REVIEW

Subcutaneous implantable defibrillator: system overview, evidence and future directions

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Abstract: Implantable cardioverter-defibrillators (ICDs) prevent sudden cardiac death (SCD) in patients at high risk of sudden arrhythmic death. Long-term studies have proven the efficacy of this system, however, implantation of endocardial leads is associated with significant procedural and long-term complications[1,2]. To overcome this complications an entirely subcutaneous implantable cardioverter defibrillator (S-ICD) has been developed. This approach is demonstrated to be safe and effective. The purpose of this review is to assess the current evidence from the clinical trials and future directions of this novel technology.
Keywords: implantable cardioverter defibrillator, ventricular fibrillation, sudden cardiac death, defibrillation threshold, inappropriate shocks.

Rezumat: Defibrilatorul cardioverter implantabil (ICDs) previne moartea subită cardiacă (SCD) la pacienții cu risc crescut de moarte subită aritmică. Studiile pe termen lung au dovedit eficacitatea acestui sistem. Cu toate acestea, implantarea sondelor endocardice este asociată cu complicații procedurale și pe termen lung semnificative[1,2]. Pentru a evita aceste complicații a fost dezvoltat un defibrilator în întregime subcutanat (SCD). Această abordare s-a dovedit a fi sigură și eficientă. Scopul lucrării de față este de a evalua dovezile actuale din studiile clinice și viitoarele direcții ale acestei noi tehnologii.
Cuvinte cheie: defibrilatorul cardioverter implantabil, fibrilația ventriculară, moartea subită cardiacă, pragul de defibrilare, șocuri inapropriate.

INTRODUCTION

S-ICD represents a viable option to transvenous implantable defibrillator (TV-ICD) for the prevention of SCD. ICD therapy is well established as a successful treatment strategy. Transvenous leads, however, still remains the weakest part of the system[3,4]. The complications associated with the TV-ICD lead to the development of an entirely subcutaneous ICD, aiming to provide the same protection of the TV-ICD but with less risk of complications. S-ICD can provide substantial advantages, particularly in young patients with a long life expectancy and an active lifestyle, which are prone to a high risk of lead fracture, and in congenital heart disease with difficult access to the right cardiac chambers. The benefits of avoiding the use of transvenous leads must be weighed against the potential need for pacing. The system has no bradycardia pacing function, only 30 seconds post shock, and no antitachycardia pacing (ATP).

OVERVIEW OF THE SYSTEM

S-ICD detects and treats malignant ventricular arrhythmias without requiring vascular access. The system includes a subcutaneous pulse generator enclosed in a titanium case and a single subcutaneous tripolar electrode with a length of 45 cm (Figure 1 (I)). The lead has polyurethane insulation and is composed of a proximal and distal electrode separated by a shocking coil with a surface area of 750 mm^2 and a size of 9F/3 mm. S-ICD system is implanted using anatomical landmarks, after recording a 3-lead surface ECG to assess the surface signals, reducing the need for fluoroscopy during implant[5]. The pulse generator is bigger than TV-ICD generator and is placed at the mid-axillary line between the 5th and 6th intercostal spaces. The electrode is positioned parallel to and 1 to 2 cm to the left sternal midline, through two subcutaneous tunnels, one from the pocket to the xiphoid incision and the second from the xiphoid to the superior incision.

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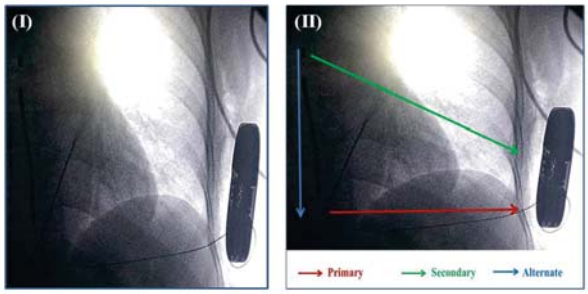

Figure 1. (I) Radiographic image of subcutaneous implantable defibrilator (S-ICD). (II) The three available sensing vector of the S-ICD primary (ring to can), secondary (tip to can) and alternate (tip to ring).

The device senses subcutaneous signals using three available sensing vectors (Figure. 1 (II)): primary (ring to can), secondary (tip to can) and alternate (tip to ring). The system automatically chooses the optimal sense vector for rhythm detection. Four separate algorithms are used to correctly identify the rhythm and prevent oversensing: rate, sinus rhythm template, dynamic morphology and QRS width analysis.

For arrhythmia termination two zones are programmable. One is the conditional zone (170-240 bpm, 10 bpm less than shock zone) using rate detection and rhythm discrimination and the other is shock zone (170-250 bpm) using only rate detection. The device testing during implantation should be performed to evaluate proper sensing, detection and charge time, to assess acute energy requirements and to evaluate post shock pacing. Postprocedure the device delivers up to five biphasic shocks per episode of 80 J. Available shock polarity is standard (coil to can) or reverse (can to coil) and can automatically be reversed if initial shock is unsuccessful. Charge time is approximately 14 seconds (sec), with a post-shock pacing at 50 bpm up to 30 sec and no ATP option available.

EVIDENCE

The main concern with any novel technology is proper performance. Several clinical trials have proven the effectiveness of S-ICD in detecting and treating lethal ventricular tachyarrhythmias. Earliest data were published by Bardy et al in 2010[5]. In their study, the best lead configuration was first identified, chosen from four different configurations, selected on the basis of specific anatomical landmarks. The suitable device configuration was with the pulse generator position left lateral and the electrode coil, of 8mm, at the left parasternal margin. Second, the defibrillation threshold (DFT) of the device was assessed in comparison to that of the conventional ICD. The S-ICD was as effective as TV-ICD for cessation of induced ventricular fibrillation but with a significantly higher energy requirement. Studies that followed this publication supported S-ICD efficacy and safety in detecting and terminating induced VT/VF episodes, the acute success rate ranging between 98%-100% (Table 1)[5-11].

Should we check DFT following S-ICD implantation? In the SIMPLE study, TV-ICD implantation without defibrillation testing was non inferior to intraoperative defibrillation testing regarding long-term efficacy of the TV-ICD or total mortality[12]. This is not the case for S-ICD and the results of two studies underline that DFT intraoperative is currently necessary. One study was published in 2013 by Kobe et al. and assessed the DFT using a step by step protocol. Success conversion rate was quite low using a protocol of 65J, 15J safety margin, with a standard shock polarity, only 89.5%. The other cases required change of shock polarity, higher energy or reposition, reaching finally an overall rate of 98%[8]. In the study published by Frommeyer et al. in 2016 the success rate of acute conversion using a protocol of 65J reached 90%, but 15% of these had a reverse polarity shock. In a small percentage of the cases (4%) a reduce safety margin, less than 10J was accepted. Ineffective repeated shocks droved to reposition of the system in 6 cases[11]. These results seem anomalous considering the initial evaluation of the lead configuration reported by Bardy which exhibited a DFT mean of 32.5±17 J for the actual S-ICD configuration[5]. Another aspect to consider is the maximum energy shock of the device, no more than 80J and no other possible interventions to improve shock efficacy

Table 1. Conversion rate of induced VT/VF

Study	Number of patients	Success conversion rate	Reposition of the can or lead
Bardy et al. NEJM 2010 (CE TRIAL)[5]	53	98%	1
Olde Nordkamp et al. JACC 2012 (Dutch trial)[6]	118	100%	-
Weiss et al. Circulation 2013 (IDE trial)[7]	304	100%	-
Kobe et al. Heart Rhythm 2013[8]	67	98.5%	2
Jarman et al. UK experience Europace 2013[9]	111	100%	-
Lambiase et al. EHJ 2014 (Effortless trial)[10]	393	98%	7
Frommeyer et al. J Am Heart Assoc 2016[11]	98	100%	6

that are available in TV-ICD systems, such as additional coil or a subcutaneous array.

What about long-term performance? Using pooled data from two large studies, Effortless and IDE trial, on 882 patients, Burke et al. showed that 90.1% of VT/VF episodes were stopped after one shock and 98.2% were terminated after up to five shocks[13]. About 37% of VT/VF episodes were self-terminated, due to longer programming time-to-therapy (19.2±5.3sec). Overall, the estimated 3 year rate of inappropriate shocks was 13.1% but this rate was reduced over time. START study results and MADIT-RIT led the operators to change programming of the device[14,15]. Higher cutoff rate and dual zone shocks programming decreased significantly the incidence of inappropriate shocks. In patients with programmed dual zone the incidence of inappropriate shocks at 3 years was significant lower (11.7%) than those with single zone (20.5%). Inappropriate therapy remains a major concern in all ICD system, regardless of whether it is a S-ICD or TV-ICD, and is associated with a decrease in the quality of life and increase in mortality[16,17]. The rate of inappropriate shocks observed in the S-ICD trials ranges between 4% to 25%, not so different from TV-ICD. These occur, however, through a different mechanism, mostly secondary to T-wave oversensing (Table 2).

If we analyze data from the S-ICD trials, the highest rate of inappropriate shocks was reported by Jarman et al. in 2012[18]. This was a small study that included only young patients with a mean age of 20 years, without ischemic or dilated cardiomyopathy. It is curious why this population exhibited the highest rate of inappropriate shocks given the fact that in this group, an S-ICD system should be strongly considered (Figure 2)[19]. The authors note this could be due to cardiac repolarization, which differs from adult population, although they did not identify any predictor factors for inappropriate shocks, secondary to T-wave oversensing (TWOS). A retrospective study which analyzed patients who received a TV-ICD found that 55% of them at 5 years follow-up would have been suitable for S-ICD. Predictors for S-ICD unsuitability were found to be QRS width, advanced heart failure and secondary prevention[22]. In a study published by Groh et al. in 2014, 8% of S-ICD candidates had inadequate signals and predictors were T-wave inversions, on standard 12 lead ECG, in DI, DII and aVF[23]. Another study, published in the same year, found as predictors factors for screening failure patients with hypertrophic cardiomyopathy, heavy weight, prolonged QRS duration and R:T ratio less than 3 in the ECG lead with the largest T wave[24]. This aspect should underline the importance of pre-implantation screening to identify the suitable patients

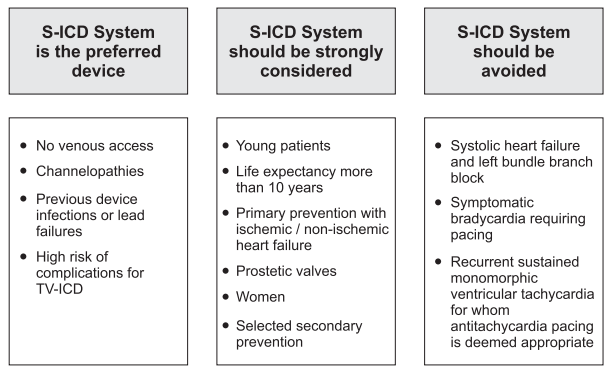

Figure 2. Recommendations for S-ICD implantation[19].

Table 2. Trial data. Rate of inappropriate shocks, re-interventions and infections

Study	Number of patients	Age (median / mean ±SD)	Ischemic or idiopathic cardiomyopathy	Follow-up duration (months)	Inappropriate shocks	Re-interventions	Infections rate
Bardy et al. 2010[5]	55	56±13	85%	10	9%	11%	4%
Dabiri Abkenari et al. 2011[20]	31	53±16	75%	9	16%	10%	3%
Olde Nordkamp et al. 2012[6]	118	50±14	57%	18	13%	14%	6%
Jarman et al. 201218	16	23	0%	9	25%	19%	0%
Aydin et al.[21] 2012	40	42±15	45%	8	5%	13%	0%
Weiss et al.[7] 2013	314	51.9±15.5	~80%	11	13%	4%	6%
Kobe et al.[8] 2013	69	45.7±15.7	52%	7	4%	4%	1%
Jarman et. Al UK experience 2013[9]	111	33	19%	13	15%	17%	10%
Lambiase et al. 2014[10]	456	47±18	53%	12	7%	6%	4%
Burke et al. (Pooled date) 2015[13]	882	50.3±16.9	70%	21.7±11.5	13%	9%?	11%

for S-ICD. On the other hand, a study from Zeb et al. in 2015 found less specific the S-ICD screening tool, especially in patients with complex congenital heart disease[25]. Templates acquired during exercise testing post-implant procedure can prevent TWOS, leading also in choosing the best sensing vector configuration[26]. New algorithms developed for TWOS may help prevent inappropriate shocks without affecting ventricular sensing arrhythmias[27].

Other points of concern are the rate of re-interventions and infections associated with S-ICD system (Table 2). Rate of re-interventions was up to 19%, being higher in the young population and mainly due to pocket erosions[18]. Rate of infections was up to 11%, higher in the pooled data published by Burke and al 13. In their data on 882 patients, only 1.7% of infections required extraction. The majority of superficial wounds responded well to antibiotic treatment. Nevertheless, the incidence declined overtime and this may be related to initial inexperience of the operators with the surgical technique of implantation. Providing a rigorous procedural preparation and improving the implantation technique by using 2-incision technique instead of 3-incision technique may have helped[28].

FUTURE DIRECTIONS

The S-ICD represents a major advancement in ICD technology. Since it was introduced on the market the system continues to evolve. Maybe, for the next generations of devices, current limitation will be addressed such as device longevity, dimension and shape, lower DFT and pacing ability.

Integration of an S-ICD system with a leadless pacing could play an important role and would widen the implant indications in those with bradycardia or in patients requiring ATP-pacing. Recently, a study published by Tjong et.al investigated the feasibility of an S-ICD with a leadless pacing device[29]. The study was first conducted on animals, and later, on human subjects. They concluded there was no interference on performance between devices, without dislodgment of the leadless pacing system after repeated shocks, from either S-ICD or external defibrillator. This same author published, shortly after, the first concept study of a combined leadless pacing prototype in a patient with an preexisting S-ICD, manufactured by the same company[30]. Ventricular tachycardia was successfully detected by the S-ICD and communication to the leadless pacing trigger with success the ATP pacing with interruption of the tachycardia.

Promising results also come from some recent studies using substernal leads placement. Lead implants were done using percutaneous sub-xiphoid approach, under fluoroscopic guidance with a peelable sheath into the substernal space. Preliminary data have shown that this approach requires lower DFT than S-ICD, providing the opportunity for greater device longevity and smaller device size[31]. Furthermore, it seems that from this extravascular space pacing was possible, overcoming the limitations of current S-ICD, without the need to integrate a leadless pacing system in the majority of patients[32].

This could mean the beginning of a new era of devices, but further studies are needed to assess the feasibility and safety of these systems.

Conflict of interest: none declared.

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