EFFORTLESS S-ICD registry: another step in the right direction

Theofanie Mela and Jagmeet P. Singh*

Cardiac Arrhythmia Service, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

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This editorial refers to ‘Worldwide experience with a totally subcutaneous ICD: early results from the EFFORTLESS S-ICD registry¶’, by P.D. Lambiase et al., on page 1657

While the clinical significance of the implantable cardioverter defibrillator (ICD) in the reduction of sudden cardiac arrest remains unequivocal, the quest for the best implantable system continues. The first successful, yet experimental, ICD system involved two electrodes between the pectoralis muscle and the rib cage, two sensing electrodes in the chest wall musculature, with a pulse generator and capacitor implanted intra-abdominally in animals.1 The first ICD implanted in a human in 1980 consisted of epicardial patches and sensing leads.2 Subsequently, the advent of transvenous ICD leads significantly reduced the morbidity of the procedure and complication rates, while improving clinical outcomes. The transvenous leads, however, came with the cost of a spectrum of vascular complications as well as design faults. Therefore, the quest for a better implantable system has continued. The totally subcutaneous ICD (S-ICD), an innovative strategy obviating the need for vascular access, has come on as a contender to fill this void.3

Evidence favouring the clinical use of the S-ICD came from the feasibility studies and European registries that preceded the Food and Drug Administration (FDA) approval of the device.1–5 Most of these studies have comprised smaller numbers with limited follow-up, calling into question the applicability of these results in real-world practice. The study now presented by Lambiase et al.,6 reporting on early data from the multicentre EFFORTLESS S-ICD registry, provides valuable information on system performance and inappropriate shock rates. This registry is a laudable effort and comprises an observational, non-randomized, standard of care evaluation of S-ICD in countries outside the USA. The term ‘worldwide experience’ in the title, however, may be a misnomer, as the registry primarily comprises only seven countries (six from Europe and New Zealand). The data set used for this analysis from April 2013 comprised 472 patients receiving the S-ICD system, with a mean follow-up of 558 days. Notably, half of these patients were collected retrospectively. Interestingly, due to the selection criteria for patients receiving the S-ICD [i.e. lack of indications for pacing, for cardiac resynchronization therapy (CRT), and for pace-termination of ventricular tachycardia (VT)], the patient cohort in this study is quite dissimilar from those in traditional ICD studies. The patients are significantly younger (average age of 49 years), and include a small number of children, and those with ischaemic cardiomyopathy (37%), idiopathic ventricular fibrillation (VT; 7%), channelopathies (13%), congenital heart disease (7%), and non-ischaemic cardiomyopathy (31%). Also, it is interesting to note that fewer than one-third had a history of congestive heart failure, and the overall mean left ventricular ejection fraction was 42%.

Registries offer a great venue for understanding the real-world safety and efficacy of device therapy and in particular provide a unique opportunity also to examine subgroups of patients that may never be studied and evaluated in randomized clinical trials (e.g. those on haemodialysis or elderly patients). Importantly, the inferences that are drawn from this should be primarily made from data collected prospectively. Although the investigators include retrospective and prospective patient groups in the study, the demographic data in the two groups remain quite comparable. It would have been of additional value if within the same centres a prospective registry of transvenous ICDs was maintained. Such a simple additional strategy could have helped to create a control arm and bring us closer to a comparative analysis on clinical outcomes, although would this still not have provided the same level of purity of a head-to-head randomized controlled clinical trial vs. transvenous ICDs.

Although S-ICD implantation is a new procedure, it is not a particularly challenging one. The whole system is implanted subcutaneously and there is very little room for a serious complication other than those related to healing of the pocket and the need for re-operation if the lead position is not optimal. The rate for which the S-ICD system had to be explanted due to an infection was 2.2% (Figure 1), higher than the range of transvenous ICDs. Undoubtedly the implications from such infections are less serious than those with transvenous devices, where endocarditis and the accompanying bacteraemia...
could be life threatening, if not recognized early and treated aggressively. Also, the removal of transvenous leads in turn is associated with an added procedural risk of major complications and mortality. The results from this registry show a much lower infection rate than previous studies had reported. This lower rate in turn could have been due to the additional familiarity gained after the first few hundred implants. From our personal experience, we can state that the manufacturers have made extraordinary efforts to educate physician operators carefully, which in turn has improved the acute procedural success. Although general anaesthesia is usually a requirement for this procedure, the absence of the need for fluoroscopy makes it attractive for operators and for niche populations, such as children and pregnant women. Of note, nine patients (2%) died during follow-up, one of which was arrhythmic. Ventricular fibrillation in this case was appropriately detected and treated, and death here was due to asystole after a series of unsuccessful shocks. Although the S-ICD system is designed to deliver a brief sequence of pacing after a shock, this is apparently not as successful as transvenous pacing.

Some of the potential concerns with the S-ICD have been arrhythmia detection, prolonged charge times, and consequently delayed therapy. The implications are not exactly known, as only a few spontaneous episodes have been studied so far in the relatively small number of patients that have received S-ICDs. However, the EFFORTLESS S-ICD registry now provides additional real-world information that may help address some of these concerns. The time to therapy in the Investigational Exemption Trial (IDE) was 14.2 s, while in this registry the mean time to therapy for spontaneous episodes was 17.5 s, with a range of 6.0–29.4 s. The IDE study was based on spontaneous events in only 16 patients, thereby making the results of this registry more meaningful, as the latter was derived from 169 spontaneous episodes in 59 patients, with 93 appropriate interventions for VT and VF in 33 (7.2%) of the patients. The efficacy of the first shock for spontaneous VT/VF termination was 88% and increased to 96% after the fifth shock. Also, 73 inappropriate shocks were delivered in 32 patients, with the majority of these as a consequence of sensing-related issues. One of the major weaknesses of the VT/VF detection of the S-ICD system is inappropriate sensing (7%), with the majority of inappropriate shocks being due to T wave or low amplitude signal oversensing. After reprogramming, only 2% of the patients experienced recurrent inappropriate shocks. The S-ICD offers two zones of therapy, a high-rate zone and a conditional zone, where the supra-ventricular arrhythmia discriminators can be applied. In the S-ICD IDE cohort, when the conditional zone was turned on, the patients were significantly less likely to experience an inappropriate shock due to any cause. Compared with the earlier studies, the incidence of inappropriate shocks was lower in the EFFORTLESS-ICD registry. This, however, needs to be interpreted in light of the differences in the populations and also the length of follow-up within the four different studies/registries (see Figure 1). To avoid this risk of inappropriate shocks due to oversensing, a stepwise diligent screening algorithm is followed prior to the implantation of the device, both at rest and in different positions of the body, as well as, ideally, during exercise. A certain percentage of patients may not be eligible candidates for S-ICD implantation following that screening. The percentage is not well known, but can be as high as 19%, if someone considers consecutive patients of an ICD clinic. This can be considered a significant limitation of this system, both for the time required for screening prior to the procedure and the uncertainty of each patient regarding their candidacy for this procedure. In our experience, this has been a drawback with regards to patients referred from remote geographic areas to our centre, as it is unclear if the patient will be a suitable candidate for the S-ICD system until after the screening. Also, the first-generation devices are bulky and may work best in patients with a larger body habitus. They also have a shorter battery life. Importantly, like most innovative and disruptive technologies that stand the test of time, one can envisage the S-ICD device continuing to evolve and the size becoming progressively smaller, the algorithms smarter, the shock times shorter, and battery life longer. Just like conventional transvenous devices, over time the S-ICD too will have remote monitoring and become compatible with magnetic resonance imaging.
The authors should be congratulated for their efforts to present this information in a systematic way and offer much needed long-term data. S-ICDs seem like a first-line strategy for specific patient subsets with limited vascular access, high infectious risk, and complex congenital anomalies. Whether it should be first line in conventional primary and secondary prevention situations remains an area of debate, with strong arguments on both sides.\textsuperscript{10,11} How the totally subcutaneous ICD compares with the conventional transvenous approach in terms of long-term clinical outcomes, quality of life, ICD generator changes, lead durability, and cost-effectiveness requires more data and follow-up. The extended follow-up in the EFFORTLESS S-ICD registry may help answer some of these lingering questions. However, the early data from this registry seem like a very good step in the right direction.

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