Surface Electrocardiogram Screening for Subcutaneous Implantable Cardioverter-Defibrillators in Japanese Patients With and Without Brugada Syndrome

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Background: Subcutaneous implantable cardioverter-defibrillators (S-ICD) could eliminate lead-associated complications. We assessed the prevalence of S-ICD ineligibility in conventional ICD recipients and compared it in patients with and without Brugada syndrome (BrS).

Methods and Results: Consecutive patients with a transvenous ICD without an indication for antibradycardia pacing were assessed. A patient was considered eligible for S-ICD if the ECG satisfied the screening template, both supine and standing, in ≥1 lead. Among 130 patients (103 men, age 57 ± 15 years), a total of 18 (13.8%) patients were ineligible. The BrS group (n=33) had a significantly higher prevalence of S-ICD screening failure as compared with the non-BrS group (P=0.003; 30% vs. 8.2%). In the BrS group, the body mass index (BMI) was significantly lower, and T/QRS amplitude in lead I was significantly higher in those who were ineligible than that in the patients who were eligible. Of the 10 BrS patients failing the screening, 4 became eligible in the right parasternal electrode position.

Conclusions: Among current ICD patients, there was a high incidence of patients with BrS who were unsuitable for S-ICD based on the left parasternal screening test. Suitability screening of patients for S-ICDs should be conducted carefully in patients with BrS, particularly if the BMI is low. Right parasternal electrode positioning should also be tested in such BrS patients.

Key Words: Body mass index; Brugada syndrome; Subcutaneous implantable cardioverter-defibrillator; Surface ECG screening

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require formal patient consent.

**Screening for S-ICD Eligibility**

The Boston Scientific ECG screening tool was used to determine eligibility for S-ICD in 2 different postures: supine and standing. As recommended by Boston Scientific, ECG recordings simulating the 3 sensing vectors of the S-ICD were analyzed. The electrode left leg (LL) was placed in the 5th intercostal space along the left mid-axillary line, electrode left arm (LA) was placed 1 cm lateral to the left sternal border and 1 cm above the xiphoid process, and the electrode right arm (RA) was placed 14 cm cranial to electrode LA on the left parasternal line (Figure 1). A ground electrode was placed on the right lower extremity. The bipolar vector lead I was derived from the RA and LA, lead II from the RA and LL, and lead III from the LA and LL, corresponding to the alternate, secondary, and primary sensing vectors of the S-ICD, respectively. A patient was considered a candidate for S-ICD implant if at least 1 lead satisfied the S-ICD screening template in both positions. In the BrS group, the screening protocol was repeated after moving the sternal electrodes (electrodes RA and LA) on the right parasternal line, with electrode LA at 1 cm lateral the right sternal border and 1 cm above the xiphoid process, and electrode RA at 14 cm superior to electrode LA (Figure 1), when the left parasternal sensing electrode position test failed.

**Surface 12-Lead ECG Analysis**

We measured the QRS axis and the T-wave axis on the

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**Table 1. Characteristics of Patients Undergoing ECG Screening for S-ICD Eligibility**

<table>
<thead>
<tr>
<th></th>
<th>Total (n=130)</th>
<th>BrS group (n=33)</th>
<th>Non-BrS group (n=97)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57±15</td>
<td>55±14</td>
<td>58±16</td>
<td>0.34</td>
</tr>
<tr>
<td>Male</td>
<td>103 (79)</td>
<td>29 (88)</td>
<td>74 (76)</td>
<td>0.16</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.65±0.09</td>
<td>1.66±0.07</td>
<td>1.65±0.09</td>
<td>0.75</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>66±14</td>
<td>64±12</td>
<td>66±15</td>
<td>0.48</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.8±4.4</td>
<td>23.2±3.5</td>
<td>24.1±4.7</td>
<td>0.329</td>
</tr>
<tr>
<td>Hypertension</td>
<td>34/96</td>
<td>21/12</td>
<td>13/84</td>
<td>0.0000006</td>
</tr>
<tr>
<td>Primary/secondary prevention</td>
<td>52 (40)</td>
<td>13 (39)</td>
<td>39 (40)</td>
<td>0.55</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-blockers</td>
<td>65 (50)</td>
<td>3 (9)</td>
<td>62 (64)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Antiarrhythmic drugs</td>
<td>64 (50)</td>
<td>10 (30)</td>
<td>54 (56)</td>
<td>0.021</td>
</tr>
<tr>
<td>QRS width (ms)</td>
<td>121±42</td>
<td>118±22</td>
<td>122±47</td>
<td>0.65</td>
</tr>
<tr>
<td>QTc interval</td>
<td>441±44</td>
<td>415±33</td>
<td>450±44</td>
<td>0.0003</td>
</tr>
<tr>
<td>QRS axis (degrees)</td>
<td>20±46</td>
<td>31±48</td>
<td>16±47</td>
<td>0.12</td>
</tr>
<tr>
<td>T-wave axis (degrees)</td>
<td>39±61</td>
<td>40±24</td>
<td>39±70</td>
<td>0.87</td>
</tr>
<tr>
<td>Angle between QRS and T axes (degrees)</td>
<td>61±54</td>
<td>36±40</td>
<td>70±56</td>
<td>0.0001</td>
</tr>
<tr>
<td>T/QRS amplitude in lead I</td>
<td>0.34±0.31</td>
<td>0.45±0.27</td>
<td>0.31±0.31</td>
<td>0.02</td>
</tr>
<tr>
<td>T/QRS amplitude in lead II</td>
<td>0.46±0.11</td>
<td>0.73±0.12</td>
<td>0.37±1.0</td>
<td>0.09</td>
</tr>
<tr>
<td>T/QRS amplitude in lead aVF</td>
<td>0.32±0.26</td>
<td>0.50±0.38</td>
<td>0.26±0.17</td>
<td>0.001</td>
</tr>
<tr>
<td>UCG</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>57±15</td>
<td>67±6</td>
<td>54±15</td>
<td>0.0002</td>
</tr>
<tr>
<td>LVd (mm)</td>
<td>51±10</td>
<td>45±4</td>
<td>53±10</td>
<td>0.0001</td>
</tr>
<tr>
<td>Xp</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTR (%)</td>
<td>46±7</td>
<td>43±5</td>
<td>47±8</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Values are shown as the mean±SD, or n (%). BMI, body mass index; BrS, Brugada syndrome; CRT, cardiothoracic ratio; ECG, electrocardiogram; LVDd, left ventricular internal dimension in diastole; LVEF, left ventricular ejection fraction; QTc, corrected QT; S-ICD, subcutaneous implantable cardioverter-defibrillators; UCG, ultrasound cardiography; Xp, X-ray photograph.
**Figure 2.** Example of surface ECG screening in a patient with Brugada syndrome. With variation of the type 1 Brugada ECG, the screening test changed from inappropriate (A) to appropriate (B). In both panels, the left ECG shows leads V1–3 of the 12-lead ECG and the right ECGs show the screening vectors of leads I–III in the supine and standing positions.

**Figure 3.** Example of surface ECG screening of another patient with Brugada syndrome. Although the ECG showed the type 1 Brugada ECG, the screening test was inappropriate (A). It was appropriate with the normal ECG (B). In both panels, the left ECG shows leads V1–3 of the 12-lead ECG and the right ECGs show the screening vectors of leads I–III in the supine and standing positions.
patient's most recent 12-lead surface ECG. The angle between the 2 vectors was evaluated as the absolute value of the minor angle. Leads I, II, and aVF were analyzed because they mimic the 3 sensing vectors of the S-ICD. The data for the T/QRS amplitude ratio in each of the 3 leads were collected. All ECGs were analyzed by 2 independent electrophysiologists. Reasons for failure were recorded for every analyzed vector and categorized into high T-wave voltages and high/low QRS complex voltages.

**Statistical Analysis**

Normally distributed continuous variables are expressed as the mean±SD, and as number and percentages for categorical variables. The differences between the continuous variables were assessed using Student’s t-test or the Mann Whitney U test. Categorical variables were compared using the chi-squared test, or Fisher’s exact test when the data were very unequally distributed among the cells of the contingency table being below 5. A multivariable logistic regression analysis was performed to identify the independent clinical predictors of S-ICD ineligibility in the BrS group. Statistical significance was defined as P<0.05. SPSS statistical software (v22, SPSS Inc., Chicago, IL, USA) was used for all analyses.

**Results**

**Study Population**

A total of 130 consecutive patients (103 men, age 57±15) satisfied our entry criteria. Of them, 33 patients had BrS (25%). The remaining 97 patients in the non-BrS group consisted of 28 patients with ischemic heart disease, 20 with hypertropic cardiomyopathy (HCM), 16 with idiopathic ventricular fibrillation (VF), 9 with dilated cardiomyopathy, 5 with sarcoidosis, and 19 miscellaneous. The indication for ICD implantation was primary prevention in 26.2% and secondary prevention in 73.8% of patients. In the BrS group, 12 subjects (36%) had a previous episode of aborted sudden death and 7 (22%) had syncope; 28 patients with BrS (85%) presented with type 1 ECG spontaneously, while the remaining 5 showed type 1 ECG only after the infusion of pilosicainide, a pure sodium-channel blocker.

Patient characteristics are summarized in Table 1. There were no differences in the demographics and comorbidities of the BrS and non-BrS patients. However, the BrS group had significantly more patients with ICD for primary prevention, shorter QTc interval, smaller angle between the QRS and T axes, and larger T/QRS amplitude ratio in leads I and aVF compared with the non-BrS group. In the ultrasound characteristics, the BrS group had significantly better left ventricular ejection fraction (LVEF) and smaller LV.

**Prevalence of S-ICD Unsuitability**

Overall, a total of 18 (13.8%) patients were ineligible for S-ICD implantation according to the surface ECG screening criteria. The BrS group had a significantly higher prevalence of S-ICD screening failure as compared with the non-BrS group (P=0.003; 10/33 [30%] in BrS vs. 8/97 [8.2%] in non-BrS).

Among a total of 780 sensing vectors (2 positions for each vector), 249 (32%) were considered ineligible in the screening test. The alternate sensing vector was the most frequently ineligible (44%), then the secondary vector (29%), followed by the primary sensing vector (25%). The main reason for failure was high T-wave voltage (82% patients, 90% sensing vectors). The amplitude of the QRS complexes and T waves, and T/QRS amplitude ratio in leads I, II, and aVF of the 12-lead ECG were compared with those in the coupling sensing vectors of the S-ICD screening test, namely, the primary, secondary, and alternate vectors in the supine position. The coefficients of determination of regression lines between the above data of amplitude in each pair were between 0.12 and 0.37, indicating that there was little relevance between ECG morphology in the 12-lead ECG and that in the S-ICD screening test.

In the BrS patients, 100 sensing vectors were ineligible among 198 vectors (51%) because of high T-wave voltage, except for 4 vectors in 2 patients with low QRS complex voltages. As in the total subjects, the alternate sensing vector was the most frequently ineligible (78%), then the secondary vector (58%), and finally the primary sensing vector (36%) in the BrS patients. The prevalence of failure was not different in the alternate sensing vector between the unsuitable and suitable BrS patients (100% vs. 65%; P=0.07), while in the other 2 sensing vectors that was significantly higher in the unsuitable patients than in the suitable patients (100% vs. 9%; P=0.00001, in the primary sensing vector, and 100% vs. 39%; P=0.0014, in the secondary sensing vector).

In the 10 BrS patients who were ineligible for S-ICD
S-ICD Screening Test in BrS

Predictors of Eligibility in BrS

Among the patients with BrS, the clinical characteristics of those who were eligible and those who were ineligible in the usual left parasternal screening were compared (Table 2). BMI was significantly lower (P=0.016; 21.0 vs. 24.1 kg/m²), and the T/QRS amplitude in lead I was significantly higher (P=0.045; 0.60 vs. 0.39) in those who were ineligible than in those who were eligible. There was a trend towards higher LVEF and smaller cardiothoracic ratio (CTR) in the ineligible group. In 31 patients (94%) the 12-lead surface ECG was recorded at the time of S-ICD screening. Among them, the prevalence of type 1 ECG was similar for those who were ineligible or eligible (P=0.88; 3/9 [33%] vs. 8/22 [36%]). Multivariate analysis assessing BMI, T/QRS amplitude in lead I, LVEF, and CTR revealed that nothing remained as an independent predictor. In the non-BrS group, the mean BMI was not different for those who were ineligible or eligible (P=0.51; 24.2 vs. 23.0 kg/m²).

In contrast, there were no significant differences in any characteristics between those who were eligible or ineligible among the BrS patients according to the bilateral parasternal screening test. Of the 4 patients who passed the right parasternal screening after failing the left parasternal screening, the mean BMI was 19.8 kg/m² and the mean T/QRS amplitude in lead I was 0.46.

Discussion

In this study based on our single-center experience, S-ICD screening failure occurred in 13.8% of current ICD recipients and was significantly more frequent in the patients with BrS compared with the non-BrS patients (30% in BrS vs. 8.2% in non-BrS, P=0.003). In the BrS group, the BMI of those who were ineligible was significantly lower than that of patients who were eligible. When the right parasternal screening was assessed together, the prevalence of S-ICD screening failure in the BrS group was minimized from 30% to 18%, which was no longer significantly different from that in the non-BrS group (8.2%, P=0.189).
Prevalence of S-ICD Unsuitability

In the S-ICD, which has a morphology-based sensing algorithm, abnormal QRS complexes and T waves can cause sensing issues, resulting in inappropriate shocks.1–3,12–17 In the EFFORTLESS Registry, 7% of patients received inappropriate shocks because of oversensing of cardiac signals, mainly the T wave.18,19 Currently, a surface ECG screening test is performed to exclude patients who might have inappropriate shocks. The reported prevalence of ineligibility for S-ICD implantation ranges from 7% to 16%.3–9 Olde Nordkamp et al reported that among greater body weight, prolonged QRS duration, R/T ratio <3 on the surface ECG lead with the largest T wave, and HCM, R/T ratio <3 in the lead with the largest T-wave was a strong predictor of failed screening for the S-ICD.4 In a report by Groh et al, T-wave inversion was the only predictor of screening failure.5 Randles et al used the previously recommended 2-vector rule, which requires at least 2 leads to satisfy the S-ICD screening template in both the supine and upright position. They reported a 15% failure rate in an unscreened cardiac patient cohort, with QRS duration as the only predictor of failure.

Although patients with BrS were included in those reports, their numbers ranged from 0% to 3%.3–9 There were very few reports about S-ICD eligibility in BrS patients prior to our study. Olde Nordkamp et al9 found that 0 of the 88 BrS patients had type 1 BrS-ECG at baseline, and the prevalence of ineligibility was 2%. Ajmaline testing evoked type 1 BrS-ECGs in 21 patients and during that testing, 5 patients had inappropriate morphology for S-ICD implantation. Conte et al reported that 61 patients with BrS had a higher rate of inappropriate morphology analysis as compared with other channelopathies (18% vs. 5%, P=0.07) and ajmaline challenge unmasked sensing failure in 14.8% of drug-induced BrS patients previously considered eligible.21

The overall S-ICD screening failure rate in the current ICD recipient was 13.8%, which was similar to previous reports. In contrast, failure in our patients with BrS in the left parasternal electrode positioning was 30%, which was comparable to that in a previous report during type 1 BrS-ECGs.20 and considerably higher than in patients with other diseases requiring an ICD. However, in contrast to the previous reports,20,21 the presentation of type 1 ECG was not related to the ineligibility of S-ICD in our BrS patients.

S-ICD Use for Patients With BrS

In previous reports, BrS was a particular challenge in regard to sensing and detection of VF in conventional ICDs. The characteristic BrS-ECG pattern carries the risk of T-wave oversensing and subsequent inappropriate therapy. Dynamic variations in ECG morphology are a further aspect of Brugada ECGs that complicate VF detection.10,22 T-wave oversensing has been reported as the leading cause of inappropriate shocks by the S-ICD in BrS patients.23

Among our patients, S-ICD eligibility fluctuated between appropriate and inappropriate in some BrS patients because of variation in ECG morphology. Therefore, we recommend multiple evaluations of S-ICD appropriateness in BrS patients to ensure that ECG vector changes do not produce inappropriate shocks.

Our data showed that the BMI of those who were ineligible was significantly lower than that of patients who were eligible with left parasternal electrode positioning in the BrS group, although it did not remain as an independent predictor in the multivariate analysis. In contrast, a report from Europe showed that increased body weight was independently associated with screening failure, but in a general cardiac disease population.6 The mean BMI of their patients was 27 kg/m² and it was speculated that this was potentially because obese patients have smaller R-wave amplitudes related to the subcutaneous fat between the heart and electrode.6 No one has studied the effect of BMI on S-ICD screening test lead ECG morphology per se, but we found 1 study that looked at the BMI effect on the 12-lead ECG® greater BMI led to lower values of R- and T-wave axes, indicating a rightward shift of both. Furthermore, R-wave voltage and T-wave amplitudes appeared to be BMI dependent, although it peaked at a BMI of 18.5 kg/m² and diminished with further increases in weight. In general, the BMI of Japanese is lower than that of Caucasians. Our patients’ mean BMI was 23.8 kg/m², considerably lower than S-ICD screening reports from Western countries whose patients’ mean BMI ranged from 27 to 29 kg/m² (>25 kg/m²). At any rate, there were no significant differences in either the axis or voltage of the R and T waves, except for T/QRS amplitude in lead I, between the eligible and ineligible groups in our study, leaving us with little explanation of why BMI might affect eligibility. We noted that lower BMI was a key feature of eligibility for S-ICD in BrS patients, but was not true of non-BrS patients.

The lead I in the surface ECG mimics the vector of the primary sensing lead, which had the highest prevalence of eligibility among the 3 sensing vectors of the S-ICD.6 The significantly higher T/QRS amplitude in lead I in the ineligible group of BrS patients might contribute to them leaving before undertaking the screening, although we found that there was little relevance between ECG morphology in the 12-lead ECG and that in the S-ICD screening test.

Utility of Right Parasternal Electrode Placement for Patients With BrS

Recently, there were some reports on the usefulness of the right parasternal screening for S-ICD in patients with HCM or congenital heart diseases.8,25,26 In the present study, right parasternal screening also improved the eligibility of patients with BrS. The 4 BrS patients who failed the left parasternal screening test, but passed the right parasternal screening, had significantly lower BMI. Interestingly, no predictive factors for S-ICD screening failure were found in the BrS group with bilateral parasternal screening. In the previous report, although there was no definitive conclusion predicting the patients who might benefit from a right parasternal position, it was speculated that the right parasternal sensing electrode position was further away from the structurally normal heart, and therefore differences appeared more marked compared with the left parasternal sensing position.26 We could not find the electrophysiological mechanisms underlying the improvement in eligibility for S-ICD according to right parasternal electrode placement because of the small number of patients.

Study Limitations

The major limitation is the small sample size. The external validity of our study is limited to the included patient group. Any assessment of eligibility for S-ICD is affected by the population under consideration.

The pre-implant screening assumes that vectors suitable at pre-implant screening fulfill the criteria of the sensing algorithm of the S-ICD when implanted and exclude
patients who fail S-ICD candidacy. The defibrillation ability of S-ICD is beyond the scope of this study.

Conclusions
Among the current cohort of Japanese ICD patients, there was a considerably high incidence of patients with BrS who were unsuitable for S-ICDs based on presently available left-sided screening criteria. The selection of patients for an S-ICD should be done carefully in patients with BrS, particularly if the BMI is low; however, right parasternal electrode positioning might be advantageous in such patients. More work is necessary on the S-ICD sensing algorithms to increase BrS patients’ eligibility for the S-ICD in order to ensure appropriate sensing.

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Funding / Conflict of Interest Statement
None.

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