New ECG Criteria for High-Risk Brugada Syndrome

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To identify high-risk patients with Brugada syndrome, the present study reviewed 60 standard 12-lead electrocardiograms from 60 patients collected by the Japanese Brugada syndrome registry. Under blinded conditions, the S wave of lead V1 was measured from the tip of r to r', and the amplitude of the ST segment in lead V2 was measured at 0.08 s from the J point. In patients with ventricular fibrillation (n=17), the S wave was significantly longer in V1 (0.085±0.007 s vs 0.075±0.011 s, p=0.001), and ST segment elevation in V2 was significantly greater (0.323±0.133 mV vs 0.236±0.129 mV, p=0.012) than in patients without fibrillation. An S wave width of 0.08 s or more in V1 had a positive predictive value of 40.5% and negative predictive value of 100% for ventricular fibrillation, with 100% sensitivity. ST elevation of 0.18 mV or more in V2 had a positive predictive value of 37.8% and a negative predictive value of 100% for ventricular fibrillation, with 100% sensitivity. Both an S wave width ≥0.08 s in V1 and ST elevation ≥0.18 mV in V2 were highly specific indicators of ventricular fibrillation and are proposed as new criteria for high-risk Brugada syndrome. (Circ J 2003; 67: 8 – 10)

Key Words: Brugada syndrome; ECG criteria; Risk; Ventricular fibrillation

Methods

We reviewed standard 12-lead ECGs that were on file at the Japanese Brugada syndrome registry2-4 and selected 60 from 60 patients because their quality was sufficient for accurate measurement of the QRS width and ST amplitude in the right precordial leads. All ECGs were recorded at a paper speed of 25 mm/s. The ECGs were from 17 patients with a history of VF, 9 patients with episodes of syncope, and 34 asymptomatic patients (Table 1). We measured the width of the S wave and ST segment elevation in leads V1 and V2 because there is usually a prominent r' in Brugada syndrome and either of these 2 leads shows the maximum ST segment elevation. We thought that conduction delay might be detected at the terminal portion of the QRS deflection, so the S wave of V1 and V2 was measured from the tip of r to r', and the amplitude of the ST segment was measured at 0.08 s from the J point. These measurement were made by 2 cardiologist who were unaware of the clinical information about the patients. Magnification was used to minimize the measuring error. When the measured values were not identical, the mean value of the 2 measurements was calculated.

Data Analysis

All variables are reported as the mean±SD for each group. The nonparametric Mann-Whitney U test was used to assess the significance of differences between the groups. Correlations between the presence or absence of

<table>
<thead>
<tr>
<th>Type of ST elevation</th>
<th>Asymptomatic n=34</th>
<th>Symptomatic n=9</th>
<th>History of VF n=17</th>
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<tbody>
<tr>
<td>Age (years) mean (SD)</td>
<td>52.3 (12.7)</td>
<td>52 (12.5)</td>
<td>46.1 (8.8)</td>
</tr>
<tr>
<td>M/F</td>
<td>32/2</td>
<td>8/1</td>
<td>17/0</td>
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<tr>
<td>Type of ST elevation</td>
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<tr>
<td>Coved</td>
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<td>6</td>
<td>16</td>
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<tr>
<td>Saddleback</td>
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<td>3</td>
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</table>

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Results

S Wave Width in Lead V1 or V2

The width of the S wave in leads V1 and V2 was identical in the majority of the patients, but was sometimes longer in V1. A gentler slope that preceded the turning point for the down slope of the negative T wave was designated as ‘S terminal delay’, which was seen at the terminal portion of the S wave in the right precordial leads (Fig 1) of approximately one-third of the patients. Terminal delay was more common and more prominent in lead V1 than V2, so we concentrated on the S wave in V1 (Fig 2). The width in V1 was greater in symptomatic patients (those with VF or syncope) than in asymptomatic patients (0.083±0.010 s vs 0.074±0.011 s, p=0.0006), and it was 0.08 s or more in all VF patients. The mean width of the S wave in lead V1 was also significantly greater in the 17 VF patients than in the 43 patients without VF (0.085±0.007 s vs 0.075±0.011 s, p=0.0011). In the present series of patients, an S wave width of 0.08 s or more in lead V1 had a positive predictive value of 40.5% and a negative predictive value of 100% for VF, with a sensitivity of 100%.

ST Amplitude in Lead V2

The ST amplitude measured at 0.08 s from the J point was obviously greater in V2 than in V1 (Fig 3). None of the patients showed ST segment elevation of less than 0.10 mV in V2. In symptomatic patients (VF or syncope), the mean ST amplitude in lead V2 was significantly greater than in asymptomatic patients (0.317±0.138 mV vs 0.217±0.117 mV, p=0.0017), and none of the VF patients had an amplitude of less than 0.18 mV. There was also a significant difference between VF patients and non-VF patients with respect to ST segment elevation (0.323±0.133 mV vs 0.236±0.129 mV, p=0.012). In this present series of patients, an ST amplitude of 0.18 mV or more in lead V2 had a positive predictive value of 37.8% and a negative predictive value of 100% for VF, with a sensitivity of 100%.

Discussion

We investigated the ECG characteristics of high-risk Brugada syndrome and found that both an S wave width ≥0.08 s in lead V1 and ST elevation ≥0.18 mV in lead V2 were highly specific indicators of patients who suffered from VF.

Broadening of the QRS complex, especially the S wave, in the right precordial leads might reflect an underlying conduction delay. Widening of the S wave was frequently observed in the symptomatic patients and might be an important indicator of increased risk. There was prolongation of the His-ventricular interval in some patients, according to the initial report on Brugada syndrome1 and the ECG also showed a right bundle branch block pattern. In the present series, most of the patients with documented VF had ‘S terminal delay’ in the right precordial leads and because this delay was more frequently observed in lead V1 than lead V2, we selected V1 for S wave measurement. Conduction delay has been suggested as having an important role in the development of ventricular arrhythmia in Brugada syndrome, and a ventricular late potential is frequently recorded in patients with Brugada syndrome in whom life-threatening ventricular arrhythmias are provoked during electrophysiological studies. Examination of multiple generations in a large family9 showed that the
QRS duration of affected individuals tended to increase as a function of age, and that serial ECGs of affected individuals demonstrated progressive QRS widening, but elevation at the J-point did not increase with age.

In the present study, the ST amplitude was also a highly specific indicator of high-risk patients with Brugada syndrome, but its positive predictive value was lower than that of the S wave width. It is important to detect high-risk patients among those who have a family history of syncope or sudden death and an ECG without obvious ST segment elevation. In this situation, the magnitude of ST elevation is not a powerful clinical indicator. It is well known that ST segment elevation varies day by day; and so may be an inadequate indicator. In recent reports, spontaneous ST segment elevation (the typical Brugada ECG pattern) was an important risk factor for high-risk Brugada syndrome. Itoh et al also pointed out that the arrhythmogenesis in Brugada syndrome might be related to the pronounced ST segment elevation! In order to distinguish the normal ST segment elevation observed in athletes from that of Brugada syndrome, the magnitude of the ST elevation and the QRS duration may be useful. Therefore, not only ST segment elevation, but also the S wave width should be measured to detect high-risk patients and we propose an S wave width in V1 ≥0.08 s and ST segment elevation ≥0.18 mV as new criteria for high-risk Brugada syndrome.

Study Limitations
This was a retrospective observational study, and only one ECG per patient was assessed, so no follow-up information on the patients was obtained. It may be important to elucidate the diurnal change in ST elevation and S wave width, because the His-Purkinje system might be also affected by autonomic tone, but we could not evaluate this important information. Accordingly, a prospective study using these new ECG criteria should be performed.

In conclusion, these ECG criteria may help differentiate high-risk patients with Brugada syndrome.

References

Appendix 1