The infection may range from localized pocket or wound infection to fulminant endocarditis. Most patients ultimately require explantation in order to treat the infection successfully. Lead malfunction or defects typically require reoperation with implantation of additional transvenous leads and abandonment of the problematic lead. Annual failure rates of transvenous leads increase with time after implantation. The estimated lead survival rate at 5 and 8 years is 85 % and 60 %, respectively. Annual failure rate of leads at least 10 years old is 20 %.[9] The S-ICD system was designed, in part, as a way to circumvent many of the complications associated with transvenous ICD implantation.

Safety analyses of the S-ICD and comparison with that of conventional ICDs are crucial to its development and clinical acceptance. Earlier S-ICD trials demonstrated a higher rate of complications than later ones, reflective of increased operator experience and improved technology. In the initial trial describing the S-ICD system, thirteen of 55 patients had device related adverse events.[12] In a Dutch cohort of 118 patients, sixteen experienced complications and adverse events

were more frequent in the initial 15 implantations.[17] In the S-ICD IDE study, which had rigorous FDA oversight, Weiss et al reported a 180-day complication-free rate of 92.1 % for all complications and, more specifically, 99 % for complications caused by the S-ICD system.[20] Early results from EFFORTLESS reported similarly low complications with complication-free rates of 97 % and 94 % at 30 and 260 days, respectively.[21] Recently, a large registry corroborated high complication-free rates of the S-ICD.[14] A propensity-matched analysis found that the in-hospital complication rates associated with S-ICD (0.9 %) were not significantly different than that of single chamber or dual chamber ICDs.[26] A second analysis found that complication rates between S-ICD and transvenous ICDs were similar, but that the nature of the complications was different. S-ICDs reduced lead complication rates but it was at the cost of non-lead related complications.[28] Reported rates of infection and hematoma formation in S-ICDs[14,22] are similar to rates previously reported in conventional ICDs.[7,8,27] However, importantly, S-ICD infections are localized and have not been associated with bacteremia or systemic involvement. Improvement in the complication rate suggests a learning curve associated with the implantation of S-ICDs. A pooled cohort from the IDE study and EFFORTLESS registry demonstrates a significantly decreased complication rate with more experienced operators.[29] Technology advances have also contributed to decreased S-ICD adverse events. Parasternal lead migration was encountered frequently in early clinical trials; however, in at least two trials, no further lead migration was observed following the introduction of a xiphoid suture sleeve to the operative protocol.[17,19]

Inappropriate shocks are associated with worsened quality of life, increased healthcare costs,[30,31] so minimizing such events has been an area of intense study for ICDs. The cause of inappropriate shocks with S-ICD have been inappropriate sensing of myopotentials, T-wave oversensing, changes in QRS morphology, or failure to discriminate supraventricular tachycardia (SVT). In one study, no further inappropriate shocks were observed following a software update specifically addressing myopotential oversensing.[19] Other software updates addressing T-wave oversensing, changes in sensing vectors during exercise, or the addition of new templates have led to reductions in inappropriate therapy.[17]

For transvenous ICDs, conservative programming of tachycardia treatment zones by prolonging detection duration or increasing threshold rates for therapy has been shown to not only reduce inappropriate shocks, but also improve mortality.[32] The Subcutaneous versus Transvenous Arrhythmia Recognition Testing (START) study demonstrated that the S-ICD discriminated SVT more effectively than transvenous ICD systems.[33] Thus, the use of dual zone programming employing a conditional zone (rate plus discriminators) markedly reduces inappropriate shocks.[34] Continued reductions in inappropriate shocks as well as improvements in device implantation and technique with new generations of the S-ICD device will likely lead to an even more acceptable safety profile. These differences in the types of lead complications and inappropriate shocks between transvenous and subcutaneous ICDs has been further supported by a recent meta-analysis.[35]

The safety profiles of a device are also affected by longevity. A device with a shorter battery life or time to the elective replacement interval (ERI) exposes the patient to more procedures with their intrinsic risks.

Conventional ICDs implanted after 2002 were found to have a mean battery life of 5.6 years.[36] Although device longevity varies somewhat with manufacturer and programmed mode, overall longevity of devices continues to improve with more recently implanted devices.[37] The manufacturer of the S-ICD initially projected device longevity of 5 years.[10] A nearly 6-year follow-up of 55 patients enrolled in the European Regulatory Trial demonstrated a device replacement rate of 47 %. The majority of devices were replaced on ERI (81 %) and the median time for device replacement was 5 years. Premature battery depletion occurred in 9 % of the initial S-ICD cohort leading to a field safety notification regarding a battery manufacturing issue. Following correction, premature battery depletion was observed in 0.6 % in the IDE trial and 0.2 % in the EFFORTLESS registry.[38] Published rates of premature battery depletion in transvenous ICDs are 8–9 %.[39,40] The second generation S-ICD system has manufacturer projected longevity of over 7 years,[11] though this will need to be validated with subsequent analyses.

Efficacy

S-ICD devices are effective in appropriately sensing and terminating VT/VF. Conversion testing is typically performed immediately following implantation with induction of VT/VF and a 65 J shock providing an adequate (15 J) safety margin.[12,16,18,19] An early trial comparing temporary S-ICD systems with transvenous ICDs found that conversion efficacy was similar, though S-ICD systems had higher defibrillation thresholds.[12] Moreover, the START study demonstrated no significant differences in ventricular arrhythmia detection for S-ICDs and transvenous devices.[33] A larger study of 899 episodes of induced VT/VF established a 99.8 % rate of successful VT/VF detection and defibrillation. In those instances where VT/VF was successfully detected, successful defibrillation was obtained in 100 % of patients.[20] An early study of 40 consecutive S-ICD patients did demonstrate a low conversion efficacy with the initial shock; however, 96.4 % had successful conversion within the five allotted shocks.[18] Recent large trials further corroborate the ability of the S-ICD system to successfully defibrillate induced VT/VF.[14,26] Failure of conversion with the first shock is predicted by patient height and BMI.[14] Conversion testing has also been performed ≥ 150 days after implantation. Of the 75 patients with evaluable results, 72 (96 %) were successfully converted at 65 J. The three other patients were successfully converted at 80 J.[20] Mean time to therapy has been reported at 14.6 and 19.2 sec[20,22] and is in line with the current paradigm for programming of defibrillation therapy for transvenous systems.[30]

Induction of VT/VF and conversion testing indicates proper device functioning in a controlled setting. However, demonstration of termination of spontaneous episodes is obligatory to show the true benefit of ICDs. Weiss et al reported 119 spontaneous VT/VF episodes in 21 patients. There were 38 discrete VT/VF episodes and 81 that occurred during VT/VF storms. The first shock conversion rate for the discrete episodes was 92.1 % and all but one was terminated with ≥ 1 shocks. The exception was an episode of monomorphic VT, which terminated spontaneously while the device was charging for a second shock.[20] In the EFFORTLESS registry, the overall successful conversion rate for spontaneous episodes was 97.4 %.[25] Other investigations have found similarly high rates of successful first shock[17] and overall shock efficacy.[22]

Limitations

Despite evidence establishing the safety and efficacy of the S-ICD, the device does have limitations. The system does not have the ability to provide chronic anti-bradycardic, anti-tachycardic pacing, or CRT. It is able to provide up to 30 sec of post-shock asystole pacing at a rate of 50 bpm.[15] The inability to provide pacing chronically emphasizes the importance of appropriate patient screening to exclude those patients with, or who may develop, bradycardic indications. In the 3-year follow-up of the EFFORTLESS registry, the S-ICD was explanted for the indication of bradycardia in 0.1 %, ATP in 0.5 %, and CRT in 0.4 % of patients.[25] Low rates of S-ICD explantation and transition to transvenous devices for bradycardia, CRT, or ATP likely reflect the importance of proper patient selection.

Conclusion

The S-ICD device is a safe and effective alternative to contemporary transvenous ICDs in selected patients. Additionally, new studies have demonstrated both safety and efficacy in broader, sicker populations.[14,26] This is being studied in even more detail in the UNTOUCHED trial of primary prevention patients with a reduced ejection fraction.[41] Though direct randomized comparisons between the two systems are currently unavailable, the Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter-Defibrillator Therapy (PRAETORIAN) trial is ongoing.[42] In selected patients, and arguably most, who qualify for ICD therapy without an indication for pacing, CRT, or ATP, the subcutaneous ICD system should be considered. ■

1. The Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. N Engl J Med 1997;**337**:1576–83. DOI: 10.1056/NEJM199711273372202; PMID: 9411221.
2. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. N Engl J Med 1996;**335**:1933–40. DOI: 10.1056/NEJM199612263352601; PMID: 8960472.
3. 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 2002;**346**:877–83. DOI: 10.1056/NEJMoa013474; PMID: 11907286.
4. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 2005;**352**:225–37. DOI: 10.1056/NEJMoa043399; PMID: 15659722.
5. Lewis GF, Gold MR. Safety and efficacy of the subcutaneous implantable defibrillator. J Am Coll Cardiol 2016;**67**:445–54. DOI: 10.1016/j.jacc.2015.11.026; PMID: 26821634.
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 2011;**58**:995–1000. DOI: 10.1016/j.jacc.2011.06.007; PMID: 21867832.
7. Kremers MS, Hammill SC, Berul CI, et al. The National ICD Registry Report: version 2.1 including leads and pediatrics for years 2010 and 2011. Heart Rhythm 2013;**10**:e59–65. DOI: 10.1016/j.hrthm.2013.01.035; PMID: 23403056.
8. Ezzat VA, Lee V, Ahsan S, et al. A systematic review of ICD complications in randomised controlled trials versus registries: is our 'real-world' data an underestimation? Open Heart 2015;**2**:e000198. DOI: 10.1136/openhrt-2014-000198; PMID: 25745566.
9. 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 2007;**115**:2474–80. DOI: 10.1161/CIRCULATIONAHA.106.663807; PMID: 17470696.
10. Lupo PP, Pelissero G, Ali H, et al. Development of an entirely subcutaneous implantable cardioverter-defibrillator. Progress in cardiovascular diseases. 2012;**54**:493–7. DOI: 10.1016/j.pcad.2012.03.006; PMID: 22687590.
11. Emblem MRI S-ICD System Product Details. Boston Scientific. Available from: http://www.bostonscientific.com/en-US/

products/defibrillators/emblem-s-icd-system.html
12. Bardy GH, Smith WM, Hood MA, et al. An entirely subcutaneous implantable cardioverter-defibrillator. N Engl J Med 2010;**363**:36–44. DOI: 10.1056/NEJMoa0909545; PMID: 20463331.
13. 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: Executive Summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm 2017. DOI: 10.1016/j.hrthm.2017.10.036.
14. Gold MR, Aasbo JD, El-Chami MF, et al. Subcutaneous implantable cardioverter-defibrillator post-approval study: clinical characteristics and perioperative results. Heart Rhythm 2017;**14**:1456–63. DOI: 10.1016/j.hrthm.2017.05.016; PMID: 28502872.
15. Rowley CP, Gold MR. Subcutaneous implantable cardioverter defibrillator. Circ Arrhythm Electrophysiol 2012;**5**:587–93. DOI: 10.1161/CIRCEP.111.964676; PMID: 22715237.
16. 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 2013;**10**:29–36. DOI; 10.1016/j.hrthm.2012.09.126; PMID: 23032867.

17. 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* 2012;**60**:1933–9. DOI; 10.1016/j.jacc.2012.06.053; PMID:23062537.

18. Aydin A, Hartel F, Schluter M, et al. Shock efficacy of subcutaneous implantable cardioverter-defibrillator for prevention of sudden cardiac death: initial multicenter experience. *Circ Arrhythm Electrophysiol* 2012;**5**:913–9. DOI; 10.1161/CIRCEP.112.973339; PMID: 22923274.

19. Dabiri Abkenari L, Theuns DA, Valk SD, et al. Clinical experience with a novel subcutaneous implantable defibrillator system in a single center. *Clin Res Cardiol* 2011;**100**:737–44. DOI: 10.1007/s00392-011-0303-6; PMID: 21416191.

20. Weiss R, Knight BP, Gold MR, et al. Safety and efficacy of a totally subcutaneous implantable-cardioverter defibrillator. *Circulation* 2013;**128**:944–53. DOI; 10.1161/CIRCULATIONAHA.113.003042; PMID: 23979626.

21. 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* 2014;**35**:1657–65. DOI: 10.1093/eurheartj/ehu112; PMID: 24670710.

22. Burke MC, Gold MR, Knight BP, et al. Safety and efficacy of the totally subcutaneous implantable defibrillator: 2-year results from a pooled analysis of the IDE Study and EFFORTLESS Registry. *J Am Coll Cardiol* 2015;**65**:1605–15. DOI: 10.1016/j.jacc.2015.02.047; PMID: 25908064.

23. Jarman JW, Lascelles K, Wong T, et al. Clinical experience of entirely subcutaneous implantable cardioverter-defibrillators in children and adults: cause for caution. *Eur Heart J* 2012;**33**:1351–9. DOI: 10.1093/eurheartj/ehs017; PMID: 22408031.

24. Jarman JW, Todd DM. United Kingdom national experience of entirely subcutaneous implantable cardioverter-defibrillator technology: important lessons to learn. *Europace* 2013;**15**:1158–65. DOI: 10.1093/europace/eut016; PMID: 23449924.

25. 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* 2017;**70**:830–41. DOI: 10.1016/j.jacc.2017.06.040; PMID: 28797351.

26. 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* 2016;**1**:900–11. DOI: 10.1001/jamacardio.2016.2782; PMID: 27603935.

27. Freeman JV, Wang Y, Curtis JP, et al. Physician procedure volume and complications of cardioverter-defibrillator implantation. *Circulation* 2012;**125**:57–64. DOI: 10.1161/CIRCULATIONAHA.111.046995; PMID: 22095828.

28. Brouwer TF, Yilmaz D, Lindeboom R, et al. Long-term clinical outcomes of subcutaneous versus transvenous implantable defibrillator therapy. *J Am Coll Cardiol* 2016;**68**:2047–55. DOI: 10.1016/j.jacc.2016.08.044; PMID: 27810043.

29. Knops RE, Brouwer TF, Barr CS, et al. The learning curve associated with the introduction of the subcutaneous implantable defibrillator. *Europace* 2016;**18**:1010–5. DOI: 10.1093/europace/euv299; PMID: 26324840.

30. Daubert JP, Zareba W, Cannom DS, et al. Inappropriate implantable cardioverter-defibrillator shocks in MADIT II: frequency, mechanisms, predictors, and survival impact. *J Am Coll Cardiol* 2008;**51**:1357–65. DOI: 10.1016/j.jacc.2007.09.073; PMID: 18387436.

31. van Rees JB, Borleffs CJ, de Bie MK, et al. Inappropriate implantable cardioverter-defibrillator shocks: incidence, predictors, and impact on mortality. *J Am Coll Cardiol* 2011;**57**:556–62. DOI: 10.1016/j.jacc.2010.06.059; PMID: 21272746.

32. Moss AJ, Schuger C, Beck CA, et al. Reduction in inappropriate therapy and mortality through ICD programming. *N Engl J Med* 2012;**367**:2275–83. DOI: 10.1056/NEJMoa1211107; PMID: 23131066.

33. Gold MR, Theuns DA, Knight BP, et al. Head-to-head comparison of arrhythmia discrimination performance of subcutaneous and transvenous ICD arrhythmia detection algorithms: the START study. *J Cardiovasc Electrophysiol* 2012;**23**:359–66. DOI: 10.1111/j.1540-8167.2011.02199.x; PMID: 22035049.

34. Gold MR, Weiss R, Theuns DA, et al. Use of a discrimination algorithm to reduce inappropriate shocks with a subcutaneous implantable cardioverter-defibrillator. *Heart Rhythm* 2014;**11**:1352–8. DOI: 10.1016/j.hrthm.2014.04.012; PMID: 24732366.

35. 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* 2017;**3**:1484–6. DOI: 10.1016/j.jacep.2017.07.017

36. Thijssen J, Borleffs CJ, van Rees JB, et al. Implantable cardioverter-defibrillator longevity under clinical circumstances: an analysis according to device type, generation, and manufacturer. *Heart Rhythm* 2012;**9**:513–9. DOI: 10.1016/j.hrthm.2011.11.022; PMID: 22094073.

37. von Gunten S, Schaer BA, Yap SC, et al. Longevity of implantable cardioverter defibrillators: a comparison among manufacturers and over time. *Europace* 2016;**18**:710–7. DOI: 10.1093/europace/euv296; PMID: 26609076.

38. Theuns DA, Crozier IG, Barr CS, et al. Longevity of the subcutaneous implantable defibrillator: long-term follow-up of the European regulatory trial cohort. *Circ Arrhythm Electrophysiol* 2015;**8**:1159–63. DOI: 10.1161/CIRCEP.115.002953; PMID: 26148819.

39. Manolis AS, Maounis T, Koulouris S, et al. "Real life" longevity of implantable cardioverter-defibrillator devices. *Clin Cardiol* 2017;**40**:759–64. DOI: 10.1002/clc.22729; PMID: 28543134.

40. Hauser RG, Hayes DL, Epstein AE, et al. Multicenter experience with failed and recalled implantable cardioverter-defibrillator pulse generators. *Heart Rhythm* 2006;**3**:640–4. DOI: 10.1016/j.hrthm.2006.02.011; PMID: 16731462.

41. Gold MR, Knops R, Burke MC, et al. The design of the understanding outcomes with the S-ICD in Primary Prevention Patients with Low EF Study (UNTOUCHED). *Pacing Clin Electrophysiol* 2017;**40**:1–8. DOI: 10.1111/pace.12994; PMID: 27943348.

42. 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* 2012;**163**:753–60. DOI: 10.1016/j.ahj.2012.02.012; PMID: 22607851.