Sinus Node Function in Patients With Brugada-Type ECG

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Background  Some studies have shown that patients with Brugada syndrome (BS) have atrioventricular conduction disturbance, but their sinus node function has not been evaluated.

Methods and Results  The patients group consisted of 59 male patients and 1 female patient with BS. Supraventricular and ventricular programmed electrical stimulation (PES) was performed. Ventricular fibrillation (VF) or sustained polymorphic ventricular tachycardia was induced by ventricular PES in 26 patients with BS (VF group), but was not induced in the other 34 patients (non-VF group). Sinus node function and conduction of the atrioventricular (AV) node in the control group, non-VF group and VF group were evaluated. Sinus node function was attenuated and the His–ventricle interval was prolonged in the VF group (corrected sinus node recovery time: 452±126 ms (VF group), 324±146 ms (non-VF group), Sino-atrial conduction time: 179±60 ms (VF group), 127±60 ms (non-VF group)).

Conclusion  The function of both the sinus node and AV node are attenuated in patients with PES-induced VF.

Key Words: AV node function; Brugada syndrome; Sinus node function; Sinus node recovery time

In 1992 Brugada et al reported 8 patients with right bundle branch block and persistent ST segment elevation in the right precordial leads! These patients experienced episodes of syncope, and polymorphic ventricular tachycardia or VF was induced by programmed electrical stimulation (PES). It has been reported that 10–20% of cases of Brugada syndrome are caused by cardiac sodium channel mutation2–4 and impaired sodium channel function can explain the characteristic ST segment morphology and the occurrence of ventricular arrhythmia5–7. If mutation of the cardiac ion channel causes BS, there might be abnormal supraventricular electrophysiology. In fact, we found that patients with BS have abnormal atrial vulnerability9 and moreover, recent studies have shown that some cases of BS are associated with supraventricular tachyarrhythmia and sinus node dysfunction10–13. The present study was therefore designed to determine the characteristics of the conduction function of the sinus node and atrioventricular (AV) node in patients with a Brugada-type ECG.

Methods

Patients  The subjects of this study were 59 male patients and 1 female patient with a Brugada-type ECG (13 symptomatic and 47 asymptomatic patients). The mean age of the patients was 47±10 years. Brugada-type ECG was defined as J wave (higher than 0.2 mV) and a coved-type or saddle back-type ST segment elevation (higher than 0.1 mV) in the right precordial leads.14 Symptomatic patients had recurrent episodes of syncope of unknown origin (4 patients) or had been resuscitated from cardiac arrest or detected event of VF (9 patients). All subjects had right bundle branch block with spontaneous ST elevation without drug provocation. There were no patients from the same family, echocardiography and right ventriculography were performed in all patients but no abnormalities were found. None of the patients showed clinical evidence of sick sinus syndrome or high-degree atrioventricular block.

The patients with BS were divided into 2 groups based on the results of the electrophysiological study (EPS): one group in which VF was induced by PES (induced VF group, n=26) and one in which VF was not induced by PES (non-induced VF group, n=34).

Electrophysiological Study  After obtaining written informed consent, an EPS was performed in 52 patients. All antiarrhythmic drugs were discontinued for at least 5 drug half-lives before the EPS. After right femoral and right jugular venous access and left femoral arterial access had been obtained, 4 quadripolar electrode catheters with a 5-mm inter-electrode distance (6-Fr, EP Technologies Inc, Boston Scientific Inc, Sunnyvale, CA, USA) were positioned in the high right atrium (HRA), His bundle region, right ventricular apex (RVA) and right ventricular outflow tract (RVOT); an octapolar catheter with 2.5 mm inter-electrode distance (6-Fr, EP Technologies Inc) was positioned in the coronary sinus, and a quadripolar electrode catheter with a 5-mm inter-electrode distance (7-Fr, Medtronic Inc, Minneapolis, MN, USA) was positioned in the postero-lateral region of the left ventricular (LV) free wall. Endocardial potentials were recorded by bipolar electrodes and filtered to record frequencies of 30–400 Hz. PES
was performed at an intensity twice the threshold and for 2 ms in duration through the distal electrodes in the HRA for evaluation of supraventricular electrophysiology. Atrial stimuli was performed at HRA for 30 s. Then sinus node recovery time (SNRT), corrected SNRT (CSNRT = SNRT – sinus cycle length), SNRT/sinus cycle length × 100% (%SNRT), atrio-His (AH) and His-ventricular (HV) interval and maximal one-to-one conduction of the AV node were estimated. Sino-atrial conduction time (SACT) was estimated by the method described by Narula et al.15 A brief atrial overdrive was performed at a cycle length 50–150 ms faster than the sinus rate, and the interval from the last paced beat to the first sinus escape was measured and then baseline sinus cycle length was subtracted and divided by 2, which yields the estimated SACT.

The protocol of ventricular stimuli included up to 3 extrastimuli (2 basic cycle lengths of 600 and 400 ms) and rapid ventricular pacing at RVA, RVOT and LV. The coupling interval of the extrastimuli was not shorter than 180 ms and ventricular rate of rapid burst pacing was up to 270 beats/min. The protocol of the ventricular EPS was the same as that previously reported.16

### Statistical Analysis
Quantitative values are expressed as means ± 1 SD. Statistical significance in differences between 2 groups was analyzed by Mann-Whitney’s t-test for unpaired values.

### Results
Table 1 shows the differences of sinus node function between the non-induced VF group and the induced VF group: SNRT did not differ; CSNRT and %SNRT were prolonged in the induced VF group compared with the non-induced VF group, and SACT was prolonged in the induced VF group compared with the non-induced VF group (p<0.01). Although abnormal values of CSNRT (>525 ms), %SNRT (>150%) and SACT (>125 ms) occurred in 6%, 18% and 44%, respectively, of patients in the non-induced VF group, the respective values were 31% (p=0.001), 42% (p=0.036), 89% (p=0.003) of patients in the induced VF group.17

#### Table 1 Sinus Node (SN) Function and Atrioventricular Node (AVN) Function in Patients With Brugada-Type ECG

<table>
<thead>
<tr>
<th>patients with Brugada syndrome</th>
<th>Non-induced VF (n=34)</th>
<th>Induced VF (n=26)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SN function</strong></td>
<td></td>
<td></td>
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<tr>
<td>Sinus cycle length (ms)</td>
<td>902±189</td>
<td>881±173</td>
<td>0.591</td>
</tr>
<tr>
<td>SNRT (ms)</td>
<td>1,227±209</td>
<td>1,333±238</td>
<td>0.161</td>
</tr>
<tr>
<td>CSNRT (ms)</td>
<td>324±146</td>
<td>452±126</td>
<td>0.001</td>
</tr>
<tr>
<td>%SNRT (%)</td>
<td>138±20</td>
<td>152±14</td>
<td>0.005</td>
</tr>
<tr>
<td>SACT (ms)</td>
<td>127±60</td>
<td>179±60</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>AVN function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximal 1:1 conduction (beats/min)</td>
<td>146±29</td>
<td>136±22</td>
<td>0.089</td>
</tr>
<tr>
<td>AH interval (ms)</td>
<td>91±20</td>
<td>98±16</td>
<td>0.307</td>
</tr>
<tr>
<td>HV interval (ms)</td>
<td>35±8</td>
<td>41±8</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Data are mean value±SD.

AH interval, atrio-His interval, CSNRT, corrected sinus node recovery time (SNRT–sinus cycle length); ERP, effective refractory period; HV interval, His-ventricle interval; NA, not assessed; PCL, paced cycle length; SNRT, sinus node recovery time; %SNRT, SNRT/sinus cycle length×100; VF, ventricular fibrillation.

Fig 1. Brugada patient with PES-induced VF in whom atrial pause was induced after cessation of atrial pacing (sinus node recovery time (SNRT)=1,735 ms).
There was no difference in AH interval between the induced VF group and non-induced VF group, but the HV interval in the induced VF group was prolonged compared with the non-induced VF group. There was no difference between the 2 groups for the maximal values of one-to-one conduction of the AV node.

Fig 1 shows a case of PES-induced VF in which sinus pause was induced after cessation of atrial pacing.

Discussion

Brugada syndrome is characterized by ST segment elevation in the right precordial leads and nocturnal sudden cardiac death from polymorphic ventricular tachycardia and VF. It has been reported that mutation of the sodium channel gene is associated with 10–20% of cases of BS. and that an abnormality in the sodium channel gene is associated with 10–20% of cases of BS4,20 and that an abnormality in the sodium channel gene is associated with 10–20% of cases of BS4,20 and that an abnormality in the sodium channel gene could explain the ECG abnormality and occurrence of ventricular arrhythmia.6,8 In fact, it has been shown that patients with BS have abnormal atrial electrophysiology; the signal-average electrogram shows abnormal late potentials21,22 and delayed potential has been found in the epicardial region of the right ventricular outflow tract.23 Kanda et al reported that abnormal intraventricular conduction delay exists in symptomatic BS24 If impairment of the cardiac ion channel causes BS, abnormal electrophysiological characteristics should be found not only in the ventricular myocardium, but also in the atrial myocardium and cardiac conduction system. In fact, patients with BS have abnormal atrial vulnerability,25,26 prolongation of the His–ventricular interval and supraventricular tachyarrhythmia, especially paroxysmal atrial fibrillation and paroxysmal supraventricular tachycardia8,9,11 The HV interval is prolonged in patients with Brugada syndrome and this may be caused by impaired cardiac ion channel functions7,29–31 Grant et al reported that long QT syndrome, BS and conduction system disease occurred in a family with SCN5A mutation and that one of the cases of BS showed prolonged sinus pause13 In the present study, the EPS showed impaired sinus node function in patients with a Brugada-type ECG. Although markedly abnormal sinus node function was not found in this study, there was latent sinus node dysfunction in patients with PES-induced VF. It is thought that attenuation of sinus node function might result from dysfunction of the cardiac ion channel, but because the sino-atrial conduction time was prolonged in patients with PES-induced VF in this study, another possible cause of the nodal dysfunction is a conduction disturbance between the sinus node cells and atrial myocardium. In fact, a conduction abnormality of the ventricle of patients with PES-induced VF has been shown by prolonged intraventricular conduction28 or signal-average electrogram21,22 Moreover, the impairment of atrial conduction in patients with BS suggests that a conduction disturbance results in impairment of sinus node function.

Although the incidence of sinus node dysfunction and of high-degree AV block is though to be low, bradycardia could induce augmentation of ST elevation and frequent VF attack22,23 Thus, the possibility of sinus node dysfunction should be taken into consideration in patients with BS.

Study Limitation

We did not perform genetic tests in the patients with BS and therefore did not detect the SCN5A mutation. Hence, it is unclear whether sodium channel dysfunction resulted in the sinus node impairment in the Brugada patients with VF induced by PES. Although the disease activity of BS is influenced by vagal nerve activity,24,25 we did not evaluate the influence of the autonomic nervous system and the results of this study may have been influenced by autonomic nerve activity.

Conclusion

There was deterioration of sinus node function in BS patients with VF induced by PES and they may have an abnormality in nodal function.

References


