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# Third-generation subcutaneous implantable cardioverter defibrillator and intermuscular two-incision implantation technique in patients with Arrhythmogenic cardiomyopathy: 3-year follow-up☆

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ABSTRACT

*Background:* Long-term data on the potential advantages of combining the third-generation subcutaneous implantable cardioverter defibrillator (S-ICD) with modern software upgrade including the "SMART Pass", modern programming strategies and the intermuscular (IM) two-incision implantation technique in arrhythmogenic cardiomyopathy (ACM) with different phenotypic variants are lacking. In this study we evaluated the long-term outcome of patients with ACM who underwent third-generation S-ICD (Emblem, Boston Scientific) and IM two-incision technique.

*Methods:* The study population included 23 consecutive patients [70% male, median age 31 (24–46) years] diagnosed with ACM with different phenotypic variants who received third-generation S-ICD implantation with the IM two-incision technique.

*Results:* During a median follow-up of 45.5 months [16–65], 4 patients (17.4%) received a at least one inappropriate shock (IS), with median annual event rate of 4.5%. Extra-cardiac oversensing (myopotential) during effort represented the only cause of IS. No IS due to T-wave oversensing (TWOS) were recorded. Only one patient (4.3%) experienced device-related complication consisting of premature cell battery depletion requiring device replacement. No device explantation because of need for anti-tachycardia pacing or ineffective therapy occurred. There was no significant difference between patients who did and did not experienced IS with regard to baseline clinical, ECG and technical characteristics. Five patients (21.7%) received appropriate shocks on ventricular arrythmias.

*Conclusions:* According to our findings, although the third-generation S-ICD implanted with the IM two-incision technique appears to be associated with a low risk of complications and IS due to cardiac oversensing, the risk of IS due to myopotential mainly during effort should be considered.

## 1. Introduction

"Arrhythmogenic cardiomyopathy" (ACM) is currently defined as a genetic heart muscle disease which can affect the right ventricle (RV), the left ventricle (LV) or both, whose most distinctive phenotypic feature is myocardial scar (fibro or fibrofatty myocardial replacement) which underlies global and/or regional ventricular dysfunction and predisposes to potentially lethal scar-related ventricular arrhythmias (VA) [1,2]. Implantable cardioverter defibrillator (ICD) is the only proven lifesaving treatment, despite significant morbidity because of device-related complications and inappropriate shocks (IS) [3–10]. The subcutaneous ICD (S-ICD) has become a recognized effective alternative to the transvenous ICD (TV-ICD) for prevention of sudden cardiac death (SCD) among at risk-patients not needing pacing or cardiac

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resynchronization therapy [11,12]. 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 VA [11,12]. Today, a new generation of S-ICD with a major software upgrade along with the intermuscular technique (IM) represent the most recent advances in reducing IS, pocket complications and improving device performance [13–16]. However, in ACM patients, the matter of its use is more complex, because of the intrinsic characteristics of the disease, which is a progressive one and associated with the possibility of electrocardiographic depolarization/repolarization changes, leading to cardiac/non-cardiac oversensing and potential IS delivery [17]. Moreover, the S-ICD cannot deliver anti-tachycardia pacing (ATP) therapy, which could be an effective "pain-free" therapy for monomorphic ventricular tachycardia (VT) in ACM [4]. Limited studies have demonstrated that S-ICD is a safe and effective therapy for treatment of both induced and spontaneous VA despite IS and a relatively high rate of surgical revision due to complications [18–20]. However long-term data on the potential advantages of the combination of third-generation S-ICD and IM two-incision implantation technique in ACM with different phenotypic variants are lacking. The aim of this single center study was to evaluate the long-term outcome of ACM patients with different phenotypic variants, according to the 2020 International Criteria ("Padua criteria") [1,2], underwent last generation S-ICD implantation with the IM two-incision technique.

## 2. Methods

### 2.1. Study population

The study population of this single center study included 23 consecutive patients [70% male, median age 31 (24–46) years; range 13–68 years] diagnosed with ACM who received de novo third-generation S-ICD (EMBLEM A219, Boston Scientific) implantation with the IM two-incision technique for the prevention of SCD, at the Department of Cardiac, Thoracic and Vascular Sciences, University of Padova, Italy between 31 October 2016 and 10 June 2022. ACM was diagnosed according to the 2010 ITF criteria and more recently to the 2020 International criteria ("Padua criteria") [1,2]. According to the 2020 International Criteria the phenotypic variants of ACM were classified as: [1] the "dominant-right" variant (i.e., the classic ARVC phenotype characterized by the predominant RV involvement, with no LV abnormalities); [2] the "biventricular disease" variant, characterized by the involvement of both RV and LV; and [3] the "dominant-left" variant characterized by LV involvement, with no RV abnormalities.

Baseline clinical characteristics, electrocardiographic abnormalities, cardiac magnetic resonance findings (CMR), indication for ICD implantation, electrocardiogram (ECG) screening, and technical device characteristics were collected. All S-ICD implants were performed by experienced operators. The local ethics committee approved the study protocol. Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

### 2.2. S-ICD implantation

Before implantation, all patients underwent screening for S-ICD eligibility using the Boston Scientific manual ECG screening tool or the automated screening tool based on the surface ECG limb lead recording over the left and/or right parasternal regions to simulate the three S-ICD sensing vectors. To be eligible for S-ICD implantation, at least one ECG lead must satisfy the template (at any gain) in both erect and supine postures. All ECGs screening were reviewed by two experienced electrophysiologists blinded to patients, clinical presentation, and outcome. When there was disagreement, the ECG for that patient was adjudicated by a third independent observer. The implantation procedure was performed in an electrophysiology laboratory under standard sterile conditions and general anesthesia, local anesthesia with conscious sedation or ultrasound-guided serratus anterior plane block as reported previously in detail [21]. Antibiotic prophylaxis was administered 1 h before the procedure. In all patients the IM two-incision technique was used for implantation, as previously reported in detail [13,16], Briefly, the IM two-incision technique abandons the superior parasternal incision and consists of creating an IM pocket (between the anterior surface of the serratus anterior muscle and the posterior surface of the latissimus dorsi muscle) for the pulse generator (PG) rather than a subcutaneous pocket using anatomical landmarks. The position of the lead and PG relative to the heart silhouette was checked by fluoroscopy. After the procedure, defibrillation testing (DT) was performed after induction of ventricular fibrillation (VF) by 50 Hz stimulation. The DT was considered successful if the device detected and terminated VF using $\leq$65 J shock. The test was considered successful in cases where the first shock failed with standard polarity but was effective at the same energy with reverse polarity without the need for implant revision. On the contrary, in the case of a 65 J shock failure and further successful test either after implant revision or at >65 J, the test was considered non sucessful. The decision to perform post-implant DT was at the discretion of the implanting physician considering also the clinical condition of the patient. In patients who did not undergo DT a synchronized 10 J shock in sinus rhythm was considered. A chest X-ray (both anterior–posterior and lateral view) was obtained the day after the procedure to confirm stable lead and PG position. Quality was judged adequate if the complete coil and PG were visualizable. The PRAETORIAN score was calculated according to a three-step approach as reported previously in detail [22]. Based on the final score, three risk categories were defined: [1] low risk of conversion failure: PRAETORIAN score of <90 points; [2] intermediate risk of conversion failure: PRAETORIAN score between $\geq$90 and < 150 points; [3] high risk of conversion failure: PRAETORIAN score of $\geq$150.

### 2.3. Device programming

The sensing vector (primary, secondary, or alternate) was automatically selected by the device at the time of implantation and optimized during supine and upright positions. In all patients, the device programming features included two tachyarrhythmia detection zones: [1] the shock-only zone, in which detection and therapy were based on rate only and [2] an additional "conditional zone," in which a morphology analysis algorithm was applied in addition to rate. Rate cutoffs were individualized for each patient based on clinical indications.

### 2.4. Follow-up and endpoints

All patients were followed up at 1 month and every 3 to 6 months thereafter. During these visits, patients' clinical conditions, S-ICD interrogations, and complications were assessed. Remote device monitoring was also used. The primary endpoint of this study consisted of IS, whereas the combined secondary endpoint consisted of IS and device-related complications. Complications included: pocket and/or lead infection requiring system extraction, pocket hematoma that led to drainage, incomplete wound healing, skin erosion of PG or electrode, blood transfusion, or prolongation of hospitalization; device-related thrombotic events; pneumothorax or hemothorax that led to intervention or prolongation of hospitalization; cardiac perforation or tamponade; lead repositioning or replacement, and other complications related to the lead or generator that required medical or surgical intervention. A lead failure was considered if it did not meet its performance specifications or otherwise perform as intended and required removal or abandonment because judged nonfunctional [23]. An ICD shock was classified as inappropriate when triggered by anything other than ventricular tachycardia or VF above the programmed rate zone,

including supraventricular arrhythmias (SVT), cardiac/noncardiac oversensing, or device or lead malfunction. Cardiac oversensing was defined as T-wave oversensing (TWOS), QRS oversensing, P-wave oversensing or oversensing due to a low amplitude signal, and other/combined types of cardiac oversensing. Noncardiac oversensing was defined as any kind of oversensing due to noncardiac causes (eg. electromagnetic interference and myopotentials). All-cause mortality or death due to any cause, appropriate ICD therapy, major adverse cardiac events, hospitalization for heart failure and heart transplantation were also reported. An appropriate shock was defined as a therapy delivered because of correctly diagnosed shockable rhythm. Captured S-ECG tracings from all shock episodes stored in the S-ICD were obtained and examined by two electrophysiologists. Episodes of inappropriate therapy were evaluated and verified with the Boston Scientific Technical support team. R-wave amplitude of the programmed sensing vector among different ACM subgroups was analyzed. The R-wave amplitude was acquired from the EGM post-implant and during follow-up. The highest positive or negative R wave peak from the 3-40 Hz signal was measured using an internal engineering tool of the Latitude system.

### 2.5. Statistical analysis

Categorical differences between groups were evaluated by using the chi-square test ($X^2$) or the Fisher exact test as appropriate. Continuous variables were expressed as mean ± standard deviation (SD) or median with 25–75% for normally distributed and skewed variables, respectively, and compared with the Student's *t*-test or the Wilcoxon rank sum test, as appropriate. A univariate binary logistic regression model was used to provide associations between baseline clinical, ECG, S-ICD technical characteristics and IS. Event-free survival curves were drawn with the Kaplan-Meier method. Patients were censored at the time of their first event or at the time of their last clinical follow-Up. A two-tailed $p$ value $<0.05$ was considered statistically significant. Data were analyzed with SPSS (IBM SPSS Statistics Version 24.0.0, Armonk, NY).

## 3. Results

### 3.1. Baseline clinical characteristics

Baseline clinical characteristics are reported in Table 1. According to the 2020 International Criteria, 9 patients (39%) showed a "dominant-right" phenotypic variant (ARVC phenotype), 12 patients (52%) a "biventricular disease" phenotypic variant, and 2 patients (9%) a "dominant-left" phenotypic variant. At CMR, late gadolinium enhancement was reported in 22 patients (95.6%). Twenty-one patients (91%) had genetic testing performed, with 13 (62%) harboring a pathogenic mutation such as, PKP2 ($n = 3$,), DSG2 (n = 3), DSP2 (n = 3), TMEM43 ($n = 1$), JUP (n = 1), RYR2 (n = 1), DSC2 (n = 1). Eight patients (34%) were implanted for secondary prevention ($n = 6$ with sustained VT; $n = 2$ presented with SCD). At the time of ICD implantation, 18 (78%) patients were being treated with a beta blocker while 6 (26%) were receiving an antiarrhythmic agent. The reason for S-ICD placement was the presence of previous TV-ICD (patients underwent lead extraction for infection or lead failure) in 2 patients (8.7%) patients. In the remaining patients, the choice of implanting an S-ICD rather than a TV-ICD was at the discretion of the physician, which was based on clinical indications.

### 3.2. S-ICD implant characteristics

Baseline technical device characteristics are reported in Table 2. Eight patients (34.8%) had all 3 suitable sensing vectors, 15 (65.2%) had at least 2 suitable sensing vectors. The secondary sensing vector was the most compatible (78.3%), followed by the primary vector (17.4%) and the alternate vector (4.3%). Two patients (8.7%) unsuitable became eligible after moving the sensing electrodes from the left to the right parasternal line. There were no cases with adjudication disagreement.

**Table 1**
Baseline clinical characteristics of the study population.

| Characteristics | $N = 23$ |
|---|---|
| Male | 16 (70) |
| Age, years | 31 (24–46) |
| BMI (kg/m$^2$) | 22 (20–25) |
| Secondary prevention | 8 (34) |
| Family history of ACM | 5 (22) |
| History of AF | 1 (4) |
| History of syncope | 6 (26) |
| History of sustained VT | 6 (26) |
| NSVT | 9 (39) |
| Previous Transvenous ICD | 2 (8) |
| ECG characteristics at implant | |
| Sinus rhythm | 23 (100) |
| AF | 0 |
| QRS duration | 95 (88–112) |
| Number of inverted T waves | 3 (2–4) |
| Epsilon wave | 2 (8) |
| PVCs >500/24 h | 19 (82) |
| LV ejection fraction | 53 (48–55) |
| RV ejection fraction | 47 (37–55) |
| Late gadolinium enhancement | 22 (95) |
| ACM phenotypic variant | |
| "Dominant-right" phenotypic variant (ARVC) | 9 (39) |
| "Biventricular disease" | 12 (52) |
| "Dominant-left" (ALVC) | 2 (8) |
| Medication at implant | |
| Beta-blockers | 18 (78) |
| Antiarrhythmic agents | 6 (26) |
| ACE-inhibitors or ARBs | 8 (34) |

Values are expressed as number/total (%) of patients or median (25th–75th percentile). Abbreviations: ACM, arrhythmogenic cardiomyopathy; ARVC, arrhythmogenic right ventricular cardiomyopathy, AF, atrial fibrillation; ALVC, arrhythmogenic left ventricular cardiomyopathy; BMI, body mass index; ECG, electrocardiogram; ICD, implantable cardioverter defibrillator; LV, left ventricular; NSVT, non-sustained ventricular tachycardia, RV, right ventricular; VT, ventricular tachycardia; PVCs = premature ventricular contractions.

**Table 2**
S-ICD implant characteristics.

| Implant characteristics | N = 23 |
|---|---|
| S-ICD model A219 | 23 (100) |
| Lead model | |
| 3501 | 20 (87) |
| 3401 | 3 (13) |
| Lead position | |
| Left parasternal | 21 (91.3) |
| Right parasternal | 2 (8.7) |
| Programmed sensing vector | |
| Primary | 4 (17.4) |
| Secondary | 18 (78.3) |
| Alternate | 1 (4.3) |
| Defibrillator testing attempted | 20 (87) |
| VF conversion at ≤65 J | 20/20 (100) |
| Shock impedance, ohm | 64 (57–88) |
| Synchronous shock | 3 (12) |
| S-ICD programming | |
| Conditional shock zone (beats/min) | 215 (210–220) |
| Shock zone (beats/min) | 250 (250–250) |

Values are expressed as number/total (%) of patients or median (25th–75th percentile).
Abbreviations: S-ICD, subcutaneous implantable cardioverter defibrillator; VF, ventricular fibrillation.

The procedure was performed under general anesthesia in 14 (61%) patients, local anesthesia with sedation in 6 (26%) and with ultrasound-guided serratus anterior plane block in the remaining 3 (patients 13%). The average procedure time ("skin to skin") was 58 ± 15 min. A post-operative chest radiography confirmed stable device and lead location in

all patients. The S-ICD generator was on or posterior to the mid-axillary line in all patients. The distance between the generator and the thoracic wall was <1 generator width in all patients. According to the PRAETORIAN score, the risk of conversion failure was classified as low in 21 patients (91.3%), intermediate in 2 (8.7%).

DT was performed in 20 (87%) patients. Ventricular fibrillation was successfully converted at ≤65 J in all patients; with standard polarity in 19 patients (95%) and with reverse polarity in one patient (5%). Overall, median shock impedance was 64 Ohm (57–88).The mean time from VF induction to effective shock delivery was 15 ± 3 s. The 3 patients who did not undergo DT, all undergo synchronized 10 J shock in sinus rhythm with a median impedance of 80 Ω (62–80). No intra-procedural complications occurred. Dual-zone programming for tachyarrhythmia detection was selected in all patients and the SMART Pass® filter was activated in 21 patients (91.3%) after implantation.

The median post-implant R-wave amplitude of the programmed sensing vector among the different ACM phenotypes variant, "Dominant-right", "biventricular disease" and "dominant-left" variant was 0.87 mV (0.76–1.50), 1.40 mV (0.96–1.55), 1.17 mV (0.87–1.46), respectively ($P = 0.58$). The median R-wave amplitude at follow-up in the "Dominant-right", "biventricular disease" and "dominant-left" variant was 1.0 mV(1.00–1.50), 1.15 mV (0.90–1.55), 1.10 mV (0.80–1.40), respectively ($P = 0.86$).

### 3.3. Follow-up

The median duration of follow-up was 45.5 months [16–65]. Four patients (17.4%) received a at least one IS (median annual event rate 4.5%), Supplemental Fig. 1. Five patients (21.7%) experienced at least one complication including IS and device-related complications. One patient (4.3%) experienced one device-related complication consisting of premature cell battery depletion requiring device replacement. Device-related complications and reasons for IS are reported in detail in Table 3. Extra-cardiac oversensing represented the only cause of IS (Fig. 1). No IS due to TWOS or SVT were recorded. We did not observe lead dislodgment in patients with IS. Clinical and technical characteristics of patients who experienced IS are reported in the Supplemental Table 1. At the time of the IS episode, the SMART Pass® filter was found activated in 3 patients out of 4 and all episodes occurred during effort. Patients with IS underwent successful device reprogramming, including changing the sensing vector and no other events occurred during follow-up in the majority of patients (3/4). Only one patient underwent device (both generator and lead) removal and TV-ICD re-implantation because of the impossibility to solve the oversensing of myopotential with device reprogramming. During follow-up, no lead or device dislodgement, lead failure, infection, skin erosion, or device explantation because of need for ATP or ineffective therapy was noted.

There was no significant difference between patients who did or did not experience IS with regard to baseline clinical, ECG and technical characteristics including R-wave amplitude of the programmed sensing vector post implantation or at follow-up.

Five patients (21.7%) received a total of 12 appropriate and successful shock on VA during follow-up (monomorphic VT in 4 patients and VF in one patient), supplemental Fig. 1. The time to therapy for spontaneous episodes was 16 ± 3 s. One patient underwent successful catheter ablation and the other 3 patients were treated with optimization of drug therapy. The follow-up was uneventful. No need for transplant or LV assist device implantation or deaths occurred in this cohort.

## 4. Discussion

In this study we evaluated the long-term outcome of patients with ACM with different phenotypic variants, according to the 2020 International Criteria ("Padua criteria") who underwent third-generation S-ICD (Emblem, Boston Scientific) implantation with modern software upgrading, and IM two-incision technique. We focused on the prevalence and type of IS, complications, their management and possible predictors. The main findings are:

I. the rate of IS remains substantial in ACM, occurring in 17% of patients despite third-generation device with SMART Pass® filter activated in most cases, device programing with high rate cutoff and optimal positioning of the device. This because the extra-cardiac oversensing due to myopotential represented the leading cause of IS. No IS due to TWO were recorded. Our results highlight the need for effective strategies to prevent IS, such as appropriate pre-implantation ECG screening and provocative testing ("stress-test") at follow-up;
II. except one case of premature cell battery depletion, no other device-related complications requiring reintervention were observed, suggesting the potential role of the IM two-incision technique in preventing complications;
III. S-ICD is effective in terminating clinical VA in the absence of a perceived need for ATP or pacing;

In patients with ACM at risk of SCD, the TV-ICD provides the most effective life-saving therapy [3]. 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. This high rate of lead-related adverse events may be explained by the peculiar ACM pathobiology which leads to progressive loss of myocardium with fibrofatty replacement, also affecting the site of RV lead implantation [3–10]. The S-ICD has become a recognized effective alternative to the TV-ICD [11,12]. The intracardiac leadless configuration makes the S-ICD a preferable choice mostly in the young patients with inherited arrhythmogenic diseases, while maintaining efficacy to interrupt life-threatening VA. However, potential limitations of the S-ICD in ACM patients, include inability to deliver ATP which may be an effective "pain free" therapy and concerns for IS due to TWOS and myopotentials because of baseline ECG depolarization/repolarization changes [4,18–20,24].

Preliminary studies from both the Hopkins [18] and the Italian registries [19] demonstrated that S-ICD can effectively treat both induced and spontaneous VA in patients with ARVC despite relatively high IS mostly due to TWOS and myopotential oversensing and device-

**Table 3**
Device-related complications and reasons for IS during follow-up.

| | n = 23 |
|---|---|
| Patients experienced at least one complication (including inappropriate shock and device-related complications) | 5 (21.7) |
| Device-related complications requiring reintervention | 1 (4.3) |
| Pocket-associated complications | 0 |
| Erosion | 0 |
| Infection | 0 |
| Lead-associated complications | 0 |
| Lead dislodgment (Within 24 h) | 0 |
| Lead failure | 0 |
| Lead infection | 0 |
| Others complications | |
| Premature cell battery depletion requiring device replacement | 1 (4.3) |
| Ineffective therapy | 0 |
| Procedure-related complication | 0 |
| S-ICD removal for complications and TV-ICD re-implantation* | 1 (4.3) |
| Patients experienced inappropriate shocks | 4 (17.4) |
| Reason for inappropriate shock | |
| Atrial fibrillation/supraventricular tachycardia | 0 |
| Cardiac oversensing | 0 |
| TWOS | 0 |
| Extra-cardiac oversensing | 4 |
| Myopotentials | 4 |

Values are expressed as number/total (%) of patients or median (25th–75th percentile). Abbreviations: TV-ICD, transvenous implantable cardioverter defibrillator, TWOS, T-wave oversensing. *Impossibility to solve the oversensing of myopotential leading to inappropriate shock with device reprogramming.

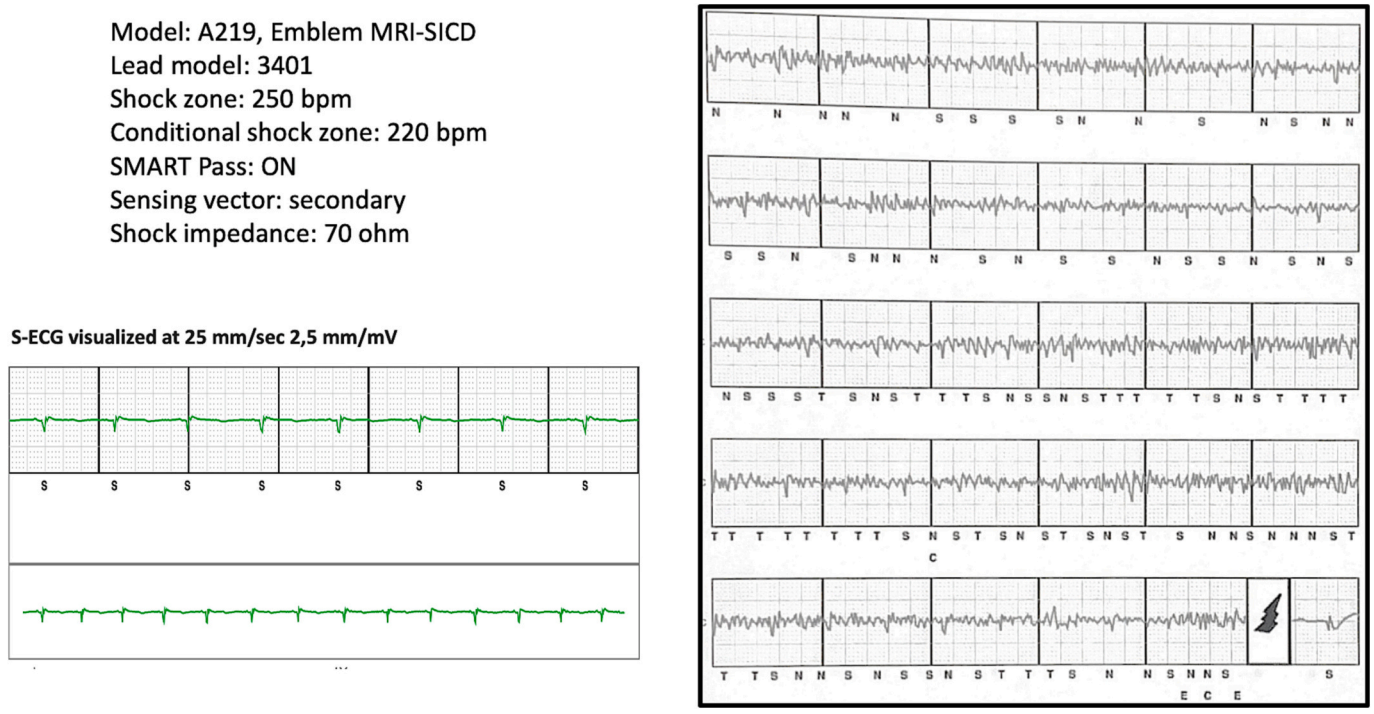


**Fig. 1.** S-ICD stored electrogram of extra-cardiac oversensing leading to inappropriate shock due to myopotential (secondary vector) during effort in a patient with arrhythmogenic cardiomyopathy (biventricular phenotypic variant).

related complications requiring surgery revision.

Recently, Wang et al. [20] compared outcomes including appropriate therapies, IS and complications between TV-ICD ($n = 88$) and S-ICD ($n = 57$) among patients with ACM from the Johns Hopkins ARVC Registry. The main clinical findings of this study were: 1) IS shocks were significantly more common in the S-ICD group (23%) than the TV-ICD group (10%); 2) while the TV-ICD group had significantly more procedure-related complications (14% vs 4%); 3) the association between ICD type and the composite of IS and complication was not statistically significant (subcutaneous vs transvenous adjusted HR: 1.43;95% CI: 0.72–2.84); 3) in patients with ARVC receiving an ICD, a subcutaneous device was not associated with more appropriate shocks despite the lack of ATP rather than TV-ICD.

The results of these previous studies mentioned above [18–20] expand the population of ACM patients who may benefit from a S-ICD. However, long-term data on the potential advantages of the combination of third-generation S-ICD with modern software upgrading, including the "SMART Pass", modern programming strategies and IM two-incision implantation technique in ACM with different phenotypic variants according to the recent 2020 International Criteria ("Padua Criteria") [1] are lacking.

### *4.1. Third-generation S-ICD and the intermuscular two-incision technique in ACM patients: what are the potential advantages?*

The S-ICD therapy has evolved over the last years and more recent data showed that the use of new implantation techniques, modern device programing with high rate cutoffs, current new generation electrogram filtering (SMART Pass filter) and discrimination algorithms, led to a significant reduction in rates of IS and device-related complications [12,13,16,17]. A new technique that uses two incisions and an IM pocket for the PG between the serratus anterior and the latissimus dorsi muscles has been introduced and is currently widely adopted [13–16]. The IM two-incision technique allows for optimal positioning of the device achieving a low PRAETORIAN score (<90), reducing shock impedance, high probability of effective defibrillation and reducing device-related complications [15,16]. The new generation S-ICD has several favorable features when compared with the first-generation S-ICD, including a smaller generator size, an increased battery life, and a software upgrade, further improving S-ICD performance while reducing inappropriate therapies, especially TWOS [16,25]. While continuous research in the field of S-ICD technology and implantation technique is ongoing, EMBLEM S-ICD and IM two-incision technique represent the most recent advances [16].

However, currently, it is unclear whether the IM technique and the new generation S-ICD may impact the occurrence of IS and device-related complications in patients with ACM. According to our results during 3-year follow-up, the rate of IS remains substantial, occurring in 17% of patients despite third-generation devices with SMART Pass® availability, modern device programming, and optimal positioning of the device and lead using the IM two-incision technique. Therefore, the IM two-incision technique does not seem to impact the occurrence of IS given the substantial rate of IS observed in our study. However, if we focused on the causes of IS, extra-cardiac oversensing (myopotentials) represented the only cause. We did not obverse IS due to TWOS. This can be explained certainly by the SMART Pass® detection filter which attenuates cardiac oversensing especially TWOS [16,25], but it could also be due to the IM technique which may improve cardiac sensing [16] shifting the type of complications towards extra-cardiac sensing [16,26]. The use of third-generation S-ICD and IM two-incision technique in the overall study population in our study may explain the slightly lower rate of IS and the absence of pocket and lead related complications compared to the study by Wang et al. [20]. Of note, in this study only 52% of patients received a third-generation device, the SMART Pass filter was available and programmed in 57% of patients and the IM technique was adopted in only 8% of patients.

Interestingly, in our study the cause of IS was myopotential oversensing. It remains to be clarified if this is related to the IM position of the S-ICD generator or not. Tsutsui et al. speculated that *Latissimus dorsi* and *musculus serratus anterior*, the large muscle surrounding an S-ICD device, could create clinically troubling myopotential from daily activities [27]. Thus, the reduction of TWOS may be offset by the

introduction of myopotentials due to the IM position especially in ACM patients with a low R-wave amplitude.

Although the rate of ACM patients that experienced IS was not negligible, it is in line with data from previous reports on TV-ICD (10–25%) [3,9,10,20,28].

Our findings suggest that possible strategies that could further reduce IS in ACM receiving S-ICD are: proper pre-implant ECG screening, device programming with high rate cutoff (shock zone >250), targeting a surface ECG R-wave amplitude >1 mV at implant may allow for better discrimination. Furthermore, it will also be important to track the sensed R-wave amplitude in various vectors at rest, during effort and with maneuvers on follow-up. A "stress-test" shortly after implantation, involving an isometric chest press, lifting and holding a weight, side planks, abdominal crunch and raising left arms, should be carefully performed. Prominent myopotential during this test should prompt immediate consideration for preventive measures such as, avoiding the affected vector(s) and patient education [29]. The feasibility of this test is supported by a recent report by van den Bruck et al. [29] that myopotential can be reportedly induced by an exercise test in many S-ICD patients, although not all the provoked myopotentials are recognized as a tachycardia [29]. Specifically, secondary and alternate vectors are allegedly more vulnerable during isometric chest press than the primary vector, which is instead more affected by side plank exercise [29]. The effectiveness of this "stress test" should be evaluated in detail in patients with ACM implanted with IM.

Moreover, due to the potential R-wave amplitude decline in ACM during follow-up predisposing to possible cardiac and/or non-cardiac oversensing it may be desirable to have at least 2/3 vectors suitable in S-ICD.

Until definitive data comparing efficacy and safety of new generation TV-ICD versus S-ICD, with updated discrimination algorithms and software are available in ACM patients, decision-making needs to be individualized, mostly taking into account potential device-related complications, likelihood of IS, and the need of antibradycardia pacing or ATP.

### 4.2. Study limitations

Although, this study is the first study with a long term follow-up which has assessed the outcome of patients with ACM having different phenotypic variants, according to the 2020 International Criteria, and who underwent third-generation S-ICD implant with the IM two-incision technique, there are some limitations. This is a retrospective single-center study. The sample size of the study population is low and surely further studies with larger study populations are needed to confirm the data from this preliminary study. Larger studies with patients affected by different cardiomyopathies and with third-generation S-ICD, are also needed to understand whether the issue of IS due to myopotentials is restricted or not to the ACM population. However, it should be considered that patients with ACM in our experience are characterize by a lower R-wave amplitude value than that observed in patients with other cardiomyopathies. This makes patients with ACM much more susceptible to myopotential problems. No direct comparison was made between TV-ICD and S-ICD or comparison between traditional technique and IM two-incision technique for S-ICD implant, but this goes beyond the aim of the present study. Certainly, large randomized studies with a predefined comparable new generation TV-ICD cohort, with updated discrimination algorithms and software would be needed to accurately define the clinical benefit or harm from device choice. Even with this long follow-up there were a relatively small number of events and this might have affected the identification of predictors. All procedures were performed by experienced operators, and therefore, our results might not be widely applicable in less experienced centers. Despite these limitations, the data presented are unique in several ways and make an important contribution to the limited published data regarding the clinical performance of third-generation S-ICD in patients with ACM.

## 5. Conclusions

According to our findings, although the third-generation S-ICD implanted with the IM two-incision technique appears to be associated with a low risk of complications and IS due to cardiac oversensing, the risk of IS due to myopotential, mainly during effort, should be considered. Strategies to avoid extra-cardiac oversensing should be adopted.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2023.04.018.

## Ethics approval statement

The study was reviewed and approved by the local medical ethics committee.

## Authors' contributions

Federico Migliore: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing - original draft; Writing - review & editing.

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Enrico Giacomin: Data curation; Formal analysis; review & editing.

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Stefano Accinelli: Data curation; Formal analysis; Funding acquisition; Supervision; Validation.

Sabino Iliceto: Supervision; Validation; Visualization; review & editing.

Domenico Corrado: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing - original draft; Writing - review & editing.

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None.

## Declaration of Competing Interest

All the authors declare that there are no conflict of interests.

## Data Availability

Data available on request from the authors.

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