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SHORT COMMUNICATION

Impact of electrocardiogram screening during drug challenge test for the prediction of T-wave oversensing by a subcutaneous implantable cardioverter defibrillator in patients with Brugada syndrome

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Abstract Screening tests conducted at rest may be inadequate for the prediction of the T-wave oversensing (TWOS) in subcutaneous implantable cardioverter defibrillator (S-ICD) candidates with Brugada syndrome (BrS) because of the dynamic nature of electrocardiogram (ECG) morphology. We evaluated the utility of ECG screening during drug challenge (DC) for prediction of TWOS in BrS patients implanted with an S-ICD. The study enrolled 6 consecutive BrS patients implanted with an S-ICD. In addition to baseline ECG screening, pre-implant screening during DC using a sodium channel blocker was performed in all patients. All patients underwent appropriate morphological analysis on baseline ECG screening; however, 2 BrS patients (33%) showed inappropriate sensing during DC. During 243 days of follow-up after S-ICD implantation, no patient experienced an appropriate shock. TWOS was confirmed during exercise testing in one of 2 patients who showed inappropriate sensing during DC. However, one patient with appropriate sensing during DC experienced recurrent episodes of inappropriate shocks due to TWOS during exercise. The present initial experience indicates that further studies are needed to detect the risk for TWOS from an S-ICD in BrS patients.

Keywords Brugada syndrome · Subcutaneous implantable cardioverter defibrillator · T-wave oversensing · Drug challenge test

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Introduction

Implantable cardioverter defibrillator (ICD) deployment is considered the main therapy in high risk patients with Brugada syndrome (BrS). The transvenous ICD (TV-ICD) has been associated with high complication rates in BrS patients fitted with an ICD [1, 2]. The subcutaneous implantable cardioverter defibrillator (S-ICD) can be an effective alternative to the conventional TV-ICD system in patients with BrS [3, 4]. However, the S-ICD uses morphology-based rhythm discrimination, and is susceptible to T-wave oversensing (TWOS), resulting in inappropriate shocks (IASs) [4]. A screening electrocardiogram (ECG) of an S-ICD can change from appropriate to inappropriate on a drug challenge test [5–9], which may lead to inadequate sensing of the S-ICD system.

Herein, we report our initial experience of S-ICD implantation in BrS patients with a drug provocation test for prediction of TWOS.

Materials and methods

Study population

This study involved 6 consecutive BrS patients implanted with an S-ICD, who were admitted to the National Cerebral and Cardiovascular Center (Suita, Japan) between February and December 2016.

BrS was diagnosed by the presence of type 1 ST-segment elevation, occurring spontaneously or after intravenous administration of a sodium channel blocker, in ≥1 right precordial leads (V_1 and V_2) placed in a standard or a superior position (up to the 2nd intercostal space) [10]. Type 1 ECG was defined as a coved-type J-point or ST elevation of ≥2 mm, followed by a negative T-wave

[11]. No patients had structural heart disease, including arrhythmogenic right ventricular cardiomyopathy. This study was approved by the Institutional Research Board of the National Cerebral and Cardiovascular Center.

Pre-implant ECG screening

All patients underwent ECG screening before S-ICD implantation at baseline and during a drug provocation test, and were found suitable for S-ICD implantation on the basis of the baseline ECG screening. The screening ECG was obtained by recording from the location of the 3 sensing electrodes of the S-ICD (can: in the fifth intercostal space along the left mid-axillary line, proximal electrode: 1 cm lateral to the left sternal border and 1 cm above the xiphoid process, distal electrode: 14 cm cranial to proximal electrode on the left parasternal line), and mimicked the sensing vectors used by the S-ICD in a standard left parasternal lead position: Leads I, II, and III corresponded to the alternate (distal electrode to proximal electrode), secondary (distal electrode to can), and primary (proximal electrode to can) vectors of the S-ICD, respectively. Pre-implant screening is judged to be effective if at least one vector consistently falls within the designated area throughout a 10-s period in both supine and standing positions. Three BrS patients underwent a screening test during the exercise test (case 2, 3, 5).

Drug provocation tests were conducted with pilsicainide (up to 1 mg/kg body weight injected at a rate of 5–10 mg/min) during standard and high costal (second and third) ECG recordings in the right precordial leads (V_1–V_3). All ECGs were recorded at 25 mm/s and 10 mm/mV. After independent analyses of ECG recordings by two cardiologists (T.K. and K.K.), a consensus was reached on each patient's diagnosis.

Implantation and device programming

All patients underwent the procedure under general anesthesia. The S-ICD (EMBLEM, Boston Scientific, Marlborough, MA, USA) was successfully implanted on the left side of the thorax using a standard technique. A defibrillation test was successfully performed with a shock of 65 J in all patients.

After implantation, automatic setup was performed, the automatically chosen sensing vector was programmed, and a QRS morphology template was also acquired. The S-ICD was programmed with 2 zones, which provided morphologic discrimination of events with rates in the conditional shock zone (≥200 beats/min). Detection cutoff rate for VF was 220 beats/min. SMART Pass filter software upgrade was applied from December 2016.

Follow-up

Clinical data were collected from all patients, including age, sex, and family history of sudden cardiac death at <45 years of age. Patients were routinely followed up 1 and 3 months after S-ICD implantation, and thereafter semiannually for device interrogation. An exercise test was performed to optimize the sensing vector of the S-ICD at one month follow-up.

Statistical analysis

Data were analyzed with JMP10 software (SAS Institute Inc., Cary, NC, USA). Numeric values are presented as the mean ± standard deviation (SD).

Results

Clinical characteristics of the study population

The clinical characteristics of the 6 BrS patients (6 male, mean age at diagnosis: 35.8 ± 9.1 years) are shown in Table 1. All patients underwent appropriate morphological analysis at baseline. However, during a drug provocation test with a sodium channel blocker, all sensing vectors became unacceptable in 2 BrS patients (cases 4, 5) (Table 2). Fewer sensing vectors were appropriate with an appearance of type 1 ECG during drug challenge.

Table 1 Clinical characteristics

Case	Age (years)	Sex	Type 1 ECG	Symptom	FH of SCD	VF induction by EPS
1	51	M	Spontaneous	Asymptomatic	+	+
2	30	M	Spontaneous	Asymptomatic	−	+
3	34	M	Spontaneous	Asymptomatic	+	+
4	41	M	Spontaneous	Asymptomatic	−	+
5	34	M	Spontaneous	Syncope	−	+
6	25	M	Drug-induced	Syncope	+	+

ECG electrocardiogram, *EPS* electrophysiological study, *FH of SCD* family history of sudden cardiac death at less than 45 years of age, *M* male, *VF* ventricular fibrillation

After implantation, automatic setup of the S-ICD chose vectors which were considered inappropriate during pre-implant screening in 3 of 6 patients (50%) (cases 1, 5, 6) (Table 2). During 243 ± 90 days of follow-up, no patients had appropriate therapy due to ventricular fibrillation. One patient (case 1) experienced IASs due to TWOS during exercise 1 month after S-ICD implantation, which occurred before evaluation of the post-implant exercise test (Fig. 1a; Table 2). In this case, the secondary vector was selected as the optimal sensing vector based on automatic setup after implantation because it was uncertain whether we should select the vector which was considered appropriate at the pre-implant screening or which was automatically selected after implantation, although the primary vector was the only acceptable sensing vector on preoperative ECG screening both at baseline and during drug challenge (Fig. 1b). TWOS was confirmed during the exercise test in the primary and secondary vectors (Fig. 1c). Therefore, the sensing vector was reprogrammed to the alternate vector and a QRS template at peak exercise was acquired. However, this patient again experienced an IAS due to TWOS during exercise in the alternate vector (Fig. 1d). In this patient, TWOS was successfully managed with SMART Pass filter (Fig. 1e). He has not experienced IASs due to TWOS for 3 months.

Among 2 patients who showed inappropriate sensing during drug challenge, TWOS was confirmed during the exercise test in one patient (case 4). In this case, the secondary and alternate vectors were appropriate at pre-implant ECG screening, and all vectors became unacceptable during the drug challenge (Fig. 2a). Automatic setup after implantation selected the secondary vector as the optimal sensing vector. However, TWOS was transiently observed in a few beats in the secondary vector at peak exercise during the exercise test (Fig. 2b). In this case, a drug provocation test could identify a patient considered at high risk of TWOS. Another patient (case 5) has experienced no TWOS to date.

Discussion

To date, the safety and efficacy of S-ICD in patients with BrS remain unknown. This study showed that TWOS was observed during exercise in 33% of BrS patients in the vectors judged as optimal at the pre-implant ECG screening and post-implant automatic setup.

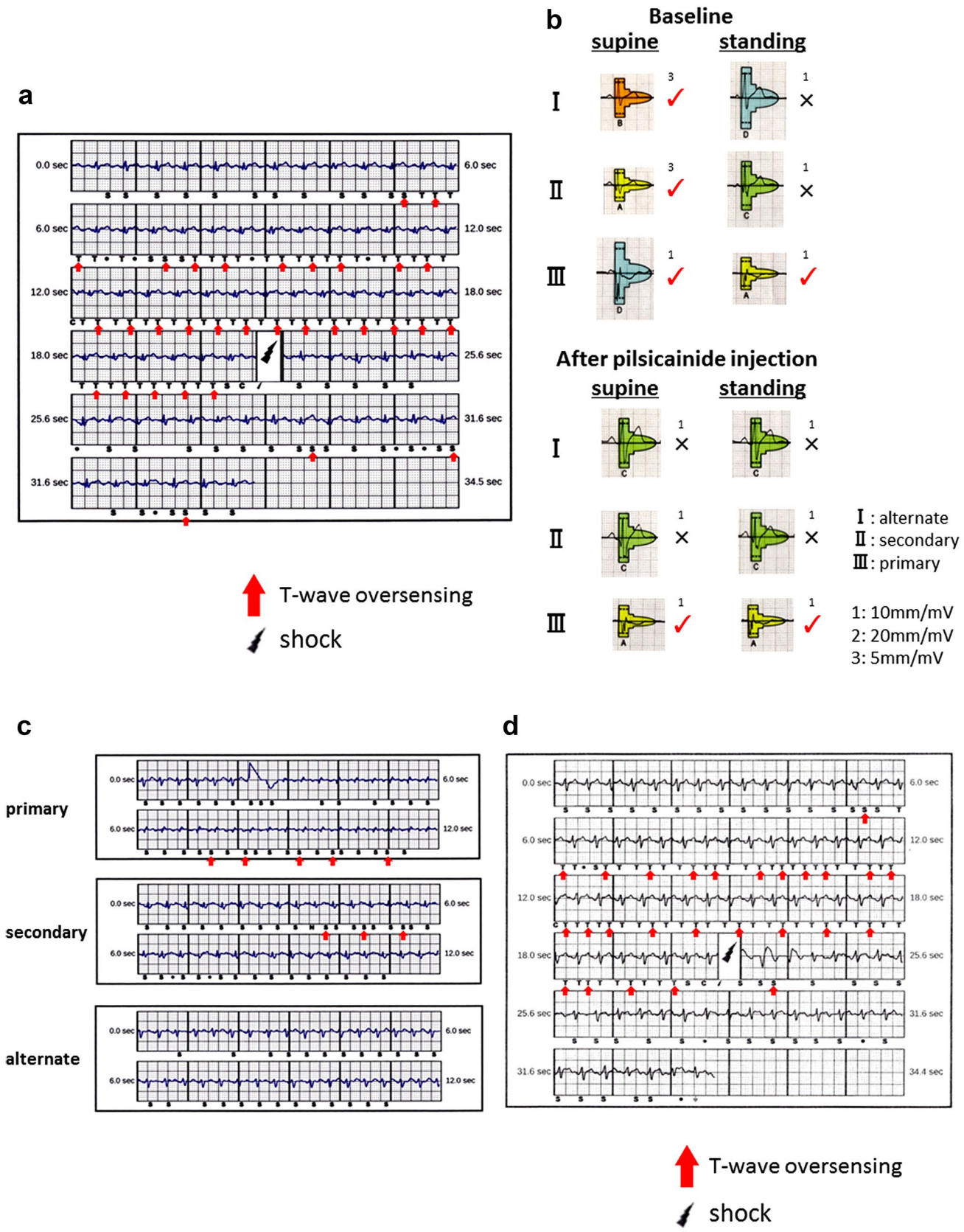
Olde Nordkamp et al. reported that the screening ECG of the S-ICD could become inappropriate with an appearance of type 1 Brugada-pattern ECG by drug provocation test in 24% of BrS patients [7]. It is considered that the drug test can evaluate the appropriateness of the S-ICD indication in BrS patients. However, no data exist to confirm the usefulness of pre-implant ECG screening during drug provocation tests in identifying patients at high risk of TWOS. This study showed that such tests could appropriately detect a patient at high risk of TWOS as shown in case 4 above. However, there was a case in which TWOS was unpredictable even with use of the drug provocation test (case 1). Conversely, the vectors judged to be inappropriate during drug challenge could be safely used as shown in case 5. ECG screening during drug challenge showed 50% sensitivity and 75% specificity to identify TWOS in BrS patients implanted with an S-ICD. It may be difficult to decide on S-ICD indications based on the results of ECG screening during drug challenge.

Post-implant exercise testing is considered essential for evaluating the presence of TWOS during exercise [12]. In this study, a post-implant exercise test revealed

Table 2 Follow-up data

Case	Pass vector pre-implant screening	Pass vector during drug test	Pass vector during exercise test	Automatically selected vector after implantation	TWOS during post-implant exercise test	Appropriate therapy	Inappropriate therapy due to TWOS
1	III	III	–	II	I, II, III	–	+
2	III	III	III	III	None	–	–
3	III	III	III	III	None	–	–
4	I, II	None	–	II	II	–	–
5	III	None	III	I	None	–	–
6	III	III	–	II	None	–	–

I alternate, *II* secondary, *III* primary, *TWOS* T-wave oversensing


a
0.0 sec
6.0 sec
12.0 sec
18.0 sec
25.6 sec
31.6 sec
34.5 sec
T-wave oversensing
shock
b
Baseline
supine
standing
After pilsicainide injection
supine
standing
I : alternate
II : secondary
III : primary
1: 10mm/mV
2: 20mm/mV
3: 5mm/mV
c
primary
secondary
alternate
d
34.4 sec
T-wave oversensing
shock

◀**Fig. 1** **a** TWOS (*red arrow*) occurred and led to an IAS during exercise 1 month after S-ICD implantation in the secondary vector, which was chosen by automatic setup of the S-ICD. **b** Only lead III was acceptable at baseline. After 50-mg pilsicainide injection, leads I and II in the supine position became inappropriate due to augmentation of the T-waves. Lead III remained appropriate. **c** TWOS (*red arrow*) was observed during exercise testing in the primary and secondary vector, but not in the alternate vector. During the exercise test, a QRS morphology template in the alternate vector was acquired at peak exercise. **d** Five months after reprogramming during exercise testing, TWOS (*red arrow*) re-occurred in the alternate vector during exercise, and led to an IAS. **e** Exercise test was performed again before and after SMART Pass filter software upgrade was applied. Although TWOS was confirmed in all sensing vectors at peak exercise before SMART Pass filter was applied, it disappeared in the alternate vector after SMART Pass filter was applied

TWOS in 2 of 6 patients (33%) with BrS. The post-implant management with exercise test and SMART Pass filter is useful to avoid TWOS in BrS patients implanted with an S-ICD.

We recognize several limitations. The small sample size may limit interpretation of the utility of drug provocation and exercise tests. Nevertheless, no study has been undertaken to date to assess the utility of ECG screening during drug provocation testing in BrS patients implanted with an S-ICD. Further studies with larger numbers of patients will be needed to confirm the results of this study.

Conclusions

It may be difficult to decide on S-ICD indications based on the results of ECG screening during drug challenge. However, BrS patients are potentially excellent candidates for an S-ICD given their young age at implantation, and without the need for anti-tachycardia or anti-bradycardia pacing. Pre- and post-implant managements that can reduce the risk of inappropriate sensing are essential. In addition to the pre- and post-implant exercise testing and use of SMART Pass filter, lifestyle education such as avoiding drugs that unmask type 1 ECG and treating febrile illness promptly would be useful. Further studies are needed to detect the risk for TWOS from an S-ICD in BrS patients.

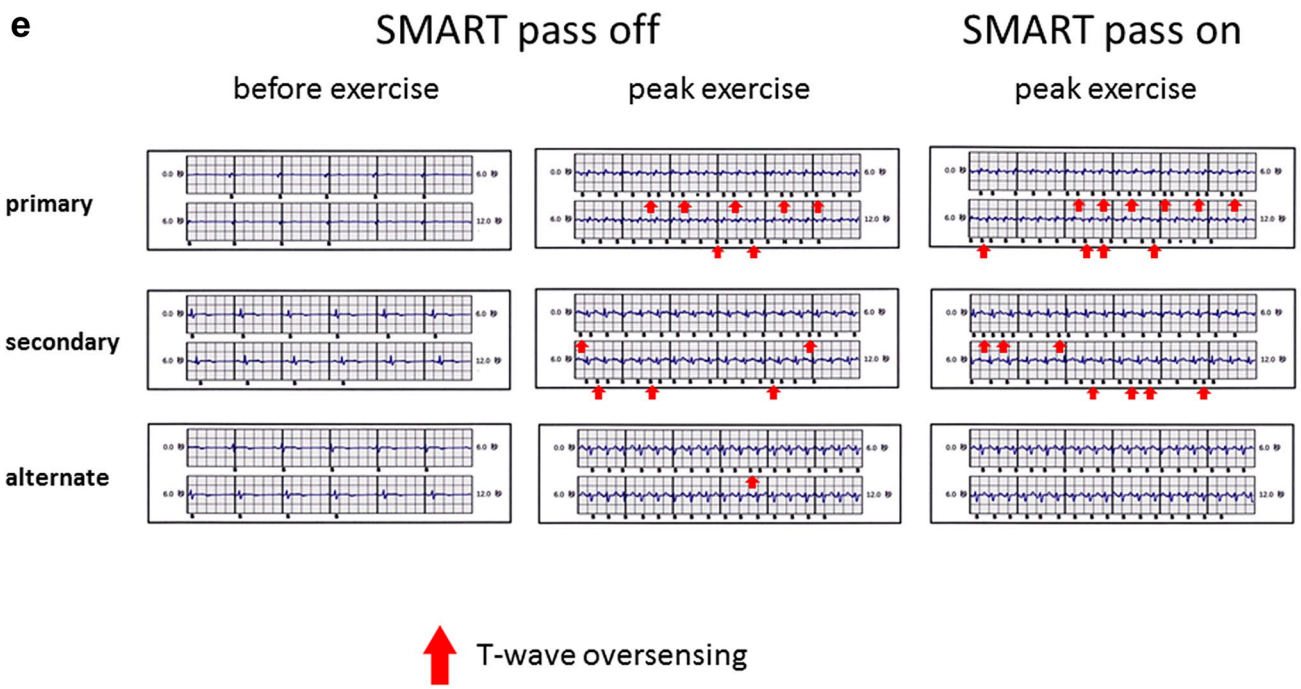


Fig. 1 continued

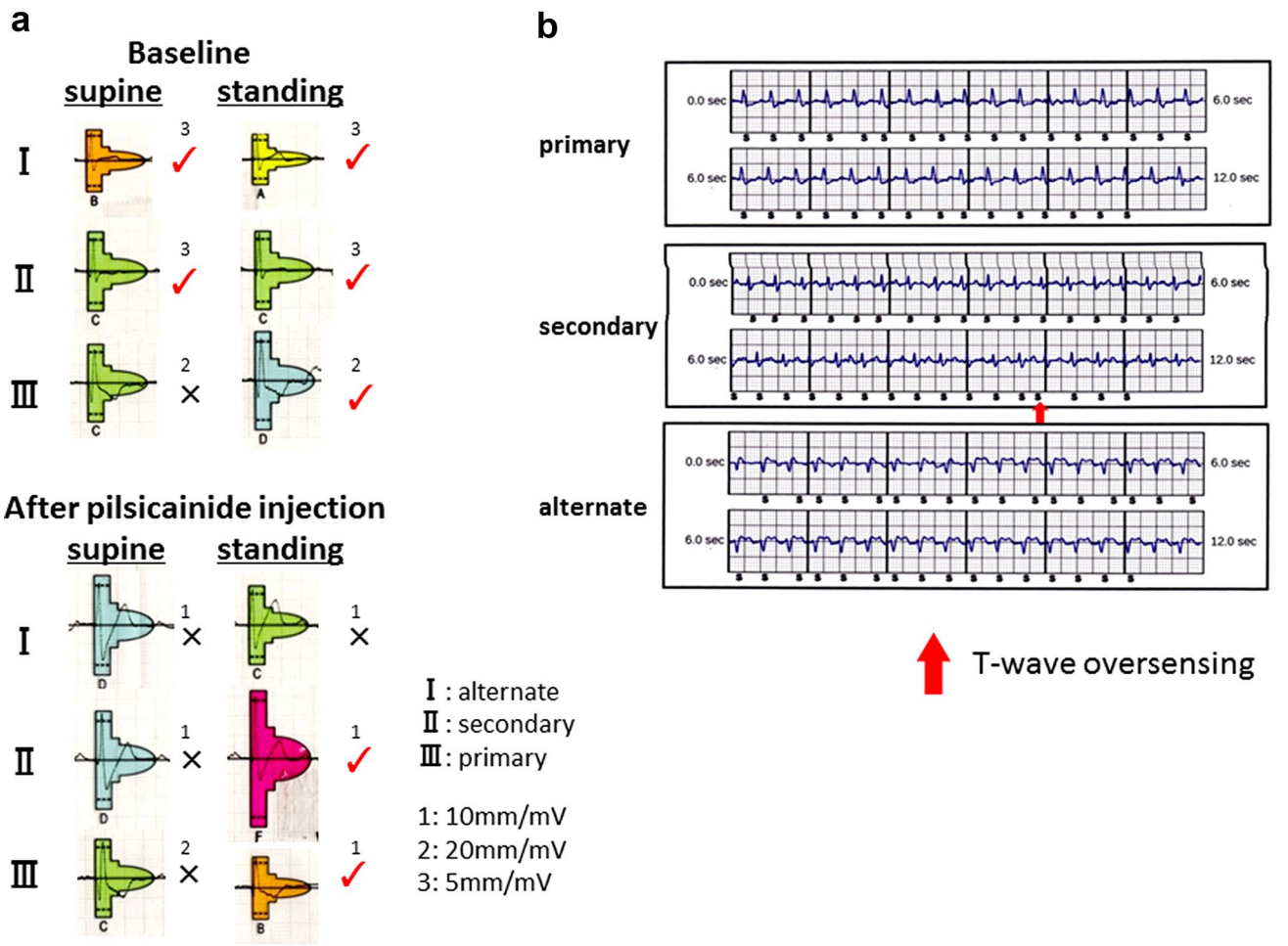


Fig. 2 **a** Lead I and II were appropriate at pre-implant ECG screening, and all vectors became unacceptable during the drug challenge. **b** Automatic setup after implantation chose the secondary vector as the optimal sensing vector. However, TWOS was transiently observed in few beats in the secondary vector at peak exercise during the exercise test

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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