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CLINICAL RESEARCH

Reduction in inappropriate therapies through device programming in subcutaneous implantable defibrillator patients: data from clinical practice

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Aims

In subcutaneous implantable cardioverter defibrillator (S-ICD) recipients, the UNTOUCHED study demonstrated a very low inappropriate shock rate on programming a conditional zone between 200 and 250 bpm and a shock zone for arrhythmias >250 bpm. The extent to which this programming approach is adopted in clinical practice is still unknown, as is its impact on the rates of inappropriate and appropriate therapies.

Methods and results

We assessed ICD programming on implantation and during follow-up in a cohort of 1468 consecutive S-ICD recipients in 56 Italian centres. We also measured the occurrence of inappropriate and appropriate shocks during follow-up. On implantation, the median programmed conditional zone cut-off was set to 200 bpm (IQR: 200–220) and the shock zone cut-off was 230 bpm (IQR: 210–250). During follow-up, the conditional zone cut-off rate was not significantly changed, while the shock zone cut-off was changed in 622 (42%) patients and the median value increased to 250 bpm (IQR: 230–250) ($P < 0.001$). UNTOUCHED-like programming of detection cut-offs was adopted in 426 (29%) patients immediately after device implantation, and in 714 (49%, $P < 0.001$) at the last follow-up. UNTOUCHED-like programming was independently associated with fewer inappropriate shocks (hazard ratio 0.50, 95%CI 0.25–0.98, $P = 0.044$), and had no impact on appropriate and ineffective shocks.

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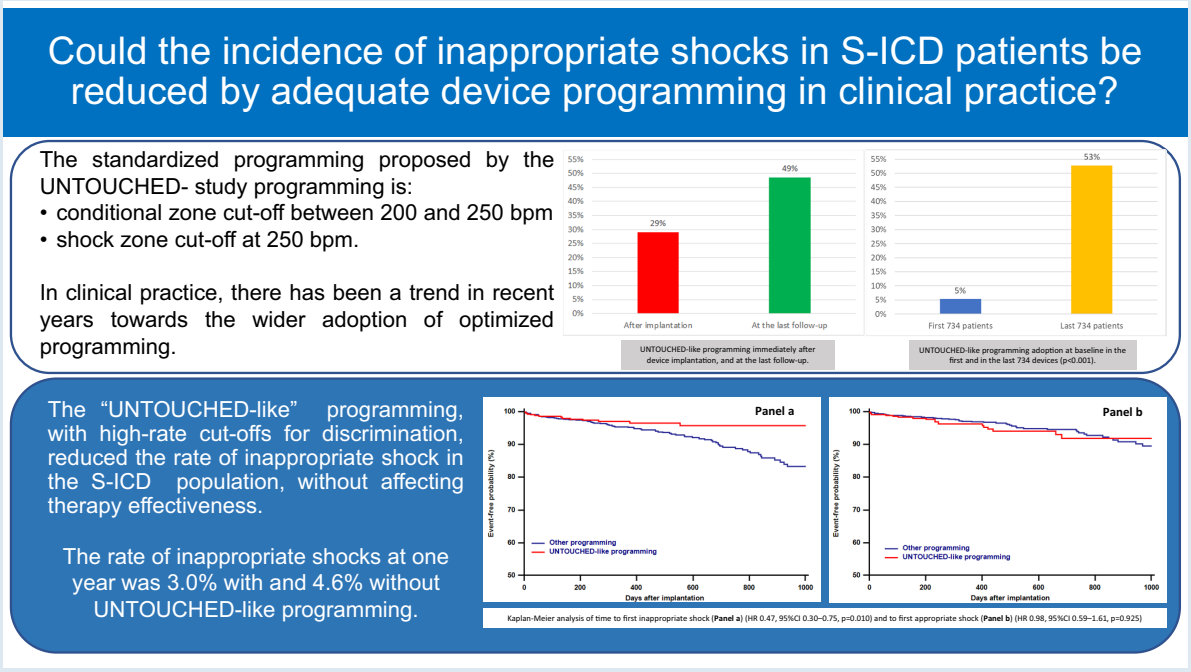
Conclusions In recent years, S-ICD implanting centres have increasingly programmed high arrhythmia detection cut-off rates, at the time of implantation in the case of new S-ICD recipients, and during follow-up in the case of pre-existing implants. This has contributed significantly to reducing the incidence of inappropriate shocks in clinical practice.

Rordorf: Programming of the S-ICD

Clinical Trial Registration URL: http://clinicaltrials.gov/Identifier: NCT02275637

Graphical Abstract



Keywords Implantable defibrillator • Subcutaneous • Programming • Inappropriate shock

What's new?

- In clinical practice, there has been a trend in recent years towards the wider adoption of optimized programming.
- Programming a conditional zone between 200 and 250 bpm and a shock zone for arrhythmias >250 bpm is associated with a lower risk s of inappropriate shocks.
- Programming high arrhythmia detection cut-off rates has no impact on appropriate and ineffective shocks.

Introduction

Observational studies have shown the overall efficacy and safety of the subcutaneous implantable cardioverter defibrillator (S-ICD) over medium- and long-term follow-up.[1–3] A randomized clinical trial has also demonstrated that the S-ICD is non-inferior to the transvenous ICD with respect to device-related complications and inappropriate shocks.[4] Moreover, the risk of major procedural complications and lead-related complications has been shown to be lower with S-ICDs than with conventional ICDs.[4,5] Previous studies have shown that device programming has an important role in the ability of the S-ICD to discriminate among arrhythmias.[2,6] Specifically, the Understanding Outcomes with the S-ICD in Primary Prevention Patients with Low Ejection Fraction (UNTOUCHED) Trial documented a very low inappropriate shock rate in S-ICD recipients on adopting standardized programming with high arrhythmia detection cut-off rates.[2] However, the programming approaches adopted in clinical practice are unknown. In this study, we analysed the clinical practice of device programming in a large S-ICD population in several implanting centres, and also the impact of device programming on the risk of appropriate and inappropriate ICD therapies.

Methods

Study design

The present study is a retrospective analysis of data collected within the framework of prospective 'Rhythm Detect' registry. The Institutional

Table 1 Baseline characteristics of the study population, implantation variables and pre-discharge device programming

	All patients ($n = 1468$)
Male gender, *n* (%)	1166 (79)
Age, years	49 ± 15
Body Mass Index, kg/m2	26 ± 4
Left ventricular ejection fraction, %	4 ± 16
Ischaemic cardiomyopathy, *n* (%)	406 (28)
Non-ischaemic dilated cardiomyopathy, *n* (%)	370 (25)
Hypertrophic cardiomyopathy, *n* (%)	231 (16)
Arrhythmic syndromes, *n* (%)	461 (31)
History of atrial fibrillation, *n* (%)	184 (13)
Chronic kidney disease, *n* (%)	145 (10)
Diabetes, *n* (%)	151 (10)
More than 1 passing vector on screening, *n* (%)	1132 (77)
S-ICD generator in subcutaneous pocket, *n* (%)	270 (18)
2-incision technique, *n* (%)	1372 (93)
Sensing vector:	
– Primary, *n* (%)	881 (60)
– Secondary, *n* (%)	499 (34)
– Alternate, *n* (%)	88 (6)
Dual-zone programming, *n* (%)	1454 (99)
UNTOUCHED-like programming of detection cut-offs, *n* (%)	426 (29)

Review Boards approved the study, and all patients provided written informed consent for data storage and analysis. From January 2013 to July 2021, consecutive patients undergoing de-novo implantation of an S-ICD (Boston Scientific Inc., Natick, MA, USA) were enrolled at 56 Italian centres (see Appendix). Before implantation, adequate S-ICD sensing was verified by means of the surface electrocardiogram screening method, which is based on a dedicated electrocardiogram morphology tool.[7] Baseline assessment comprised the collection of demographic data and medical history, clinical examination, 12-lead electrocardiogram, and echocardiographic evaluation. After implantation, patients were followed up in accordance with the standard practice of the participating centres until March 2022.

Implantation procedure and device programming

According to physician preference, the pulse generator was positioned in a subcutaneous pocket or in an intermuscular position (between the serratus anterior and the latissimus dorsi muscles). For lead deployment, physicians adopted the 3-incision technique, i.e. pocket incision, xiphoid incision, superior incision at the sternomanubrial junction, or the 2-incision technique, i.e. the superior incision is avoided by positioning the lead by means of a peel-away sheath introducer.[8,9] The decision to perform acute defibrillation testing was left to the discretion of the implanting physician. Programming of the parameters for the detection of ventricular tachycardia or ventricular fibrillation was also left to the discretion of the implanting centre. Physicians were free to set parameters on hospital discharge and adjust them during follow-up, in order to fit the specific characteristics of the patient and on the basis of the best available evidence. Device programming was defined 'UNTOUCHED-like' in the case of a conditional zone cut-off set between 200 and 250 bpm and a shock zone cut-off at 250 bpm. For the aim of this analysis, we excluded old-generation pulse generators, which were not equipped with the SMART Pass filter. We compared the status of the S-ICD parameters on pre-discharge examination with the values from the last available follow-up examination. To describe the evolution of the practice regarding S-ICD programming over the years, we sorted the procedures by implantation date, and we defined and compared two equally sized groups.

Definition of outcomes

The primary endpoint of the study was the rate of inappropriate shocks. An S-ICD shock was classified as inappropriate when it was delivered for any rhythm other than ventricular fibrillation or ventricular tachycardia. Secondary endpoints consisted of appropriate shock and ineffective S-ICD therapy. For the analysis of therapy efficacy, we reported when the first shock successfully converted the ventricular arrhythmia to sinus rhythm and the final efficacy.

Statistical analysis

Descriptive statistics are reported as means ± SD for normally distributed continuous variables, or medians and interquartile range (25th–75th percentile) in the case of skewed distribution. Normality of distribution was tested by means of the non-parametric Kolmogorov–Smirnov test. Categorical variables are reported as percentages. Differences were compared by means of Mann–Whitney or Wilcoxon non-parametric tests for non-Gaussian variables. Differences in proportions were compared by means of a Chi-square analysis. Analysis of the time to the first event was made by means of the Kaplan–Meier method. Cox proportional hazards models were used to determine the association between patients' characteristics and the occurrence of events during the follow-up period, and to estimate the hazard ratios (HRs) and the 95% confidence intervals (CIs) of an episode. For the analysis of the association between device programming and shocks, the observation periods started when the patient was discharged from the hospital, ended at the time of the first endpoint (first inappropriate shock for the primary endpoint analysis, or first appropriate shock for the secondary endpoint analysis), or were censored at the end of the follow-up period or when the device parameters for the detection of ventricular tachycardia or ventricular fibrillation were reprogrammed. A P value <0.05 was considered significant for all tests. All statistical analyses were performed by means of R: a language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study population

A total of 1468 consecutive de-novo S-ICD implantations were performed within the observation period. *Table 1* shows the baseline clinical characteristics and the implantation variables of the patients in analysis. The S-ICD generator was positioned in a standard subcutaneous pocket in 270 (18%) patients, and the 2-incision technique was adopted in 1372 (93%) procedures. Cardioversion at a shock energy of ≤65J was tested in 1103 (75%) patients. In patients who underwent testing, success was reported in 1082 (98%) cases.

S-ICD programming on hospital discharge and during follow-up

Pre-discharge device programming is reported in *Table 1*. The median conditional zone cut-off rate was 200 bpm (25th–75th percentile: 200–220) and the shock zone cut-off was 230 bpm (25th–75th percentile: 210–250). UNTOUCHED-like programming of detection cut-offs was adopted in 426 (29%) patients immediately after device implantation. The distribution of the conditional zone and the shock zone cut-off rates programmed on hospital discharge is reported in *Figure 1*. Values are compared with those reported at the time of the last follow-up examination. During follow-up, the conditional zone cut-off rate was changed in 184 (13%) patients, but the median value remained 200 bpm (25th–75th

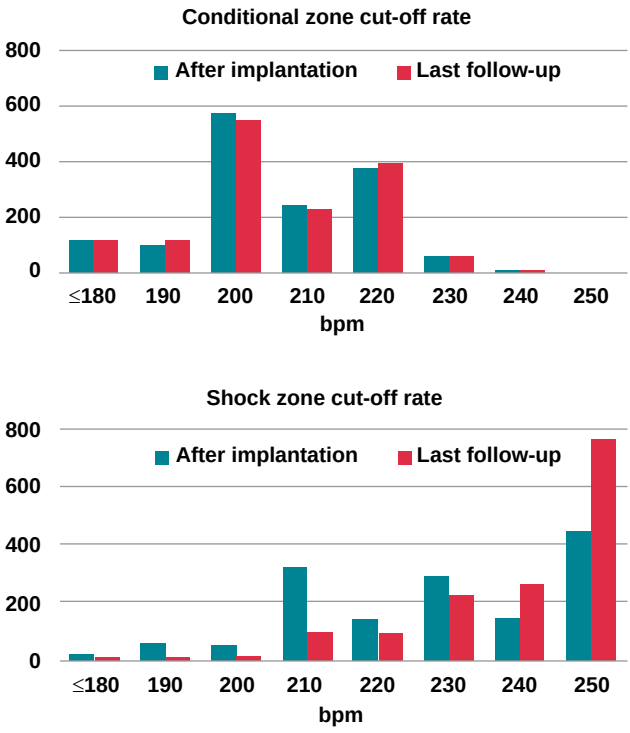


Figure 1 Distribution of the conditional zone and the shock zone cut-off rates programmed after device implantation and at the time of the last follow-up examination.

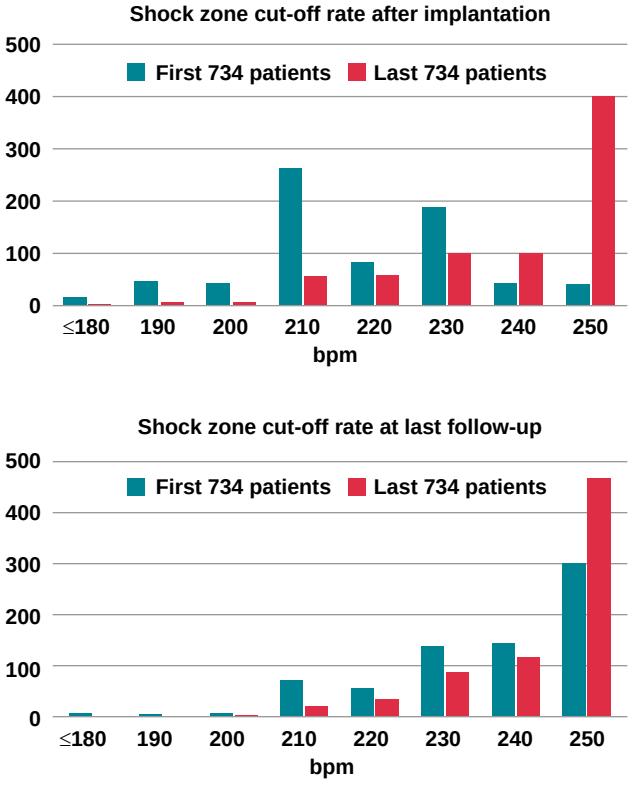


Figure 2 Changes in the distribution of the shock zone cut-off rates programmed in the first and in the last 734 devices (after device implantation and at the time of the last follow-up examination).

percentile: 200–220) ($P = 0.846$ vs. hospital discharge). The shock zone cut-off was changed in 622 (42%) patients and the median value increased to 250 bpm (25th–75th percentile: 230–250) ($P < 0.001$ vs. hospital discharge). The number of cases in which UNTOUCHED-like programming of detection cut-offs was adopted significantly increased to 714 (49%, $P < 0.001$) at the last follow-up visit. In all patients, the SMART Pass filter was activated since the time of implantation. During follow-up, the sensing vector was reprogrammed in 200 (14%) patients, with no significant changes in the distribution of vectors programmed: Primary in 866 (59%), Secondary in 499 (34%), Alternate in 103 (7%).

Table 2 Causes of inappropriate shocks

	Number of patients (%)	Reaction (number of patients)
Inappropriate Shock Therapy	103 (7.0)	
– Noise from entrapped subcutaneous air	11 (0.7)	Solved without action (11)
– Atrial fibrillation or supraventricular tachycardia	18 (1.2)	Reprogramming (10); Change in medication [a] (6); Atrial fibrillation ablation (1); Atrial fibrillation ablation after change in medication (1)
– T-Wave oversensing	20 (1.4)	Reprogramming (19); Explantation after Reprogramming (1)
– Other cardiac oversensing	15 (1.0)	Reprogramming (14); Explantation after Reprogramming (1)
– Non-cardiac oversensing	39 (2.7)	Reprogramming (37); Explantation (2 [b])

[a]Increased amiodarone and/or beta-blockers dosage
[b]After verification of lead failure.

On sorting patients by implantation date, we observed that in the first 734 patients, the shock zone cut-off was set to 210 bpm (25th–75th percentile: 210–230) on implantation and reprogrammed to a median value of 240 bpm (25th–75th percentile: 230–250) on follow-up ($P < 0.001$ vs. hospital discharge). In the last 734 patients, the shock zone cut-off was already set to 250 bpm (25th–75th percentile: 240–250) on implantation and no significant changes were made on follow-up. The distribution of the shock zone cut-off rates is reported in *Figure 2*. On pre-discharge examination, UNTOUCHED-like programming of detection cut-offs was adopted in 39 (5%) of the first 734 patients, and in 387 (53%) of the last 734 patients ($P < 0.001$).

Outcome analysis

In the study population, over a median follow-up of 23 months (25th–75th percentile: 10–31), inappropriate shocks were reported in 103 (7%) patients. The details of the events are reported in *Table 2*. Eleven cases (0.7%) were due to entrapped subcutaneous air surrounding the electrode and occurred before hospital discharge. Overall, the vast majority of cases ($n = 99$, 96%) were managed without requiring S-ICD explantation. The S-ICD was reprogrammed in response to the first inappropriate shock event in 82 patients. In particular, the detection cut-off rates were increased in 45 patients, the sensing vector was changed in 14 patients, both changes were made in 23 patients. After the first inappropriate shock, 8 out of 103 patients experienced additional episodes during a median period of 11 months (25th–75th percentile: 4–19). Six patients experienced 2 episodes, one patient 3 and one patient 4 episodes. Among the 68 patients with increased cut-off rates after the first episode, the recurrence of inappropriate shocks was reported in eight patients. *Figure 3* reports the Kaplan–Meier analysis of time to first inappropriate shock after implantation in patients with ($n = 426$) and without ($n = 1042$) UNTOUCHED-like programming on pre-discharge (hazard ratio 0.47, 95%CI 0.30–0.75, $P = 0.010$). The rate of inappropriate shocks at 1 year was 3.0% (95%CI 1.2–4.8) with and 4.6% (95%CI 3.2–6.0) without UNTOUCHED-like programming.

The results of the regression analysis of variables associated with inappropriate shock occurrence are shown in *Table 3*. Among patient characteristics, gender and history of atrial fibrillation were independently associated with inappropriate shocks. Moreover, patients with a single passing vector on screening were more exposed to inappropriate shocks. UNTOUCHED-like programming was independently associated with fewer inappropriate shocks. Appropriate shocks were

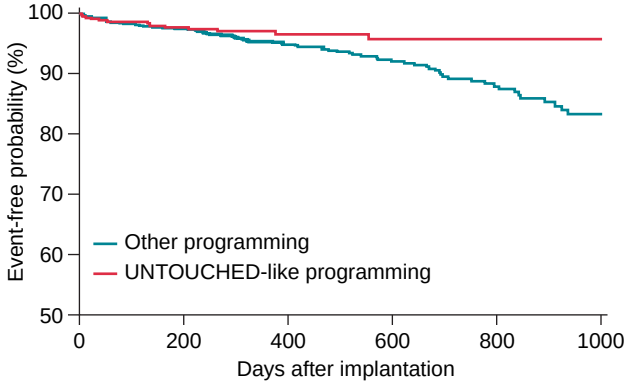


Figure 3 Kaplan–Meier estimates of time to first inappropriate shock (hazard ratio 0.47, 95%CI 0.30–0.75, $P = 0.010$). The observation periods were censored at the end of the follow-up period or when the device parameters for the detection of ventricular tachycardia or ventricular fibrillation were reprogrammed.

Table 3 Regression analysis of factors associated with inappropriate shocks

	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	P	HR	95% CI	P
Female gender	0.45	0.23–0.86	0.016	0.23	0.08–0.62	0.004
Age	0.99	0.98–1.00	0.106	–	–	–
Body Mass Index	0.99	0.94–1.04	0.985	–	–	–
Left ventricular ejection fraction	1.00	0.99–1.01	0.780	–	–	–
Ischaemic/Non-ischaemic dilated cardiomyopathy	0.80	0.49–1.30	0.367	–	–	–
History of atrial fibrillation	2.32	1.42–3.77	0.001	2.13	1.22–3.73	0.008
More than 1 passing vector on screening	0.45	0.26–0.79	0.006	0.48	0.27–0.84	0.011
S-ICD generator in subcutaneous pocket	0.72	0.43–1.18	0.197	–	–	–
2-incision technique	1.13	0.56–2.26	0.734	–	–	–
Primary sensing vector	0.75	0.50–1.13	0.173	–	–	–
Secondary sensing vector	1.02	0.67–1.57	0.924	–	–	–
Alternate sensing vector	2.15	1.17–3.93	0.014	2.03	0.98–3.98	0.064
UNTOUCHED-like programming on implantation	0.47	0.26–0.85	0.012	0.50	0.25–0.98	0.044

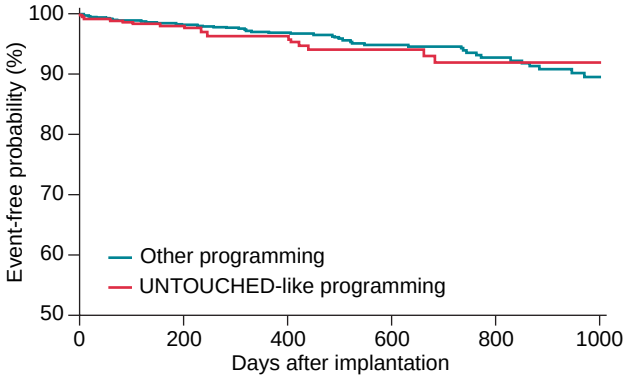


Figure 4 Kaplan–Meier estimates of time to first appropriate shock (hazard ratio 0.98, 95%CI 0.59–1.61, $P = 0.925$).

delivered in 100 (7%) patients. *Figure 4* reports the Kaplan–Meier analysis of time to first appropriate shock after implantation in patients with and without UNTOUCHED-like programming (hazard ratio 0.98, 95%CI 0.59–1.61, $P = 0.925$). The first shock was effective in 94 (94%) patients, and the final conversion rate was 98% (98 out of 100). There was no significant difference in the rate of first ineffective shocks (hazard ratio 0.82, 95%CI 0.11–6.14, $P = 0.851$) between groups. During the observation period, 3 (0.2%) patients (all of them without UNTOUCHED-like programming) experienced syncope associated with a self-terminated tachyarrhythmia.

Discussion

This is the first study to demonstrate that the incidence of inappropriate shocks in S-ICD patients can be significantly reduced by adequate device programming in clinical practice. Specifically, the standardized programming proposed by the UNTOUCHED study,[2] with high-rate cut-offs for discrimination, performed better than various programming strategies involving lower cut-offs. We also showed that, in clinical practice, there has been a trend in recent years towards the wider adoption of optimized programming.

Observational studies have confirmed the overall efficacy and safety of S-ICD[1–3] and the positive patient acceptance.[10] Moreover, randomized trials and meta-analysis demonstrated that the S-ICD is non-inferior to the transvenous ICD with respect to device-related complications and inappropriate shocks,[4] and superior with respect to lead-related complications[4,5,11] However, S-ICD therapy is less established than transvenous ICD therapy, with all the consequent limitations. Indeed, S-ICD implanters display a learning curve with respect to implant-related complications[12] and new implantation techniques.[9] Moreover, different anesthesia/analgesia approaches[13] have been proposed, and improvements in S-ICD device technology have been shown to reduce the rate of inappropriate shocks.[14] Moreover, an analysis

from the S-ICD Clinical Investigation (IDE Trial) demonstrated that the addition of a second shock zone with an active discrimination algorithm was strongly associated with a reduction in inappropriate shocks and did not result in prolongation of detection times or increased syncope.[6] Subsequently, the authors of the UNTOUCHED study proposed standardized programming with discrimination algorithms active from 200 to 250 bpm, and demonstrated that its use could reduce the rate of inappropriate shock in the S-ICD[2] population. The UNTOUCHED programming modality is consistent with the high rates and relatively long-detection durations used for transvenous ICDs in the Multicenter Automatic Defibrillator Implantation Trial-Reduce Inappropriate Therapy (MADIT-RIT), which demonstrated marked reductions in inappropriate therapies and mortality[15] and established this programming as optimal. As recommended in consensus documents for primary prevention patients,[16] such programming is now part of the standard of care for transvenous devices and, according to Gold *et al.*,[2] it should also be adopted routinely in S-ICD patients, in order to avoid unnecessary shocks. The present study revealed that this S-ICD programming approach has been increasingly adopted in clinical practice, and that most patients currently receive this device programming on implantation or, at the latest, on follow-up.

On comparing different programming approaches, we confirmed the effectiveness of the UNTOUCHED programming modality in reducing inappropriate shocks, without affecting therapy effectiveness. We recorded a one-year rate of inappropriate shocks of 3.0% with optimal programming. This result is in line with, or even better than, the UNTOUCHED study, which reported a similar rate (3.1%) of inappropriate shocks[2] in a population 7 years older than ours. It also compares favorably with the annualized rate of 6.4% in patients with single-chamber and S-ICD devices reported in a meta-analysis,[17] and with the 4.8% 1-year rate in the long-detection arm of the transvenous ICD cohort of the Avoid DeliVering TherApies for Non-sustained Arrhythmias in ICD PatiEnts III (ADVANCEIII).[18] In the S-ICD, the detection rate, but not the duration, is programmable. The mean time from detection to shock is 15 s, i.e. slightly longer than in the delayed-therapy arm of MADIT-RIT.[15] Early studies showed that, with S-ICDs, inappropriate shocks were most commonly due to T-wave oversensing. In the present analysis, this remained one of the most frequent etiologies of inappropriate therapies, involving 1.4% of the study cohort, in line with the data from the UNTOUCHED trial (1.6%).[2] Nonetheless, our results revealed the general improvement in S-ICD performance over the years, which is mainly attributable to the evolution of discrimination algorithms. Indeed, in our study cohort, which included new-generation SMART Pass enabled devices only, the one-year inappropriate shock rate was 3.0% with and 4.6% without UNTOUCHED-like programming; this is lower than the 8.1% rate reported in the Evaluation oF Factors ImpacTing CLinical Outcome and Cost EffectiveneSS of the S-ICD (EFFORTLESS) registry,[1] which included only 8% of SMART Pass enabled devices. In the UNTOUCHED trial the proportion of new-generation devices was 60%. In addition to the low rate, it should be noted that most inappropriate shocks in the present study were successfully managed by reprogramming the device, and only 4 (0.3%) necessitated system removal.

In addition to UNTOUCHED-like programming, clinical factors that were multivariable predictors of inappropriate shocks were: gender and history of atrial fibrillation. Among procedural and programming factors, a single passing vector on screening was also associated with a higher risk of inappropriate shocks, while no association was seen between inappropriate shocks and the adoption of the 2-incision technique. These results are at variance with previous findings of the UNTOUCHED study,[2] which reported no association with the number of passing vectors on screening, but more inappropriate shocks with the 2-incision technique. Nevertheless, a recently published comparison between 2-incision and 3-incision technique from the S-ICD post-approval study[19] corroborated our findings, since the authors found no difference in inappropriate therapies between study groups.

The present findings not only elucidate how the S-ICD should be used in order to obtain a better outcome, but also show that the achievable performance of the S-ICD is even better than that observed in the first trials, which suffered from the limitations of an immature technology and an amendable programming strategy.

Limitations

The limitations of our study should be acknowledged. First, its observational and retrospective design may have introduced an inherent bias. Second, the variable follow-up duration could have influenced the probability of device reprogramming, i.e. longer follow-up yielding more reprogramming needs/opportunities. Nonetheless, all patients in the analysis underwent at least one in-office visit during follow-up. Third, consecutive patients implanted with an S-ICD were included in the study. This makes the population heterogeneous and the results less comparable to those of the UNTOUCHED study that was a primary prevention trial in patients with low ejection fraction. However, our aim was to describe the programming approaches adopted for patients who currently receive an S-ICD in clinical practice, that are known to constitute a selected group that includes a minority of MADIT-II like subjects with ischaemic heart disease,[20] thus more expected to experience ventricular fibrillation than slow ventricular tachycardias.

Conclusions

The cultural achievements in ICD therapy, gained by transvenous ICD and earliest S-ICD clinical trials have impacted on the use of S-ICD in recent years, promoting an updated programming that favours high ventricular rate for arrhythmia detection. In new S-ICD recipients, this is done at the time of implantation, while in the case of pre-existing implants, it is done during follow-up. This behaviour has contributed significantly to reducing the incidence of inappropriate shocks in clinical practice.

Supplementary material

Supplementary material is available at *Europace* online.

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Conflict of interest: R.R. received speaker fees from Abbot and Boston Scientific. P.F. received speaker fees from Boston Scientific and research or educational grants from Abbott and Boston Scientific. G.L.B. reports speaker fees (small amount) from Boston Scientific, Medtronic, Biotronik, Abbot, Microport, Zoll. M.L. and S.V. are employees of Boston Scientific. The other authors report no conflicts.

Data availability

The experimental data used to support the findings of this study are available from the corresponding author upon request.

Appendix

List of participating centres

- Azienda ospedaliera 'G. Brotzu', Cagliari: B. Schintu, A. Scalone, G. Tola, A. Setzu;
- Azienda Ospedaliera Mater Domini, Catanzaro: A. Curcio;
- Azienda Ospedaliera Universitaria Senese, Siena: A Santoro, C Baiocchi, R Gentilini, S Lunghetti;
- Circolo e Fondazione Macchi, Varese: F. Caravati;
- Clinica Montevergine, Mercogliano, Avellino: F. Solimene, G. Shopova, V. Schillaci, A. Arestia, A. Agresta;
- Fatebenefratelli Hospital, Rome: S. Bianchi, P. Rossi, F. M. Cauti;
- Fondazione Poliambulanza, Brescia: C. La Greca, D. Pecora;
- 'Giovan Battista Grassi' Hospital, Ostia, Rome; F. Ammirati, L. Santini, K. Mahfouz, C. Colaiaco;
- IRCCS Fondazione Policlinico 'S. Matteo', Pavia: R. Rordorf, A. Vicentini, S. Savastano, B. Petracci, A. Sanzo, E. Baldi, M. Casula;
- Istituto Auxologico Italiano—IRCCS, Milan: GB. Perego, V. Rella;
- Istituto Clinico Sant'Ambrogio, Milan: L. Ottaviano;
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References

1. Boersma L, Barr C, Knops R, Theuns D, Eckardt L, Neuzil P *et al.* Implant and midterm outcomes of the subcutaneous implantable cardioverter-defibrillator registry: the EFFORTLESS study. *J Am Coll Cardiol* 2017;**70**:830–41.
2. Gold MR, Lambiase PD, El-Chami MF, Knops RE, Aasbo JD, Bongiorni MG *et al.* Primary results from the understanding outcomes with the S-ICD in primary prevention patients with low ejection fraction (UNTOUCHED) trial. *Circulation* 2021;**143**:7–17.
3. Lambiase PD, Theuns DA, Murgatroyd F, Barr C, Eckardt L, Neuzil P *et al.* Subcutaneous implantable cardioverter-defibrillators: long-term results of the EFFORTLESS study. *Eur Heart J* 2022;**43**:2037–50.
4. Knops RE, Olde Nordkamp LRA, Delnoy PHM, Boersma LVA, Kuschyk J, El-Chami MF *et al.* Subcutaneous or transvenous defibrillator therapy. *N Engl J Med* 2020;**383**:526–36.
5. Rordorf R, Casula M, Pezza L, Fortuni F, Sanzo A, Savastano S *et al.* Subcutaneous versus transvenous implantable defibrillator: an updated meta-analysis. *Heart Rhythm* 2021;**18**:382–91.
6. Gold MR, Weiss R, Theuns DA, Smith W, Leon A, Knight BP *et al.* Use of a discrimination algorithm to reduce inappropriate shocks with a subcutaneous implantable cardioverter-defibrillator. *Heart Rhythm* 2014;**11**:1352–8.
7. Francia P, Ziacchi M, De Filippo P, Viani S, D'Onofrio A, Russo V *et al.* Subcutaneous implantable cardioverter defibrillator eligibility according to a novel automated screening tool and agreement with the standard manual electrocardiographic morphology tool. *J Interv Card Electrophysiol* 2018;**52**:61–7.
8. Knops RE, Olde Nordkamp LR, de Groot JR, Wilde AA. Two-incision technique for implantation of the subcutaneous implantable cardioverter-defibrillator. *Heart Rhythm* 2013;**10**:1240–3.
9. Migliore F, Allocca G, Calzolari V, Crosato M, Facchin D, Daleffe E *et al.* Intermuscular two-incision technique for subcutaneous implantable cardioverter defibrillator implantation: results from a multicenter registry. *Pacing Clin Electrophysiol* 2017;**40**:278–85.
10. Vicentini A, Bisignani G, De Vivo S, Viani S, Savarese G, Francia P *et al.* Patient acceptance of subcutaneous versus transvenous defibrillator systems: A multi-center experience. *J Cardiovasc Electrophysiol* 2022;**33**:81–9.
11. Healey J. The ATLAS Trial: Avoiding Transvenous Leads in Appropriate Subjects. Presented at Heart Rhythm 2022 in San Francisco, CA on April 30, 2022.
12. Knops RE, Brouwer TF, Barr CS, Theuns DA, Boersma L, Weiss R *et al.* The learning curve associated with the introduction of the subcutaneous implantable defibrillator. *Europace* 2016;**18**:1010–5.
13. Ziacchi M, Bisignani G, Palmisano P, Scalone A, Martignani C, Elvira Mocavero P *et al.* Serratus anterior plane block in subcutaneous implantable cardioverter defibrillator implantation: A case-control analysis. *J Cardiovasc Electrophysiol* 2020;**31**:144–9.
14. Theuns DAMJ, Brouwer TF, Jones PW, Allavatam V, Donnelley S, Auricchio A *et al.* Prospective blinded evaluation of a novel sensing methodology designed to reduce inappropriate shocks by the subcutaneous implantable cardioverter-defibrillator. *Heart Rhythm* 2018;**15**:1515–22.
15. Moss AJ, Schuger C, Beck CA, Brown MW, Cannom DS, Daubert JP *et al.* Reduction in inappropriate therapy and mortality through ICD programming. *N Engl J Med* 2012;**367**:2275–83.
16. Wilkoff BL, Fauchier L, Stiles MK, Morillo CA, Al-Khatib SM, Almendral J *et al.* 2015 HRS/EHRA/APHRS/SOLAECE expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. *Heart Rhythm* 2016;**13**:e50–86.
17. Auricchio A, Hudnall JH, Schloss EJ, Sterns LD, Kurita T, Meijer A *et al.* Inappropriate shocks in single-chamber and subcutaneous implantable cardioverter-defibrillators: a systematic review and meta-analysis. *Europace* 2017;**19**:1973–80.
18. Gasparini M, Lunati MG, Proclemer A, Arenal A, Kloppe A, Martínez Ferrer JB *et al.* Long detection programming in single-chamber defibrillators reduces unnecessary therapies and mortality: the ADVANCE III trial. *JACC Clin Electrophysiol* 2017;**3**:1275–82.
19. El-Chami M, Weiss R, Burke MC, Gold MR, Prutkin JM, Kalahasty G *et al.* Outcomes of two versus three incision techniques: results from the subcutaneous ICD post-approval study. *J Cardiovasc Electrophysiol* 2021;**32**:792–801.
20. D'Onofrio A, Pieragnoli P, Biffi M, Nigro G, Migliore F, Francia P, *et al.* Subcutaneous implantable cardioverter defibrillator implantation: an analysis of Italian clinical practice and its evolution. *Int J Cardiol* 2018;**272**:162–167.