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Editorial

Implantable defibrillator in patients with inherited arrhythmogenic diseases: Are inapproppriate shocks preventable?

Life-threatening ventricular arrhythmias and sudden cardiac death (SCD) in young individuals may be of genetic origin and related to inherited arrhythmogenic diseases (IAD), either cardiomyopathies or channelopathies. In patients with IAD at risk of SCD, the implantable cardioverter-defibrillator (ICD) provides the most effective life-saving therapy. Young patients with IAD have a predominantly arrhythmia-related prognosis, so that they may survive for many decades with nearly normal life expectancy thanks to the protection against SCD provided by the ICD. (1,2). However, the improvement of survival by the ICD therapy is associated with a significant rate of inappropriate discharges and lead-related complications which may lead to an increase of long-term morbidity and mortality. Particularly, inappropriate shocks (IS) caused by either supraventricular tachycardia or abnormal sensing (due to T-or P-wave oversensing, lead fracture or electromagnetic interference) have the potential to reduce the patient''s qualityoflife and compromise the ICD therapy acceptance. Accordingly, the risk/benefit ratio should be carefully assessed when considering ICD implantation for primary prevention, mostly in patients with IAD, and a high priority should be given to prevent IS by means of adequate device type, targeted device programming, and modern discriminating software [1,2]. In recent years, device manufacturers focused technological improvements on the reduction of inappropriate ICD interventions, which resulted into more effective device programming models and improved arrhythmia detection algorithms [3,4]. The SmartShock Technology™ (SST) by Medtronic, Minneapolis, USA, consists of a systematic adoption of novel enhanced detection algorithms in conjunction with routine implementation of a contemporary evidence-based ICD programming (long detection time and antitachicardia pacing use). In the PainFree SST study [4] this combined approach was demonstrated to substantially lower the rate of IS in a large "real-word" population of ICD patients. However, data on the outcome of patients with IAD who received new-generation ICDs with SST technology are lacking.

In the current issue of the *Journal,* Auricchio et al. [5] conducted a subanalysis of the PainFree SST patients cohort, by specifically addressing rates of IS, appropriate therapies, complications and mortality in patients with IAD. The authors found that patients with IAD experienced a low annual rate of IS (1.6%), similarly to control patients with non-inherited diseases. This result differs from that of the large meta-analysis of Olde Nordkamp et al. [1] in which the annual rate of IS in young patient with IAD was three times greater (4.7%). This discrepancy may be explained by the different age and clinical characteristics of study patients as well as by different ICD models, manufacturers and programming. This further supports the advantage of adopting novel enhanced detection algorithms associated with routine implementation of modern programming strategies, such as SST by Medtronic. Of note, the incidence of IAS reported by Auricchio et al. [5] is in line with that of 1.7%/year reported by a previous study of our group in a larger population of patients with genetic cardiomyopathies and channelopathies, who received devices from different manufacturers, and programmed with a minimal threshold for intervention of 300 ms [2]. These findings may suggest that high rate-cut-offs are sufficient for preventing IS in IAD patients; however, they allow reducing inappropriate therapies due to supraventricular tachycardias, but are not enough effective to decrease the number of IAS shocks due to lead malfunction which is the main cause of device-related complications. The availability of modern discrimination algorithms permits to further prevent IS from other (more common) causes such as T-wave oversensing, lead failure and myopotentials [3,4]. Thus, the results of the study by Auricchio et al. [5] indicate that the continuous improvement of detection algorithms may have a large impact on the patient's quality of life, mostly in young IAD patients who will have ICDs for a much larger part of their life. Moreover, they [5] confirmed that dual-chamber ICD is not associated with a significant reduction in IS in IAD patients as reported by previous studies [1,3]. As a corollary, single-chamber ICD appears to be the most appropriate option for young patients with IAD, given its lower rate of lead-related complications in comparison with dual-chamber devices.

The study by Auricchio et al. [5] shows limitations predominantly related to the small sample of patients and the incomplete spectrum of IAD, which does not include important diseases such as hypertrophic cardiomyopathy, dilated cardiomyopathy, catecholaminergic polymorphic ventricular tachycardia and short QT syndrome [1]. This limitation may lead to misinterpretation of the beneficial impact on IS among IAD patients receiving devices with SST. Other limitations include the relatively short follow-up period and the retrospective study design. Moreover, all patients enrolled in the study received devices with discrimination algorithms of a single manufacturer.

The subcutaneous ICD (S-ICD) has become a recognized effective alternative to the transvenous ICD (TV-ICD) for prevention of SCD among at risk-patients not needing pacing or cardiac resynchronization therapy [6]. The S-ICD allows to reduce the risk of systemic infection and lead failure, which is the most common complication of TV-ICD often requiring surgical revision, while maintaining efficacy to interrupt life-threatening ventricular arrhythmias The intracardiac leadless

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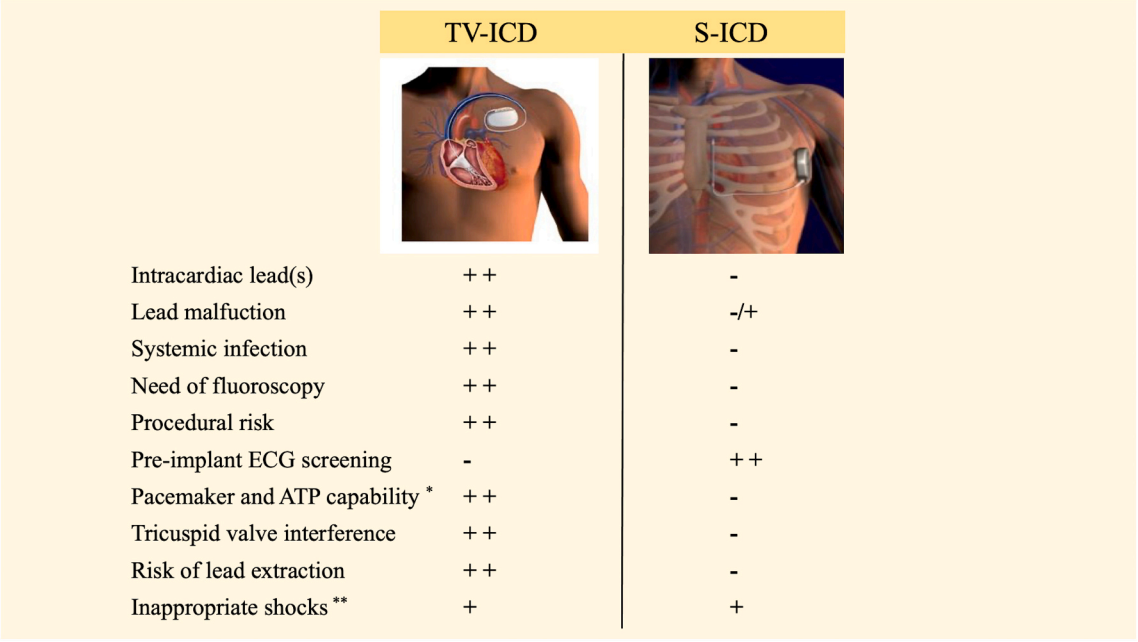

Fig. 1. Transvenous ICD versus subcutaneous ICD in patients with inherited arrhythmogenic diseases.
The figure shows pro and cons of transvenous ICD versus subcutaneous ICD in patients with inherited arrhythmogenic diseases. Future engineering advances are expected to improve S-ICD performance with regard to i) the time-delayed strategy in tachyarrhythmia sensing algorithms for non-treated, self-terminating episodes of ventricular tachycardia/ventricular fibrillation; ii) number of shock therapies for interrupting ventricular arrhythmias; iii) communication between S-ICD and leadless pacemaker for linking defibrillation therapy and antibradycardia/antitachicardia pacing (*).
** Recent data with last generation of S-ICD reported similar rates of inappropriate shocks.
ATP: antitachicardia pacing: TV-ICD: transvenous ICD; S-ICD: subcutaneous ICD.

configuration makes the S-ICD a preferrable choice mostly in young IAD patients with a long life expectancy [2]. Early studies on the S-ICD demonstrated the effectiveness of the first-generation devices, despite IS rates relatively high. The S-ICD therapy has evolved over the last years and more recent data show that the use of high rate cutoffs, current generation electrogram filtering, and discrimination algorithms, led to a significantly reduction of IAS rates of S-ICD, with a reported rate of 2.4%/year with "generation 3" devices, a figure even lower than that of TV-ICD with modern programming [6].

However, few studies exist on the S-ICD performance in IAD patients. Because of predisposing ECG depolarization/repolarization changes, these patients have an increased risk of double QRS counting or P- and/or T-wave oversensing, potentially inducing to IS delivery. On the other hand, S-ICD is unable to deliver antitachycardia pacing which may be an effective "pain-free" therapy. In the Effortless study cohort of patients with channelopathies receiving S-ICD, the incidence of IS was 8.5% over 3.2 years of follow-up and the annualized IS rate lower for the S-ICD than TV-ICD patients (2.7%/year vs 3.8%year) [7]. A recent study by Kuschyk et al. [8] assessed the long-term outcome of S-ICD patients compared to TV-ICD in a cohort of patients with IAD including cardiomyopathies and channelopathies. In keeping with the study results of Auricchio et al. [5], the Kuschyk's study demonstrated a relative low incidence of IS with an annual rate of 1.9%year and no statistically significant differences between S-ICD and TV-ICD (although lower in the S-ICD patients, i.e., 1.4%/year vs 2.5%/year). These findings may be explained by the use of second generation devices in most S-ICD patients and modern programming strategies in both type of devices. Of note the risk of cardiac oversensing, including T-wave oversensing is particularly relevant in patients with arrhythmogenic cardiomyopathy, who need specific strategies to prevent IS, such as appropriate pre-implantation ECG screening, accurate implantation technique, appropriate device programming and modern software upgrading, including the "SMART Pass" [9,10]. Until definitive data comparing efficacy and safety of new generation TV-ICD, with updated discrimination algorithms and software, versus S-ICD are available in IAD patients, decision-making needs to be individualized, mostly taking into account potential lead-related complications, likelihood of IS, and the need of anti-bradycardia or antitachycardia pacing. The demonstration of the SST added value for reduction of IS is an important "new"insight to guide the choice of the most appropriate device in patients with IAD (See Fig. 1).

Declaration of Competing Interest

None.

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