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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