Discrimination of Brugada Syndrome Patients From Individuals With the Saddle-Back Type ST-Segment Elevation Using a Marker of the Standard 12-Lead Electrocardiography

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Background In the clinical situation, the saddle-back (S-B) type is more frequently detected than the coved type. In the present study, the discrimination of Brugada syndrome from the S-B type individuals using a marker of the standard 12-lead electrocardiography (ECG) was attempted.

Methods and Results The study group consisted of 55 individuals with the S-B type in whom pilsicainide provocation test (PLC test) was carried out. The time from the onset of the QRS wave in lead V2 (IV2) to the peak of the late R-like wave in the QRS wave (PV2), and the time from IV2 to the offset of the QRS wave in lead V5 (EV5) were measured. The coved type was induced by the PLC test in 29 cases (N-C group), but not in the remaining 26 cases (N-N group). The (IV2–PV2)–(IV2–EV5) value before the PLC test was greater in the N-C group than in the N-N group. The negative predictive value of ‘(IV2–PV2)–(IV2–EV5) ≥ 0’ was 76.4% for the prediction of a positive PLC test.

Conclusions A ‘(IV2–PV2)–(IV2–EV5) ≥ 0’ is a useful ECG marker for the discrimination of Brugada syndrome in the S-B type individuals. (Circ J 2007; 71: 546–549)

Key Words: Brugada syndrome; Diagnosis; Electrocardiogram

Brugada syndrome is characterized by the coved type ST segment elevation in the right precordial leads on the standard 12-lead electrocardiogram (ECG)! During clinical evaluations, such individuals are detected by ECG with an incidence of 0.05%. The coved type ECG, type 1, according to the recommendations of the European Society of Cardiology (ESC); does not have a persistent morphology and is changeable to the saddle-back type (S-B type; type 2 or type 3 in ESC recommendations). The S-B type ECG is more frequently detected than the coved type ECG in the normal clinical situation. For the S-B type individuals, Na channel blockade is recommended to show the nature that will induce the coved type.

In the present study, the discrimination of Brugada syndrome from the S-B type individuals using a marker of the ECG morphology was attempted.

Methods

Subjects
In our institution, 142 individuals with a right bundle branch block type pattern and ST-segment elevation in the right precordial leads on the standard 12-lead ECG, ie, type 1, type 2, and type 3 according to the ESC recommendation, were detected from January 1996 to August 2004. Out of those subjects, 55 individuals with the S-B type consented to the pilsicainide (Na channel blockade) provocation test (PLC test), and were entered in this study.

The subjects consisted of 8 females and 47 males, aged 54±16 years old. In their natural course, no coved type ST segment elevation had ever been pointed out in their ECG. Twenty-three individuals had a history of syncope or survived from sudden death and the remaining 32 individuals were asymptomatic. Seventeen individuals had a family history of sudden death (<45 years old). In all the subjects, no obvious heart disease was observed, and the routine blood tests, ECG, chest X-ray, exercise test and echocardiogram were carried out. Furthermore, in 29 subjects that consented to coronary angiography and left ventriculography, those studies were additionally carried out.

ECG Recording
The standard 12-lead ECG was recorded in the supine position using a 6-channel ECG recorder (Fukuda-denshi, Tokyo, Japan).

PLC Test
Pilsicainide (1.0mg/kg) was administrated intravenously over 10 min. Before, during, and after (1, 3, 5, 10, 20, 30, 60, 120 min) the administration, an ECG was recorded until recovery of the ECG morphology change.

Measurements of the ECG Markers
Because it is simple to measure the ECG markers, leads...
V2 and V5, simultaneously recorded were used in the current study. The time from the onset of the QRS wave in lead V2 (IV2) to the peak of the late R-like wave in the QRS wave (PV2), and the time from IV2 to the offset of the QRS wave in lead V5 (EV5) were measured using a magnifying glass (magnification: ×10, PEAK SCALE LUPE). Furthermore, the difference with the previous 2 measurements ((IV2–PV2)–(IV2–EV5)) was discussed. The measurement method is shown in Fig 1. The (IV2−PV2)−(IV2−EV5) value is expressed as PV2−EV5 hereafter.

**Statistical Analysis and Classification of the Participants**

The data are indicated in milliseconds and the mean ± standard deviation. Statistical analysis was calculated using a multiple comparison (Scheff) and Student’s t-test. A p-value of <0.05 was considered to be significant.

The subjects were divided into 2 different groups depending on the response to the PLS test. Namely, the subjects in whom the coved type morphology was induced were in the N-C group, and in those in whom it was not induced were placed in the N-N group.

A coved type morphology was defined as a domed ST elevation with a peak of over 0.2 mV following the QRS, gradually decreased, and continued to a negative T-wave.

‘PV2−EV5=0’ implies that the end of the QRS in V5 and the peak of the late R in V2 were simultaneously recorded. The subjects were divided into those with a PV2−EV5 ≥0 and those with that <0 using the ECG before the PLC test.

In these 2 groups, to predict the PLC test, positive sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were used.

**Ethics**

The present study was permitted by the committee of medical ethics at St. Marianna University School of Medicine. The clinical prognosis normally known in the world and the risks of each examination were explained. The examination was carried out in the individuals that signed a written consent.

**Results**

**Case**

A 40-year-old male with the S-B type presented to our...
institution and was asymptomatic. Because of a family history of sudden death, a PLC test was carried out. The routine examinations ruled out any existing obvious heart disease. No ECG abnormality had ever been pointed out in any of the yearly clinical check-ups, nor did the patient undergo any hospital care. As shown in Fig 2, the S-B type before the PLS test changed to the coved type. Before the test, the PV2 – E V5 was measured and found to be +20 ms. The patient was placed into the PV2 – E V5 ≥ 0 group.

Results of the PLC Test
In 29 subjects, the coved type morphology was induced, but not in the remaining 26 cases. Therefore, the 29 subjects were classified into the N-C group and remaining 26 into the N-N group.

The difference in the PV2 amplitude between that measured before and that after the pilsicainide administration (ΔPV2 amplitude) is shown in Fig 3. The ΔPV2 amplitudes did not change in the N-N group, but were widely distributed from 0 to 7 mV in the N-C group. The difference between the 2 groups was observed to be a more increasing amplitude in the N-C group (+2.3±1.9 mV) than in the N-N group (+0.1±0.3 mV) (p<0.0001).

Comparison of the PV2 – E V5 Value Between the N-C Group and N-N Group
The PV2 – E V5 value before the PLS test was greater in the N-C group than in the N-N group (Fig 4), and was +2±6 ms and −5±6 ms, respectively (p<0.0001). Furthermore, the individuals with a value ≥0 were more frequently included in the N-C group.

After the PLC test, the PV2 – E V5 value was also frequently observed to be greater than 0 in the N-C group, but less than 0 in the N-N group. However, the relationship between the ΔPV2 amplitude and PV2 – E V5 value could not be determined in either group as shown in Fig 5. On the ECG during the PLC test, for the PV2 – E V5 ≥ 0, 25 subjects in the N-C group and 13 in the N-N group were included. Furthermore, for the PV2 – E V5 <0, 4 subjects in the N-C group and 13 in the N-N group were included.

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Discussion
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The right bundle branch-block type pattern and ST-segment elevation in the right precordial leads in Brugada syndrome is morphologically changeable day by day. Such morphologies include the coved type and S-B type which
are proposed, as type 1, type 2 and type 3, in the recommendation from the ESC. For the diagnosis of Brugada syndrome, the coved type must be confirmed during the natural clinical course or Na channel blockade provocation test.

The S-B type is detected with an incidence of 1.0–6.0% during clinical evaluations in healthy individuals. However, they were not all Brugada syndrome cases. To reveal the coved type pattern, a Na channel blockade provocation test is believed to be useful. In the current study, the coved type was shown in approximately one-half of the subjects with the S-B type.

The ST-segment elevation observed in Brugada syndrome is understood by 2 different theories. Namely, the first is that there is a local conduction delay in the right ventricular outflow tract (RVOT); and the second is that there is a difference in the amplitude during early phase 1 of the myocardial action potential between the epicardial myocytes and endocardial myocytes in the RVOT. A difference in the amplitude during the early phase of the action potential appears as a J-wave on the ECG.

The 2 different theories possibly indicate that there is a morphological characteristic on the ECG just after the QRS wave, which corresponds to a ventricular late potential in the former, and J-wave in the latter. In a description by Wilde et al, the terminal portion of the QRS in the Type 2 and Type 3 Brugada type ECG (R' wave) was defined as gradually depressed and to be moved towards the ST segment. This potential that produces a gradual depression might be indicated as a ventricular late potential, or J-wave.

However, the probability of the detection of a Brugada type ECG morphology is well-known to be higher if recorded from the upper intercostal spaces than the standard recording positions. Brugada type ECG are considered to reflect a local abnormality of the heart.

We expected that the QRS width might be extended only in the right precordial leads in Brugada syndrome. The timing of the end of the QRS was actually measured to make a comparison between the right precordial leads and left precordial leads in individuals with the S-B type. As a result, there were individuals who had QRS in both the right and left precordial leads simultaneously end, and those who had a delay in the ending of the QRS in the right precordial leads. We had the impression that the end of the QRS in the right precordial leads was later compared to that in the left precordial leads in Brugada syndrome.

If the peak of the late R in lead V2 and the end of the QRS in lead V5 are simultaneously recorded, the end of the QRS in V2 ought to delay. A ‘PV2–EV5 ≥ 0’ in this study meant that the QRS in lead V2 ended later than that in lead V5. About half of the subjects had a ‘PV2–EV5 ≥ 0’.

The difficulty in the measurements was with the discrimination of the end of the QRS in the right precordial leads. However, the end of the QRS in lead V5 was clearly discriminated. For that reason, for the measuring point in the right precordial leads, the peak of the late R was used in this study. Before the PLS test, the PV2–EV5 values significantly increased in the N-C group, and furthermore, the majority of the cases with a PV2–EV5 ≥ 0 had a positive PLC test, but a small number of cases with a PV2–EV5 < 0 also had a positive test. Using such a marker, the NPV of the coved type inducibility was 76.4%. If the end of the QRS could be discriminated in lead V2, the data was good. Therefore, a delay in the end of the QRS in the lead V2 for the S-B type was considered to be useful for predicting Brugada syndrome.

Clinical Implications

The S-B type was frequently detected during normal clinical evaluations, however, it did not include all Brugada cases. We propose that when the end of the QRS in lead V2 is delayed from the end of the QRS in lead V5, the individuals with the S-B type should be classified as patients who have a masked substrate of Brugada syndrome. However, because the discrimination of the end of the QRS in lead V2 is often difficult, the PV2 is useful as a substitute for the end of the QRS in lead V2.

A ‘PV2–EV5 ≥ 0’ is possibly a useful marker for an automated detection of the ECG.

Conclusion

For the S-B type before the PLC test, the end of the QRS in lead V2 had a delay in comparison to the EV5 in the subjects with a positive PLC test. Even for the comparison between PV2 and EV5, the NPV of PV2–EV5 ≥ 0, was observed to be 76.4% for the prediction of a positive PLC test. This marker was useful for the discrimination of Brugada syndrome in the S-B type subjects.

References


