Myopotential Oversensing Is a Major Cause of Inappropriate Shock in Subcutaneous Implantable Defibrillator in Japan

Kenta Tsutsui, MD, Ritsushi Kato, MD, Sou Asano, MD, Yoshifumi Ikeda, MD, Hitoshi Mori, MD, Mai Tawara, MD, Sayaka Tanaka, MD, Saki Hasegawa, MD, Shintaro Nakano, MD, Siro Iwanaga, MD, Toshihiro Muramatsu, MD and Kazuo Matsumoto, MD

Summary

Previous study has identified marked differences in patient characteristics and causes of inappropriate shock (IAS) between Japan and the Western societies in terms of subcutaneous implantable cardioverter-defibrillator (S-ICD). However, evidence of IAS in Asian populations including Japan has been limited to one observational study.

Thus, we conducted a single-center registry study that tracks the postoperative course of 61 consecutive patients who received S-ICD from February 2016 to January 2020. Our findings showed that IAS occurred in 9.8% of the study population (6/61), which is comparable to the previously reported incidence. Remarkably, T-wave oversensing did not result in an IAS (0/6). Instead, myopotential oversensing was determined to have caused the most IAS events (4/6), while atrial fibrillation ranked second (2/6). A provocation maneuver (e.g., abdominal clench, push-ups, lifting a heavy item) reproduced myopotential noise disguised as R-waves, which should potentially trigger an IAS if uninterrupted. R-wave amplitude of the IAS group appeared relatively low compared to that of the non-IAS group although this finding was not tested significant. Furthermore, no temporal changes were noted in R-wave amplitude between the time of implantation and IAS events, suggesting that it is neither constantly low nor acutely dropped R-wave amplitude but a relatively high noise level that drives IAS. All the myopotential-IAS patients were found to be male. Right-sided lead implantation was associated with a higher incidence of IAS.

This study highlights the fact that IAS continues to occur due to myopotential noise oversensing instead of T-wave oversensing. To minimize the risk of IAS, it is desirable to search and secure high R-wave voltage.

Key words: Subcutaneous ICD (S-ICD), Screening, Myopotential

Subcutaneous implantable cardioverter defibrillator (S-ICD), an emerging alternate to conventional transvenous implantable cardioverter defibrillator (tv-ICD), has rapidly gained popularity worldwide. In 2019, the Japanese Circulation Society gave a Class I indication to S-ICD for those who are determined to be eligible for tv-ICD and do not require pacing or cardiac resynchronization. However, to date, besides anecdotal case reports, S-ICD evidence that specifically features Japanese population has been limited to merely one early single-center experience and another two-center observational study. Thus, the Japanese guideline recommendation critically depends on extrapolation of information from non-Asian-dominant societies such as Europe, Oceania, and the USA. This paucity of Asian evidence not only casts some doubt on the credibility of Japanese guideline statement but also potentially hampers the further optimized use of S-ICD in Japan/Asia. Therefore, it is crucial to accumulate S-ICD studies to determine whether inter-social difference in S-ICD exists.

Specifically, compared to EFFORTLESS/IDE registry, the previous Japanese S-ICD recipients were characterized by older mean age at implantation (60% versus 48%), more secondary prevention (60% versus 35%), more channelopathy (35% versus 20%), and better mean left ventricular ejection fraction (LVEF, 64.9% versus 43%). Furthermore, the major cause of inappropriate shock (IAS) was substantially different; the majority of IAS was found to be caused by myopotential in the Japanese study (60%), while the most common cause of IAS in EFFORTLESS was identified to be T-wave oversensing or low-amplitude signals (63%). One may attribute this difference in physical characteristics unique to Asians. However, a relatively small sample size of the study (60 patients from 2 hospitals) precludes simple extrapolation of this observation to the whole Japanese S-ICD population. Therefore, to confirm this observation, we conducted another Japanese registry study by examining consecutive
patients who received S-ICD in our institute.

Methods

This is a single-center observational study. The protocol of this research was approved by an institutional ethics committee within Saitama Medical University (#19-223), and it conforms to the provisions of the Declaration of Helsinki (as revised in Fortaleza, Brazil, October 2013).

Patients: Sixty-one consecutive patients who underwent S-ICD implantation at our hospital from February 2016 through January 2020 were included in the study cohort. All implantation was performed in accordance with a guideline published from the Japanese Circulation Society; all the patients had an indication for ICD and did not require pacing.1

Preoperative surface ECG screening (S-ECG): In order to evaluate the eligibility for S-ICD, the preoperative screening with the manual screening tool (MST) with a template provided by Boston Scientific Inc. was performed in all cases on the day before the implantation. The screening is considered a failure if all ECG waveforms from these three vectors do not fit into the template, which is designed to include only those with an ECG morphology recommended by the manufacturer; otherwise, when ECG waveform of at least one of three vectors fits into the template, it is considered a success. For those who failed the preoperative ECG screening in the left sternal border but passed the right sternal border, an S-ICD lead was implanted along the right sternal border.

S-ICD implantation and configuration: An eligible patient underwent an S-ICD implantation as previously described. All implantations were performed under general anesthesia using combined sevoflurane and intravenous infusion of propofol, dexmedetomidine hydrochloride, and fentanyl.

A defibrillation threshold test was routinely performed during the implantation. SMART Pass was turned on upon its release for those who received S-ICD before 2017 or turned on upon implantation since 2017, and it was maintained active during the follow-up if possible.

Postoperative follow-up: In order to evaluate the predictability of postoperative in-device EGM, which is used for detecting normal and abnormal cardiac rhythms, we compared amplitudes of R- and T-wave and a ratio of both (dubbed as “R/T ratio”) between preoperative S-ECG during the MST screening and those of initial postoperative device EGM around 3 hours following the implantation.

Additionally, to investigate the time-dependent changes in the ECG parameters, we systematically gathered amplitude of R- and T-waves and R/T ratio in primary, secondary, and alternate vectors of the in-device electrogram (EGM) periodically during an outpatient clinic visit every 6 months. We further compared these parameters between IAS and appropriate shock subgroups.

Telemetry home monitoring was also provided to all patients to monitor their general status and ventricular tachycardia (VT)/ventricular fibrillation (VF) events each month. Based on the information gathered from the home monitoring system, two dedicated device nurses provided monthly regular phone session to all S-ICD patients to monitor and address patient’s daily concerns.

Event classification: The classification committee comprised of three experienced investigators (K.T., Y.I., and R.K.), who reviewed the shock events independently. Heart rhythm was classified as VT, VF, normal sinus rhythm, sinus tachycardia, atrial fibrillation (AF), and supraventricular tachycardia (SVT). Shocks delivered for non-VT/VF were classified as inappropriate.

Statistical analysis: Data are expressed as mean ± standard deviation. For numerical values between two groups, nonparametric t-test was used. Intergroup difference was assessed by two-way analysis of variance and multiple comparison, where applicable. Contingency tests were performed using Fisher’s exact test. P < 0.05 was considered statistically significant unless otherwise mentioned.

Results

Patient characteristics: Characteristics of the study population and subgroups of those who experienced no shocks, appropriate shocks, IAS from all causes, and IAS induced by myopotential are summarized in Table I. The overall population age ranged from 12 to 76 years old, with 88% of male sex, 46% of primary prevention, and 48% of mean LVEF. The most common etiology was channelopathies (33%, i.e., Brugada syndrome, long-QT syndrome, and idiopathic VF combined), followed by ischemic heart disease (25%) and dilated cardiomyopathy (20%). The follow-up period ranged from 14 to 1450 days, with the mean and median values being 732 and 708, respectively. There were no significant differences in these parameters listed in Table I across the subgroups of non-shock, appropriate shock, and IAS groups except for an incidence of right-sided lead implantation between non-shock and myopotential-IAS groups (4% versus 75%, P = 0.0017, see the latter part of Result section) and that of ischemic heart disease between non-shock and appropriate shock groups.

Efficacy of S-ICD: During the mean follow-up period of 732 days, seven patients (11.4%) experienced an appropriate shock (Figure 1A). First shock efficacy and the total shock efficacy were 85.7% (6/7) and 100%, respectively. Namely, one patient required multiple shocks for VT/VF. An appropriate shock event tended to occur earlier than IAS (117 ± 107 versus 436 ± 312 days from implantation, P < 0.05). All the appropriate shocks in this study occurred within 1 year after the S-ICD implantation (Figure 1A).

Key characteristics of the appropriate shock group are summarized in Table I. They had Brugada syndrome (3/7), dilated cardiomyopathy (1/7), vasospastic angina (2/7), or hypertrophic cardiomyopathy (1/7) as etiology. Primary and secondary prevention have accounted for 3/7 (43%) and 4/7 (57%), respectively, and had either VT (3/7) or VF (4/7). Following a shock event, all patients received additional treatment such as quinidine for Brugada syndrome, amiodarone for dilated cardiomyopathy, and radiofrequency ablation for a monomorphic VT in a case with hypertrophic cardiomyopathy. Subsequently, no recurrent appropriate shocks were observed following the first shock.
Table I. Patient Characteristics of the Study Population

|                      | All   | Non-shock | Appropriate shock | IAS, all causes | IAS, myopotential-induced | P, Non-shock versus appropriate shock group* | P, Non-shock versus myopotential-induced IAS group* |
|----------------------|-------|-----------|-------------------|-----------------|---------------------------|---------------------------------------------|---------------------------------------------------|
| n                    | 61    | 49        | 7                 | 6               | 4                         | N/A                                         | N/A                                               |
| Age                  | 48 ± 17 | 46 ± 17 | 52 ± 12           | 51 ± 18         | 49 ± 16                   | 0.418                                       | 0.776                                             |
| Male                 | 54 (88%) | 45 (87%) | 6 (86%)           | 100%            | 100%                      | 0.501                                       | 1.000                                             |
| Follow-up period     | 752 ± 422 | 752 ± 360 | 918 ± 322        | 891 ± 353       | 891 ± 353                 | 0.085                                       | 0.081                                             |
| Day from implantation to the first shock | N/A | N/A | 117 ± 107 | 436 ± 312 | 304 ± 185 | N/A | N/A |
| Primary prevention   | 28 (46%) | 24 (46%) | 3 (43%)          | 3 (50%)         | 3 (75%)                   | 1.000                                       | 0.610                                             |
| Height (cm)          | 168 ± 8  | 167 ± 8  | 172 ± 8          | 171 ± 5         | 171 ± 6                   | 0.149                                       | 0.452                                             |
| Body weight (kg)     | 69 ± 16  | 69 ± 17  | 66 ± 13          | 71 ± 9          | 69 ± 7                    | 0.735                                       | 0.948                                             |
| Body mass index      | 24.1 ± 4.8 | 24.4 ± 5.0 | 22.2 ± 3.3 | 24.3 ± 3.9 | 23.3 ± 3.8 | 0.278 | 0.681 |
| Right-sided lead position | 6 (10%) | 2 (4%) | 2 (28%) | 3 (50%) | 3 (75%) | 1.000 | 0.397 |
| LV EF (%)            | 48 ± 22  | 46 ± 22  | 58 ± 19          | 53 ± 21         | 56 ± 24                   | 0.291                                       | 0.239                                             |
| Channelopathies*     | 20 (33%) | 17 (33%) | 3 (43%)          | 3 (50%)         | 2 (50%)                   | 0.691                                       | 0.612                                             |
| IHD                  | 15 (25%) | 13 (25%) | 0                | 1 (17%)         | 0                         | 0.016                                       | 0.117                                             |
| DCM                  | 12 (20%) | 12 (23%) | 1 (14%)          | 1 (17%)         | 1 (25%)                   | 1.000                                       | 1.000                                             |
| HCM                  | 6 (10%)  | 5 (10%)  | 1 (14%)          | 1 (17%)         | 1 (25%)                   | 0.028                                       | 1.000                                             |
| VSA-related VT/VF    | 5 (8%)   | 4 (8%)   | 2 (28%)          | 0               | 0                         | 0.156                                       | 1.000                                             |

LVEF indicates left ventricular ejection fraction; LAD, left atrium diameter; LVDd, left ventricle diastolic diameter; IHD, ischemic heart disease; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; VSA, vasospastic angina.; and N/A, not applicable. * Idiopathic VF, Brugada syndrome and long-QT syndrome combined. ** Unpaired t-test for continuous variables, Fisher’s exact test for contingency.

Figure 1. Kaplan-Meier curves for shock-free survival from appropriate shock (left) and inappropriate shock (right).

Inappropriate shocks: On the other hand, IAS has reportedly occurred in six patients (9.8%) during the study (Table I, Figure 1B left). There were no IAS-associated serious injuries, death, or cardio- or cerebrovascular accidents. T-wave oversensing was not observed as a reason of IAS (0/6). Instead, myopotential oversensing was determined to be the most common cause of IAS events (4/6, Figure 1B right), followed by AF with rapid ventricular response (2/6).

Table II details the information of four myopotential-
induced IAS patients encountered in this study. All of them were male. Duration between the implantation and the first IAS shock event ranged from 6 to 488 days. An IAS was recorded during vigorous exercise in two patients (#12 and #18) and during daily activities in other two cases (#11 and #30).

The in-device EGM of these myopotential-induced IAS patients retrieved during the post-shock interrogation revealed that myopotential noise disguised cardiac signals (A). Myopotential can be induced in the secondary and primary vectors in this patient (B).

Figure 2. A representative case of myopotential-induced IAS. The in-device EGM retrieved during the post-shock interrogation revealed that myopotential noise disguised cardiac signals (A). Myopotential can be induced in the secondary and primary vectors in this patient (B).

Table II. Detail of Four Myopotential-Induced IAS Patients

| Patient # | #11 | #12 | #18 | #30 |
|-----------|-----|-----|-----|-----|
| Age       | 41  | 53  | 36  | 70  |
| Sex       | Male| Male| Male| Male|
| Year implanted | 2016 | 2016 | 2017 | 2018 |
| Days from surgery to event | 6 | 488 | 424 | 298 |
| R-wave amplitude, alternate (mV) | 0.6 | 0.8 | 0.8 | 0.8 |
| R-wave amplitude, secondary (mV) | 1.1 | 2.0 | 0.8 | 0.8 |
| R-wave amplitude, primary (mV) | 1.2 | 1.8 | 0.4 | 1.6 |
| Etiology | Brugada | DCM | Brugada | HCM |
| Indication | Secondary prevention | Primary prevention | Primary prevention | Primary prevention |
| Causal activity | Raising left arm to dry off back following taking bath | Raising a bucket filled with 20 L of water | Workout | Lying down watching TV, left side down |
| Lead position | Right sternal border | Right sternal border | Right sternal border | Left sternal border |
| Affected vectors | Primary, secondary | Primary, alternate | Secondary, alternate | Primary, secondary |
| Solution | Changed the sensing vector to Alt | Changed the sensing vector to secondary | Changed the sensing vector to primary | Changed the sensing vector to Alt |

There appears to be a trend that the R-wave amplitude was lower in myopotential-IAS group than those in non-IAS group in alternate and primary vectors although this difference missed to reach statistical significance in the secondary vector (Figure 3, alternate, 1.7 ± 0.8 mV versus 0.9 ± 0.5 mV, P = 0.043; secondary, 2.4 ± 1.1 mV versus 1.4 ± 0.5 mV, P = 0.094; primary, 2.8 ± 1.4 mV versus 1.3 ± 0.6 mV, P = 0.035); and (3) there were no temporal changes in R-wave amplitude between the time of implantation and IAS (Table III), indicating that the R-
I n t H e a r tJ
September 2020 917

MYOPOTENTIAL-INDUCED INAPPROPRIATE SHOCK IN S-ICD

III.

Longitudinal Changes in R-wave, T-wave, and R/T Amplitude Ratio in Non-IAS and IAS Groups

| Parameter       | Vector | Group    | 0 month | 6 months | 12 months | 18 months | 24 months |
|-----------------|--------|----------|---------|----------|-----------|-----------|-----------|
| R-wave amplitude| Alternate | Non-IAS | 1.1 ± 0.5 | 0.9 ± 0.4 | 0.8 ± 0.5 | 0.8 ± 0.4 | 1.0 ± 0.8 |
|                 |         | IAS      | 1.1 ± 0.1 | 1.0 ± 0.8 | 0.7 ± 0.2 | 0.6 ± 0.2 | 0.7 ± 0.2 |
|                 | Secondary | Non-IAS | 0.8 ± 0.8 | 1.2 ± 0.3 | 1.2 ± 0.2 | 1.1 ± 0.2 | 1.3 ± 0.2 |
|                 |         | IAS      | 1.4 ± 0.5 | 1.2 ± 0.3 | 1.2 ± 0.2 | 1.1 ± 0.2 | 1.3 ± 0.2 |
|                 | Primary  | Non-IAS  | 2.0 ± 1.0 | 1.8 ± 0.9 | 1.8 ± 0.9 | 1.7 ± 0.9 | 1.7 ± 0.8 |
|                 |         | IAS      | 1.3 ± 0.5 | 0.9 ± 0.5 | 0.9 ± 0.6 | 1.0 ± 0.5 | 1.2 ± 0.3 |
| T-wave amplitude| Alternate | Non-IAS | 0.15 ± 0.09 | 0.16 ± 0.09 | 0.16 ± 0.07 | 0.17 ± 0.09 | 0.21 ± 0.15 |
|                 |         | IAS      | 0.23 ± 0.11 | 0.30 ± 0.29 | 0.15 ± 0.05 | 0.18 ± 0.13 | 0.10 ± 0.00 |
|                 | Secondary | Non-IAS | 0.27 ± 0.13 | 0.25 ± 0.11 | 0.26 ± 0.11 | 0.29 ± 0.11 | 0.27 ± 0.13 |
|                 |         | IAS      | 0.20 ± 0.12 | 0.23 ± 0.11 | 0.13 ± 0.04 | 0.20 ± 0.12 | 0.10 ± 0.00 |
|                 | Primary  | Non-IAS  | 0.31 ± 0.17 | 0.28 ± 0.14 | 0.32 ± 0.20 | 0.24 ± 0.13 | 0.22 ± 0.14 |
|                 |         | IAS      | 0.28 ± 0.13 | 0.20 ± 0.12 | 0.15 ± 0.05 | 0.18 ± 0.04 | 0.13 ± 0.05 |
| R/T ratio       | Alternate | Non-IAS | 8.4 ± 5.0 | 7.0 ± 4.5 | 6.4 ± 4.7 | 5.7 ± 4.2 | 6.5 ± 4.6 |
|                 |         | IAS      | 4.2 ± 2.3 | 4.5 ± 2.1 | 5.3 ± 2.8 | 4.1 ± 1.2 | 6.7 ± 1.9 |
|                 | Secondary | Non-IAS | 8.0 ± 4.5 | 7.9 ± 4.1 | 7.3 ± 3.0 | 6.6 ± 3.0 | 8.4 ± 5.0 |
|                 |         | IAS      | 9.4 ± 6.3 | 7.8 ± 4.8 | 9.8 ± 2.3 | 7.5 ± 3.8 | 13.3 ± 1.9 |
|                 | Primary  | Non-IAS  | 7.7 ± 4.4 | 6.8 ± 2.3 | 7.0 ± 4.2 | 8.90 ± 5.4 | 9.4 ± 4.9 |
|                 |         | IAS      | 5.0 ± 2.3 | 5.8 ± 2.3 | 6.8 ± 5.8 | 5.5 ± 1.7 | 12.0 ± 3.3 |

To prevent recurrence, the sensing vector was changed to the least susceptible one to myopotential during the provocation maneuver. In addition, the patients were instructed to avoid the mimicking activity or at least limit the action duration as short as possible. Device nurses have closely communicated with these patients on regular hospital visits and over the phone via the telemetry home monitoring system. Despite all effort, one patient suffered from multiple IAS due to different kinds of daily activities such as riding a bicycle, push-ups, abdominal clench, etc. For this patient, the continuous education and communication eventually led to the IAS elimination after a few months following the first IAS.

In two patients, AF with rapid ventricular response resulted in an IAS. These patients subsequently received a strict rate control medication such as beta-blocker and/or verapamil. In addition, one patient was advised to abstain from alcohol, which appeared responsible for the worsened rate control. In another patient, excruciating pain due to severe urinary retention identified to be caused by upper urinary tract hemorrhage caused rapid AF that triggered IAS, but this was adequately addressed via surgical repair. These experiences suggest the importance of pharmacological/non-pharmacological rate management in S-ICD patients with AF.

R-wave amplitude was correlated between S-ECG and the initial in-device EGM: R-wave amplitudes of preoperative S-ECG and postoperative in-device EGM in all vectors were determined to be correlated (Figure 4A, alternate, \( Y = 0.4699X + 0.5104, P < 0.0003, r^2 = 0.24 \); secondary, \( Y = 0.4783X + 0.5460, P < 0.0001, r^2 = 0.48 \); and primary, \( Y = 0.6215X + 0.7501, P < 0.0001, r^2 = 0.55 \)). However, the T-wave amplitude of S-ECG and in-device EGM was not correlated in the alternate and primary vectors, and that in secondary vector merely reached statistical significance with less robust fitness (Figure 4B, alternate, \( Y = 0.2365X + 0.1942, P = \text{N.S.} \); secondary, \( Y = 0.2735X + 0.1942, P = \text{N.S.} \); and primary, \( Y = 0.3045X + 0.1942, P = \text{N.S.} \)).

Figure 3. A subgroup analysis that compares the R-wave amplitude between the non-IAS (black) and IAS (magenta) patients. There were no significant differences in all vectors studied. * indicates significant difference.
\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure4.png}
\caption{Correlations in R-wave amplitude (top row), T-wave amplitude (middle row), and R/T amplitude ratio (bottom row) between the surface ECG gained during the mandatory preoperative screening test (x-axis) and initial in-device EGM (y-axis) in alternate (left column), secondary (center column), and primary (right column) vectors. R-wave in all three vectors was considered to be statistically correlated. However, the relationships in T-wave amplitude and R/T ratio between the surface screening ECG and EGM were less evident.}
\end{figure}

\begin{align*}
Y &= 0.2526^*X + 0.1902, \quad P = 0.0025, \quad r^2 = 0.17; \text{ and primary,} \\
Y &= -0.01071^*X + 0.3097, \quad P = \text{N.S.}
\end{align*}

This low or no correlation in T-wave amplitude between S-ECG and in-device EGM was preserved in R/T ratio (Figure 4C, alternate, \(Y = 0.3381^*X + 3.632, \quad P = 0.0188, \quad r^2 = 0.11\); secondary, \(Y = -0.05328^*X + 6.382, \quad P = \text{N.S.}; \text{ and primary,} \\
Y = -0.04794^*X + 7.718, \quad P = \text{N.S.}).

**Follow-up:** A longitudinal periodic follow-up of in-device R-wave amplitude, T-wave amplitude, and R/T ratio revealed that those of both non-IAS and IAS patients remain stable after implantation (Table III), suggesting that, at least in our cohort, it is not an acute or chronic change in these parameters that causes an IAS event.

During the study period, pocket infection occurred in one patient, who received an S-ICD for Brugada syndrome and primary prevention. Acute pocket hemorrhage following the implantation has required reoperation in three patients. All the patients in this subgroup had been treated with oral anticoagulation/antithrombotic agents, which was temporarily stopped for a short period of time (~a week) until hemostasis was achieved. One patient who experienced multiple appropriate shocks for a VT/VF event due to inability to use amiodarone for bradycardia crossed over to tv-ICD to support the use of amiodarone.

One patient died of progressive and refractory heart failure; she had dilated phase of hypertrophic cardiomyopathy and VT/VF, to which the cause of her death was not attributed.

**Right-sided lead was at a higher risk of myopotential-IAS:** Right-sided lead implantation was found associated with a higher incidence of myopotential-induced IAS when compared to the left-sided implantation (50% versus 2%, \(P = 0.0017\)). Failed preoperative screenings due to prominent high T-wave amplitude and for low cardiac signals were the reasons for the right-sided lead implantation in three and one cases, respectively. Individual data plots of the time-dependent changes in R-wave amplitude of the in-device electrogram did not differ between the sides of implantations (Table II). Illustrative chest X-ray images of IAS patients with the lead implanted along left and right sternal border are shown in Figure 5.

**Discussion**

**Major findings:** The major findings of this present study are as follows: (1) The occurrence of IAS in this study was up to 9.8% during the mean observational period of ~2 years. In contrast to the similar incidence of IAS between this present study and EFFORTLESS/IDE, instead of T-wave oversensing, a common cause of IAS was
Persistent myopotential noise oversensing: In this previous study, T-wave oversensing did not result in IAS. Although the exact mechanism remains unclear, possible underlying factors are as follows: (1) In Japan, the mandatory, centralized, and organized proctor training program provides new S-ICD implanters with standard techniques that avoid cardiac oversensing, (2) adequate screening combined with biological characteristics unique to Asian population may be advantageous to avoid T-wave oversense; and (3) SMART Pass, a 9 Hz high-pass filter was introduced in Japan shortly after launching the S-ICD in 2016. As a result, Japanese S-ICD patients have arguably been less exposed to the older non-SMART Pass enabled system, which is associated with four-fold higher likelihood of T-wave oversensing-induced IAS than the newer SMART Pass enabled system.101

Our study also indicates that being free from T-wave oversensing did not result in a reduced IAS incidence. Despite an adequate screening, which was useful for T-wave oversensing prevention, IAS due to myopotential oversensing continues to occur with the onset spreading over the study period (Figure 1B), which further leads to an assumption that it is difficult to determine who may suffer from myopotential oversense but also when the myopotential noise results in an IAS.

Although right-sided S-ICD lead position was associated with a higher risk of myopotential-induced IAS, the detailed mechanisms and external validity of the finding remain unclear because of the small size and the retrospective and observational design of this present study. Thus, this must be interpreted with caution. Indeed, among the four myopotential-IAS patients, right-sided lead did not result in distinguishably smaller R-wave amplitude compared to left-sided implantation in each vector (Table II). Rather, not only right-sided lead but also left-sided lead implantation ended up modestly lower R-wave amplitude over time in IAS group compared to the non-IAS group (Table II). Moreover, in two of the three IAS patients with right-sided S-ICD lead implant, the sensing vectors susceptible to clinically relevant myopotential were primary and secondary, which should involve the location of S-ICD generator rather than that of the lead (#11, #12 in Table II). Until this finding is validated by a larger, less bias-susceptible study, the possibility that patients with S-ICD leads implanted along the right sternal border may be at a higher risk of myopotential-induced IAS remains speculative.

What can we do to avoid myopotential-related IAS?: By systemic examination of the corresponding S-ECG and EGM parameters, we were able to determine that the preoperative ECG screening was predictive of future postoperative R-wave amplitude (Figure 4A). However, the S-ECG did not predict the postoperative T-wave amplitude (Figure 4B, C). We went on to find that average R-wave and T-wave amplitude and R/T ratio in each vector remained stable over time after discharge in both overall and IAS experienced subgroups (Table III). Although it was not consistently significant, R-wave amplitude in IAS group appeared lower than that in non-IAS group (Figure 3). These observations suggest, but not probe, that it is the high noise level rather than time-dependent deterioration in S-ECG/EGM parameters that causes myopotential-induced IAS. In other terms, the R-wave amplitude is the only predictable and controllable parameters before implanting an S-ICD to a new patient, highlighting the importance of preoperative search for high R-wave amplitude to minimize the risk of the myopotential-induced IAS.

In our study, the majority of myopotential IAS in-
volved primary and secondary vectors. Our hypothesis is that *Latissimus dorsi* and *musculus serratus anterior*, the large muscle surrounding an S-ICD device, tend to create clinically troubling myopotential from daily activities. This finding also emphasizes the importance of alternate vector, of which two responsible electrodes are away from *Latissimus dorsi* and *musculus serratus anterior*, as a backup when primary and secondary signals are contaminated by myopotential. However, we do not recommend the routine use of alternate vector in all S-ICD patients for “primary prevention” because of the downside of this technique, i.e., if the vector is manually set to alternate (or any), SMART Pass will be automatically turned off; and it will never be available again until we give up the manual setting; further, it remains unclear whether the benefit of doing so outweighs the risk. Thus, manual fixation to alternate (or others) is recommended for selected patients for secondary prevention.

Although myopotential noise level cannot be foreseen by preoperative screening, “stress test” shortly after surgery can be considered a possible strategy that can assess this risk; with an S-ICD system implanted, each patient is asked to perform the commonly troubling activities such as raising left arms, side plank, and abdominal crunch with the shock delivery being temporally turned off. Prominent myopotential during this test should prompt immediate consideration for preventive measures such as avoiding the affected vector(s) and patient education even though the provoked noise may not necessarily be marked as “noise” during the test due to the complex tachycardia detection algorithm. Besides, which vector is most/least vulnerable to myopotential noise can also be assessed. The feasibility of this idea is supported by a recent report that myopotential can be reportedly induced by exercise test in nearly all S-ICD patients, if not all the provoked myopotentials are recognized as a tachycardia. 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. The effectiveness of this “stress test” should be evaluated in future research.

Exercise test may be beneficial in the context of myopotential-induced IAS by thorough reassessment of device setting including re-acquiring the in-device EGM template. It is of interest whether the exercise stress test can effectively reduce the risk of myopotential-induced IAS; furthermore, this idea warrants a future study. A recent case report suggests the usefulness of lead revision in a patient with myopotential oversensing-induced IAS, which may be a crucial bailout strategy. This finding also emphasizes the importance of alternate vector, of which two responsible electrodes are away from *Latissimus dorsi* and *musculus serratus anterior*, as a backup when primary and secondary signals are contaminated by myopotential. However, we do not recommend the routine use of alternate vector in all S-ICD patients for “primary prevention” because of the downside of this technique, i.e., if the vector is manually set to alternate (or any), SMART Pass will be automatically turned off; and it will never be available again until we give up the manual setting; further, it remains unclear whether the benefit of doing so outweighs the risk. Thus, manual fixation to alternate (or others) is recommended for selected patients for secondary prevention.

In conclusion, we found that the IAS occurred at up to 9.8% during the mean observational period of ~2 years in our cohort, which seems comparable to those in previous studies. Instead of T-wave oversensing, myopotential noise caused IAS in most patients, which sharply contrasts with the studies in the Western societies. This present study underscores the importance of vigorous search for high R-wave during the preoperative screening, particularly in the alternate vector, which tends to be least vulnerable to myopotential noise. To reduce the future risk of myopotential-induced IAS, the “stress test” mimicking commonly troubling activities with the shock delivery being temporally turned off in an early stage of postoperative period may be considered.

**Acknowledgments**

We would like to thank our device nurses Risa Kanai and Yoshitaka Terasaki who supported our research as in-
dispensable members of the patient care team. We are also grateful to medical engineer team of SIMU led by Shinji Yokoyama.

Disclosure

Conflicts of interest: None.

Author contributions: K.T. performed data analysis and wrote the manuscript. K.T., S.A., H.M., M.T., S.T., H.S., Y.I., and R.K. were responsible for patient care, including surgery and outpatient follow-up. K.T., R.K., and Y.I. were responsible for data classification as independent reviewers of shock events. S.N., S.I., T.M., and K.M. critically reviewed the manuscript. All authors approved the manuscript upon submission.

References

1. Kurita T, Nogami A, Abe H, et al. 2018 JCS/JHRS Guideline on Non-Pharmacotherapy of Cardiac Arrhythmias. Available at: https://www.j-circ.or.jp/cms/wp-content/uploads/2018/07/JCS2018_kurita_nogami191120.pdf. Accessed August 4, 2020.
2. Nishii N, Tachibana M, Morimoto Y, et al. Initial experience with the subcutaneous implantable cardioverter-defibrillator in a single Japanese center. J Arrhythm 2017; 33: 338-41.
3. Sasaki S, Tomita H, Tsurugi T, et al. Safety and efficacy of subcutaneous cardioverter defibrillator in patients at high risk of sudden cardiac death- primary Japanese experience. Circ J 2018; 82: 1546-51.
4. Boersma I, Barr C, Knops R, et al. Implant and midterm outcomes of the subcutaneous implantable cardioverter-defibrillator registry: The EFFORTLESS study. J Am Coll Cardiol 2017; 70: 830-41.
5. Burke MC, Gold MR, Knight BP, et al. Safety and efficacy of the totally subcutaneous implantable defibrillator: 2-year results from a pooled analysis of the IDE study and EFFORTLESS Registry. J Am Coll Cardiol 2015; 65: 1605-15.
6. Lambiase PD, Barr C, Theuns DA, et al. Worldwide experience with a totally subcutaneous implantable defibrillator: Early results from the Effortless S-ICD Registry. Eur Heart J 2014; 35: 1657-65.
7. Kawabata M, Goya M, Sasaki T, et al. Surface electrocardiogram screening for subcutaneous implantable cardioverter-defibrillators in Japanese patients with and without Brugada syndrome. Circ J 2017; 81: 981-7.
8. Groh CA, Sharma S, Pelchovitz DJ, et al. Use of an electrocardiographic screening tool to determine candidacy for a subcutaneous implantable cardioverter-defibrillator. Heart Rhythm 2014; 11: 1361-6.
9. León Salas B, Trujillo-Martín MM, García García J, et al. Subcutaneous implantable cardioverter-defibrillator in primary and secondary prevention of sudden cardiac death: A meta-analysis. Pacing Clin Electrophysiol 2019; 42: 1253-68.
10. Theuns DAMJ, Brouwer TF, Jones PW, 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.
11. Brisben A. How the S-ICD (subcutaneous implantable cardiac defibrillator) senses cardiac signals to minimize cardiac oversensing and maximize rhythm discrimination. J Electrocardiol 2018; 51: S38-43.
12. van den Bruck JH, Sultan A, Plenge T, et al. Incidence of myopotential induction in subcutaneous implantable cardioverter-defibrillator patients: Is the oversensing issue really solved? Heart Rhythm 2019; 16: 1523-30.
13. Kooiman KM, Knops RE, Olde Nordkamp L, Wilde AA, de Groot JR. Inappropriate subcutaneous implantable cardioverter-defibrillator shocks due to T-wave oversensing can be prevented: Implications for management. Heart Rhythm 2014; 11: 426-34.
14. Sasaki T, Nakamura K, Naito S. Subcutaneous implantable cardioverter defibrillator lead repositioning for preventing inappropriate shocks due to myopotential oversensing in a post-fulminant myocarditis patient. Int Heart J 2019; 60: 466-9.
15. Noel A, Ploux S, Bulliard S, et al. Oversensing issues leading to device extraction: When subcutaneous implantable cardioverter-defibrillator reached a dead-end. Heart Rhythm 2020; 17: 66-74.
16. OECD. Obesity. Update 2017; 2017. Available at: http://www.oecd.org/health/obesity-update.htm. Accessed February 1, 2020.