Fragmentation in Body Surface Potential Mapping Recordings from Patients with Brugada Syndrome

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Abstract

Brugada syndrome (BrS) causes sudden death in patients with structurally normal hearts. Manifestation of BrS in the ECG is dynamic and most patients do not show unequivocal signs of the syndrome during ECG screening. Fragmentation of QRS complexes in BrS patients has been linked to a worse prognosis and higher risk. In this study we aim to determine the spatial location of fragmented ECG signals in BrS and controls in order to elucidate its potential role in the diagnosis of BrS and the identification of patients with a higher risk. We obtained 67-lead Body Surface Potential Mapping recordings of 38 BrS, 28 Right Bundle Branch Block (RBBB) patients and 16 controls. Fragmentation of QRS complexes appeared in the anterior torso of symptomatic BrS patients with a higher incidence than in asymptomatic individuals. P waves of symptomatic BrS patients were more fragmented than in other groups.

1. Introduction

Brugada syndrome (BrS) is a heritable arrhythmia syndrome that causes sudden death in young adults with structurally normal hearts. BrS is diagnosed in basis on the clinical and familiar history of the patient and a characteristic electrocardiogram (ECG) pattern displaying a coved-type ST segment \( \geq 0.2 \text{mV} \) in right precordial leads (referred as type I ECG) [1].

Since BrS is reflected only as an electrical disorder, the ECG is the only not invasive technology that allows, up to the date, to diagnose the disease, which does not show any sign in the different modalities of medical image. Nevertheless, the standard ECG presents limitations derived from the incomplete representation of the electrical field generated by the heart that is obtained from his projection in the 12 standard derivations.

The technology known as Body Surface Potential Mapping (BSPM) is an advanced electrocardiographic technology whose aim is to determine the global distribution of the electrical field generated by the heart by the simultaneous record of potentials in multiple locations of the thoracic surface. In addition, BSPM has been used in the diagnosis and planning of interventions in other pathologies as atrial flutter, atrial fibrillation or Wolf-Parkinson-White [2-4]. By all this, there has been demonstrated that BSPM records contain diagnostic information not contained in the standard ECG.

It has been suggested that the ventricular complexes of patients suffering BrS present a high degree of fragmentation due to conduction abnormalities, which would be tied to a worse prognosis [5-6]. Presence of fragmented QRS complexes has been linked to a higher risk of suffering syncope or fibrillation. The objective of the present study is to determine the topological representation of fragmentation in ECG waves on the torso of BrS patients and evaluate the potential use of this measurement as risk predictor.

2. Methods

2.1. Patient population

In this study, 38 patients diagnosed with BrS were included. 32 BrS patients were included in the Asymptomatic group, for patients who were symptomless, but present type 1 ECG; and 6 patients were included in the Symptomatic group, who had syncope or have an implantable cardioverter-defibrillator (ICD). In added BSPM recordings from 28 patients diagnosed with Right Bundle Branch Block (RBBB) and 16 controls were compared with BrS recordings. The clinical diagnosis of BrS and RBBB was established as described previously [7]. Selected control subjects had no history of previous heart disease and a normal resting ECG.
2.2. BSPM recording

A total of 64 chest and back leads were acquired simultaneously for each subject during 2 minutes. Electrodes were mounted as described previously [8] (see Fig. 1). Signals were acquired at a sampling rate of 2048 Hz, with a resolution of 1 μV and a bandwidth of 500 Hz. Standard ECG leads were computed from BSPM leads recorded at positions more similar to the standard ECG leads (Fig. 1).

![Figure 1. Electrode position in our BSPM system. Black circles correspond to the approximated location of precordial, right and left arm leads.]

2.3. ECG signal processing

ECG signals were processed using Matlab 7.10.0 (The Mathworks Inc.). First, baseline was estimated by filtering with a Butterworth 10th order low-pass filter with a cut-off frequency of 0.6 Hz after decimation to a sampling frequency of 51.2 Hz. Baseline was interpolated to 2048 Hz and subtracted to the original recording. Then, ECG signals were filtered with a 10th order, low-pass Butterworth filter with a cut-off frequency of 70 Hz. Power spectral density of all signals was computed by using Welch periodogram with a hamming window of 8 seconds and 50% overlap. Leads presenting more than 0.5% of their spectral content at 50 Hz were filtered with a 2nd order IIR notch filter centered at 50 Hz. All leads were visually inspected after filtering and leads with noticeable noise were excluded from further analysis.

QRS complexes were detected by selection of local maxima after steeper slopes in a simplified ECG obtained by polyline splitting [9]. Then, averaged PQRST complexes were obtained by template matching-averaging. Fiducial points in averaged beats were detected by selecting points preceding or following segments with steeper slopes in a simplified beat obtained by polyline splitting. Fiducial point detection was then manually verified. P onset and T offset served as anchoring points for baseline estimation on the averaged beats and remaining baseline was subtracted. All ECG leads were normalized to the maximum amplitude value.

2.4. Measurement of fragmentation

We implemented two methods for measuring fragmentation in QRS complexes and P waves: (1) quantification of the number of spikes in each wave and (2) detection of notched waves. Spikes within the QRS complex or P wave were defined as positive local maxima or negative local minima with a slope preceding or following the local maxima/minima above a threshold. Fig. 2 shows the spikes detected in two QRS complexes.

A notched QRS complex or P wave was defined as a wave presenting at least two consecutive spikes with the same polarity. QRS complex in Fig. 2.A would not be defined as notched, whereas QRS complex in Fig. 2.B would be defined as notched.

![Figure 2. Measurement of fractionation. Arrows identify spikes detected in QRS complexes. Dotted lines show onset and offset of QRS complex. A: QRS complex with two spikes and classified as not notched. B: QRS complex with three spikes and classified as notched.]

2.5. Statistical analysis

Number of spikes in QRS complexes and P wave were measured and values were given as mean ± std. Comparisons among groups were made using an unpaired Student’s t test. A p value lower than 0.05 was considered significant.

3. Results

3.1. Fragmentation of QRS complexes

Fragmentation measurements of QRS complexes of our population under study are summarized in Table 1. QRS complexes of BrS patients presented significantly less spikes than those of RBBB patients and controls. There were no statistical differences between the number of spikes in the QRS complex of asymptomatic and symptomatic BrS patients. Number of spikes of QRS complexes was dependent on the location of the ECG lead on the body surface, as it can be observed in Fig. 3.
Table 1.
Fragmentation measurements of QRS complexes.

<table>
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<tr>
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<th>BRUGADA</th>
<th>BRUGADA</th>
<th>RBBB</th>
<th>CONTROL</th>
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<tbody>
<tr>
<td></td>
<td>Asympt.</td>
<td>Sympt.</td>
<td>N=28</td>
<td>N=16</td>
</tr>
<tr>
<td>nS</td>
<td>2.49±0.44</td>
<td>2.54±0.49</td>
<td>3.13±0.64</td>
<td>2.99±0.45</td>
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<tr>
<td>nN</td>
<td>47±23%</td>
<td>58±38%</td>
<td>88±51%</td>
<td>86±59%</td>
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<tr>
<td>nNA</td>
<td>21±17%</td>
<td>34±23%</td>
<td>42±27%</td>
<td>28±21%</td>
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nS: number of spikes QRS complexes, nN: percentage of notched QRS complexes, nNA: percentage of notched QRS complexes in the anterior torso.

QRS complexes of controls presented more spikes on the back, on the left superior and right inferior areas, and spikes were found in the precordial area. RBBB patients presented more spikes above V₁ and V₂ leads and above V₃-V₄. BrS patients presented a surface distribution of fragmentation of QRS complexes similar to that of controls.

QRS complexes of BrS patients were also less notched than those of controls and RBBB patients. Again, notched QRS complexes in RBBB patients were located anteriorly whereas notched QRS complexes of controls were predominantly found distant to the precordial area (see Fig. 4). Symptomatic BrS patients, however, presented more notched QRS in the anterior torso than asymptomatic BrS patients and controls, although differences were not significant.

3.2. Fragmentation of P waves

Fragmentation measurements of P waves of our population under study are summarized in Table 2. P waves of symptomatic BrS patients presented more spikes than those of controls, RBBB patients and asymptomatic BrS patients (p=ns). P waves with more spikes appeared more predominantly in the precordial area, as it can be observed in Fig. 5. Symptomatic BrS patients also presented more notched P waves than asymptomatic BrS patients, controls and RBBB patients (p=ns).

Table 2.
Fragmentation measurements of P waves

<table>
<thead>
<tr>
<th></th>
<th>BRUGADA</th>
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<th>RBBB</th>
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<tbody>
<tr>
<td></td>
<td>Asympt.</td>
<td>Sympt.</td>
<td>N=28</td>
<td>N=16</td>
</tr>
<tr>
<td>nS</td>
<td>2.15±0.49</td>
<td>2.95±1.08</td>
<td>2.06±0.65</td>
<td>2.22±0.66</td>
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<tr>
<td>nP</td>
<td>44±18 %</td>
<td>63±22%</td>
<td>38±23%</td>
<td>46±23%</td>
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</table>

Figure 3. Number of spikes constituting QRS complexes. A: Controls, B: RBBB, C: Asymptomatic BrS, D: Symptomatic BrS. Mean values in each group of patients are represented.

Figure 4. Maps of percentage of notched QRS complexes. A: Controls, B: RBBB, C: Asymptomatic BrS, D: Symptomatic BrS.

Figure 5. Number of spikes constituting P waves. A: Controls, B: RBBB, C: Asymptomatic BrS, D: Symptomatic BrS.

Figure 6. Maps of percentage of notched P waves. A: Controls, B: RBBB, C: Asymptomatic BrS, D: Symptomatic BrS.
4. Discussion

Fragmentation of QRS complexes has been proposed in the literature as a risk predictor in BrS patients [5-6]. We have found that fragmentation indexes based on the number of spikes within the QRS complex are not good risk predictors, since QRS complexes of even control subjects present multiple spikes everywhere in the torso surface that may be reflecting non-pathological changes in the direction of the depolarization wavefront. Fragmentation indexes based on the presence of consecutive spikes with the same polarity (notched waves) appeared to be more sensitive for predicting cardiovascular risk than those based on spike counts. Symptomatic BrS patients presented more notched QRS complexes on the anterior torso than asymptomatic BrS or controls. Measurements obtained from non-standard positions distant from the heart may not be useful for predicting cardiovascular risk since they typically present high indexes of fragmentation even in control subjects. This higher fragmentation could be related to conduction disturbances, as proposed in the literature, that may be related to a lower sodium availability. However, conduction disturbances in BrS patients may be less accentuated in BrS patients than in RBBB patients and thus fragmentation indexes should be interpreted with care.

P waves of symptomatic BrS patients appeared to be more fragmented than those of other groups of patients, including those of RBBB patients. This finding could be consistent with a conduction slowing that may be observed both in the atria and the ventricles as a consequence of the mutation responsible of the syndrome. RBBB patients, in whom there is a block in the ventricular conduction system, do not present high fragmentation in their P waves. Most differences observed between symptomatic BrS patients and other groups were not found to be significant. This may be due to the limited number of symptomatic patients included in this study. A larger population of symptomatic BrS patients should be studied in order to determine the reproducibility of our results in a general population.

5. Conclusion

Fragmentation of QRS complexes appeared in the anterior torso of BrS Symptomatic patients with a higher incidence than in BrS Asymptomatic individuals. P waves of BrS Symptomatic patients were more fragmented than in other groups.

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References


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