Complete right bundle branch block and QRS-T discordance can be the initial clue to detect S-ICD ineligibility

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Abstract

Background—In order to minimize inappropriate shocks of subcutaneous implantable cardioverter-defibrillator (S-ICD), it is important to recognize who is suitable for S-ICD indication. This study aimed to clarify what types of cardiac disease are likely to fulfill the S-ICD screening criteria and ineligible factors for S-ICD in the standard 12-lead ECG.

Methods— A total of 348 patients with heart disease were enrolled. They were assessed supine and standing ECG recording to simulate the 3 S-ICD sensing vectors and standard 12-lead ECG, simultaneously. Clinical and ECG characteristics were analyzed to compare the patients who are eligible and ineligible with S-ICD screening ECG indication.

Results—The mean age of study patients was 49±21 years and 244 (70%) were men. Nineteen percent of patients were unsuitable for S-ICD. There was no significant difference in ineligibility for S-ICD among cardiac diseases (p=0.48). Univariate analysis showed complete right bundle branch block (CRBBB), QRS-T discordance in lead II, and QRS-T discordance in 3 leads (I, II, and aVF) were more frequent in patients who were ineligible for S-ICD than in the eligible group. Multivariate regression analysis showed CRBBB and QRS-T discordance in 3 leads were independent predictors for ineligibility of S-ICD.

Conclusion— There are no differences in eligibility of S-ICD among types of cardiac

diseases. CRBBB and QRS-T discordance were independent predictors for ineligibility.

Abbreviations:

ECG=electrocardiogram; ICD=implantable cardioverter-defibrillator;

S-ICD=subcutaneous implantable cardioverter-defibrillator;

CRBBB= complete right bundle branch block; BMI=body mass index;

LVEF=left ventricular ejection fraction; LA=left arm; RA=right arm; LL=left leg;

IRBBB=incomplete right bundle branch block; AF=atrial fibrillation;

SD=standard deviation; IVF=idiopathic ventricular arrhythmia.

Introduction

An implantable cardioverter-defibrillator (ICD) effectively prevents sudden cardiac death when used in primary and secondary preventions[1, 2, 3, 4]. Several serious complications, however, relating to conventional transvenous ICD leads including lead infection, venous thrombosis and cardiac perforation were reported.

Subcutaneous implantable cardioverter-defibrillator (S-ICD) does not require placement of leads directly into the heart, so that S-ICD could keep away from these complications relating to transvenous ICD leads. Moreover, since lead injury is continuously increasing along with an interval after transvenous ICD implantation[5, 6, 7], S-ICD is expected to avoid the troubles concerning cardiac leads. Therefore, S-ICD is more likely to be adapted for use in the younger population because younger patients are expected the longer prognosis. These advantages of S-ICD compared to transvenous ICD suggests an increase in the number of S-ICD implantation in near future.

The most common problem of S-ICD systems in the real world is inappropriate shocks being administered because of T wave oversensing[8, 9]. To avoid this problem, the manufacturer has developed a system to identify patients who are likely to be unsuitable for S-ICD, using supine and standing surface ECG screening templates. Although some investigations have been reported on the eligibility of S-ICD from Western countries, the

type distribution of heart disease is supposed to be different from country to country and among races. Thus, how many patients with heart disease are eligible for S-ICD implants according to this surface ECG screening template in the Asian population including Japan is unclear. In addition, this specific ECG system templates proposed for selection of S-ICD eligibility is uncommon and not convenient for actual clinical practice, parameters derived from the standard 12-lead ECG are expected to eliminate easily unsuitable patients from candidates of S-ICD implantation.

This study aimed to clarify what type of cardiac diseases are more likely to fulfill the surface ECG screening criteria for S-ICD implantation and what parameters obtained with the standard 12-lead ECG can predict ineligibility for S-ICD implantation.

Methods

Patients

The consecutive 450 subjects who need farther examination for heart disease, regardless ICD indication, at Okayama University Hospital from December 2015 to May 2016 were recruited. Following patients were excluded from this study: patients less than 5 years old (n=14), patients without significant heart disease as results of

precise examination (n=32), the patients with paced QRS complex (n=48), patients who were unable to stand for the required time to record a standing ECG (n=5), and those who did not consent to this study (n=3). The remaining 348 patients were included in this study. We assessed the participant's clinical characteristics including age, sex, body mass index (BMI), clinical diagnosis, and left ventricular ejection fraction (LVEF). LVEF was assessed by disk method[10] in echocardiography. All study protocols were approved by the institutional review board at Okayama University Hospital.

Screening waveform

Subjects were assessed using supine and standing ECG limb lead recordings to simulate the 3 S-ICD sensing vectors (Figure 1). The left arm (LA) electrode was positioned 1 cm laterally to the left sternal border and 1 cm above the xiphoid process. The right arm (RA) electrode was 14 cm superior to the LA electrode. The left leg electrode (LL) was positioned in the 5th intercostal space on the mid-axillary line, and the neutral electrode was on the lower torso where other lead positions were undisturbed. The primary lead vector extended from the LA to the LL. The secondary lead vector extended from the RA to the LL. The alternate lead vector extended from the RA to the LA.

All of the patients were screened in 3 increments (5, 10, and 20 mm/mV) with the paper speed of 25mm/sec for a period of 10 seconds.

S-ICD screening ECG analysis

Candidacy was determined via the Boston Scientific screening template (Natick, MA) (Figure 2a, b). Patients were eligible for S-ICD when at least 1 sensing vector in any of the same leads in the supine and standing position in all QRS-T complexes of the 10-second ECG strip at any 3 gains was present. All ECG readings were analyzed by 2 independent blinded observers.

Standard 12-lead ECG

The standard 12-lead ECG was recorded in the same day when the electrocardiography of the S-ICD screening ECG was obtained. We collected ECG parameters including QRS duration, QT interval in lead II, presence or absence of a negative T wave, complete right bundle branch block (CRBBB), incomplete right bundle branch block (IRBBB), complete left bundle branch block (CLBBB), atrial fibrillation (AF), and QRS-T discordance in leads I, II and aVF. Additionally, the amplitude of R wave was calculated in leads I, II, and III. QRS-T discordance was defined as oppositely-oriented

vectors of QRS and T wave.

Statistical analysis

Categorical variables are presented as the number of patients (percentage), and continuous variables are expressed as mean ± SD or median (interquartile range). For each variable, differences were evaluated using the Pearson χ^2 test for categorical variables and the Student's t test or the Mann–Whitney U test for continuous variables.

Logistic regression analysis was applied for assessing the effect of standard 12-lead characteristics on S-ICD eligibility according to surface S-ICD ECG screening template. We used the SPSS software program (IBM SPSS Statistics, Chicago) for all analyses. A *p* value <0.05 were considered to be statistically significant.

Results

Baseline patients' characteristics

Table 1 shows the baseline clinical characteristics of the study patients. A total of 348 patients satisfied the inclusion criteria. The population was predominantly male (70%) with a mean age of 49 years. The most common disease was Brugada syndrome (n=104,

30%) followed by congenital heart disease (n=75, 22%).

Eligibility of patient's heart diseases

Results of the eligibility with the S-ICD screening tool among diseases of patients at baseline are shown in Table 2. There were no significant differences in the eligibility for S-ICD among the types of cardiac disease (p=0.48).

Predictors of failure on 12-lead ECG

Table 3 shows the results of the standard 12-lead ECG characteristics for patients who were eligible for left parasternal screening (n=281) versus those who were ineligible (n=67). The presence of CRBBB, QRS-T discordance in lead II, and QRS-T discordance in all 3 leads (I, II and aVF) in the standard 12-lead ECG were significantly more frequent in ineligible patients than in eligible. Patients with a negative T wave tended to fail the S-ICD screening criteria, but this was not significantly different (p=0.6). Additionally, there were more patients in the ineligible subgroup with a wider QRS (108±36 ms vs 99±28 ms, p=0.15) and longer QT interval (430±47 ms vs 418±48 ms, p=0.7) than eligible subgroup, but those two were not also significant.

The results of univariate and multivariate analyses for comparison of factors associated with S-ICD screening ineligibility are shown in Table 4. Univariate analysis was applied for evaluating the association of predictive factors of ineligibility for S-ICD. CRBBB, QRS-T discordance in lead II, and QRS-T discordance in 3 leads (I, II and aVF) were more frequently found in patients who were ineligible for S-ICD screening criteria than in those who were eligible. Moreover, multivariate regression analysis showed that CRBBB and QRS-T discordance in 3 leads (I, II and aVF) were independent predictors for failing screening ECG of S-ICD.

Discussion

Main findings

To the best of our knowledge, this is the first clinical study to describe the eligibility of candidates for S-ICD according to preimplantation ECG screening in Asian patients. We found that 19% of patients failed the indication for S-ICD. There were no significant differences for eligibility among types of cardiac disease. CRBBB and QRS-T discordance in 3 leads (I, II and aVF) were independent predictors for ineligibility of S-ICD in the standard 12-lead ECG. This is the first study that described CRBBB is a

significant ineligible factor for S-ICD by multivariate logistic regression analysis.

Eligibility among cardiac diseases

Most previous studies that included a relatively large number of patients as a study population and used the S-ICD screening template reported that more than 90% of patients were appropriate for S-ICD, if the single lead matched the template as a passing indication[11,12,13]. However, 81% of patients adhered to the template ECG in our study. We could not clarify the reason(s) of the low eligibility in our study compared to previous investigations. Initially, we considered that this finding on eligibility was due to differences in the patients' baseline heart diseases; in our study, only 7% of the test population had ischemic heart disease, whereas previous reports showed that approximately 50% were patients with ischemic heart disease[11, 12, 13]. However, in our study, there was no significant difference in eligibility for S-ICD among different types of cardiac disease. Whether or not participants with ICD were included in the study may be another reason. The patients in this study were assessed for eligibility regardless of already-implanted ICD, while previous reports with relatively large number of participants included only patients with ICD indication. Thus, we assessed the eligibility in the patients with ICD. Among 348 patients, 137 patients had ICD. 21 patients (15.3%)

with ICD were ineligible for S-ICD screening ECG. This percentage is a bit higher than that in all patients. However, the result still showed lower eligibility than previous report[11,12,13].We speculate that racial differences might contribute, at least in part, to the low eligibility, and thus further studies in Asian populations are needed.

Prediction of ineligible factors in the standard 12-lead ECG for indication of S-ICD

Similar to conventional transvenous ICD, effort should be made to ensure avoidance of an inappropriate cardiac shock from an S-ICD. Louise et al. reported that the most common cause of inappropriate shock of S-ICD was cardiac signal oversensing (73%), such as T-wave oversensing[13]. S-ICD is not monitored by intracardiac but monitored subcutaneous ECG which mimics the body surface ECG. Therefore, the standard 12-lead ECGs, which are recorded on the body surface, are expected to be useful for predicting inappropriate operations, such as cardiac signal oversensing of S-ICD. Previous reports have shown that patients with a negative T wave[11,14,15], extension of the QRS duration[12], left bundle branch block[16], a small R/T ratio[13], or QT interval prolongation[15] in the standard 12-lead ECG tended to fail the screening template. In our study, these parameters tended to be ineligible of S-ICD, but the tendency did not reach the

statistically significant level. CRBBB, QRS-T discordance in lead II, and QRS-T discordance in 3 leads (I, II, and aVF) were predictors of failure for S-ICD template in univariate analysis. Multivariate analysis showed that CRBBB and QRS-T discordance in 3 leads (I, II, and aVF) were significant predictors for ineligibility of S-ICD. To the best of our knowledge, this is the first report to show that CRBBB is a predictive factor for ineligibility for treatment with S-ICD. To avoid inappropriate shocks of S-ICD, new appearances of CRBBB and QRS-T discordance in 12-lead ECG are possible signs for reconsidering eligibility of the S-ICD during follow up.

We tried to detect a common point between S-ICD screening ECG and standard 12-lead ECG. However, it was difficult to predict the morphology of S-ICD ECG from 12-lead ECG since S-ICD ECG changed dramatically from 12-lead ECG. The reason why CRBBB is an ineligible factor was unknown since QRS interval was not a significant predictor of ineligibility in this study. Among 131 patients who showed QRS-T discordance in 12-lead ECG in this study, 108 patients had also QRS-T discordance in S-ICD screening ECG. The patients with QRS-T discordance tended to be ineligible for S-ICD compared to the patients without QRS-T discordance in standard 12-lead ECG (82% vs 58%, $p<0.01$).

Louise et al. reported that heavy body weight is a factor (appropriate: 83±14 kg vs

failure: 92±16 kg) for failure of the S-ICD screening template[13]. Weinstock et al. also described that patients' BMI is an ineligible factor of S-ICD[16]. In our study, mean body weight was 58 kg and BMI was 22 kg/m^2, and only few patients had body weight more than 80kg. There was no significant difference in weight and BMI between eligible and ineligible patients. The relatively lean body and a narrow variation range of these variables compared with those in the western countries may explain the less contribution of these variables to S-ICD eligibility in our study.

Limitations

There are several limitations in this study. First, only a single center was included, and a relatively small number of participants were analyzed. Multicenter study including large number of patients should be conducted. Second, the number of patients with ischemic cardiomyopathy was relatively small compared with previous studies[11,12,13]. However, compare to western country, the implantation of ICD for patients with ischemic heart disease is much less in Japan[17]. Additionally, considering the risks and benefits of an S-ICD, the most appropriate diseases for S-ICD are congenital heart diseases because sometimes there is no venous access for ICD[18]. Patients with Brugada syndrome and idiopathic ventricular arrhythmia (IVF) also appeared to be appropriate

for S-ICD because most of them had a normal LVEF and did not need ventricular pacing. In this study, 77% of the patients had Brugada syndrome, congenital heart disease, hypertrophic cardiomyopathy or IVF. Therefore, our population can be considered as real world of S-ICD implantation.

Finally, evaluation of the screening ECG and the standard 12-lead ECG was only performed once while at rest. This situation is likely to be insufficient for patients with diurnal variation and day-to-day variations of ECG (e.g., patients with Brugada syndrome or those suffering from congenital long QT syndrome) [19, 20, 21]. Most inappropriate shocks were considered to be induced by T wave oversensing during exercise, particularly in younger patients. To evaluate more detail who matches is an appropriately to S-ICD, screening ECG should be performed during exercise testing in addition to ECG at rest.

Conclusion

In this study, 19% of potential patients for S-ICD were considered unsuitable for S-ICD when evaluated with a surface ECG screening template. There was no significant difference in eligibility among the types of cardiac disease. CRBBB and QRS-T

discordance in 3 leads (I, II, and aVF) with the standard 12-lead ECG were independent predictors for failure of indication for S-ICD. During follow up after implant of S-ICD, the morphological changes in QRS in the standard 12-lead ECG can be the initial clue that the patients with S-ICD become ineligible for this device.

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Figure legends

Figure 1.

S-ICD components, sensing vectors, and ECG lead positions.

RA, right arm; LA, left arm; LL, left leg.

The primary lead vector extended from the LA to the LL. The secondary lead vector extended from the RA to the LL. The alternate lead vector extended from the RA to the LA.

Figure 2a.

The screening template was designed by the S-ICD manufacturer (Boston Scientific).

Figure 2b.

Eligible and ineligible examples of S-ICD screening by ECG.

Figure3

Representative case of 12 lead ECG with CRBBB and QRS-T discordance failed S-ICD screening ECG

Left: Standard 12-lead ECG shows QRS-T discordance in lead Ⅱ and aVF and CRBBB.

Right: S-ICD screening ECG shows all leads are ineligible for S-ICD screening template.