Inferior and lateral electrocardiographic repolarization abnormalities in Brugada syndrome

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Abstract

**Background:** Repolarization abnormalities in the inferior-lateral leads in Brugada syndrome (BS) have not been systematically investigated.

**Methods and Results:** 280 patients (age: 41±18y, 168 males) with BS were screened for inferior-lateral repolarization abnormalities. The repolarization abnormalities were classified either as Early Repolarization Pattern or coved ≥ 2 mm Brugada Pattern and as spontaneous or class I antiarrhythmic drug (AAD) induced. 32 patients (11%) had inferior-lateral spontaneous Early Repolarization Pattern. These patients were less likely to be asymptomatic at first presentation (13 of 32 pts vs 156 of 248 pts, p=0.02) and spontaneous type I ECG was more frequent among them (38% vs. 21%, p=0.05). The spontaneous Early Repolarization Pattern occurred more frequently among patients with BS than in 283 family members not having BS (11% vs 6%, p=0.03). Class I AAD administration provoked inferior-lateral coved Brugada Pattern in 13 patients with BS. These patients had longer baseline PR intervals (206±48 vs. 172±31 ms, p<0.001) and class I AAD induced QRS interval prolongation (108 to 178 ms vs 102 ms to 131 ms, p<0.001). In 3 patients the class I AAD provoked coved Brugada Pattern was only present in the inferior leads.

**Conclusions:** Inferior-lateral Early Repolarization Pattern occurs spontaneously relatively frequently in BS. These patients have a more severe phenotype. Class I AAD administration provokes inferior-lateral coved Brugada Pattern in 4.6% of patients. We report for the first time 3 patients in whom the class I AAD provoked coved Brugada Pattern was only observed in the inferior leads.

**Keywords:** Electrocardiography, death, sudden, Brugada syndrome
Introduction

The Brugada syndrome (BS) is characterized by ST elevation in the right precordial leads (V1-3) and an increased risk of arrhythmic sudden death (1). In 2002 a consensus report defined the diagnostic ECG abnormality as a coved type ST elevation in the presence of at least a 2 mm J wave (type I ECG pattern) in the right precordial leads (V1 to V3) either occurring spontaneously or after a class I antiarrhythmic drug (AAD) challenge (2,3). However, sporadic cases have been reported, where the coved type Brugada ECG pattern was also observed in the inferior or lateral ECG leads (4-7). The majority of these patients presented with the same clinical characteristics as patients with the typical form of BS. All these findings suggest that BS has a phenotype variant in which the coved type Brugada pattern manifests not only in the right precordial but also in the inferior-lateral leads. The incidence and the clinical characteristics of this inferior-lateral Brugada phenotype variant have not been investigated yet.

Additionally, several case reports (8-11) and recently a multicenter study (12) described patients with idiopathic ventricular fibrillation and accentuated J wave or early repolarization pattern in the inferior-lateral leads. The incidence of early repolarization pattern in the inferior-lateral leads in BS has not been investigated yet.

In the current study we aimed to determine the incidence and characteristics of spontaneous or class I AAD test induced inferior-lateral repolarization abnormalities in a large unselected population of patients with BS.

Methods
Patient population

Since 1992, all patients diagnosed with BS and their relatives tested for the syndrome are included in a registry at our center and followed up in a prospective fashion. All patients included gave informed consent to participate in the registry. The ethical committee of the UZ Brussel - VUB has approved the study protocol. The database for the purpose of this study was assessed in December 2007.

Patients were included in the current study if they met all of the following criteria: 1, documentation of spontaneous or drug induced $\geq 2\text{mm}$ coved (type I) Brugada ECG pattern in at least one right precordial lead in the index patient or in a first degree relative; 2, $\geq 1\text{mm}$ J point elevation in at least one inferior (leads II, III, aVF) or lateral (I, aVL) limb lead. 563 patients in the database were screened for inclusion in the analysis. The clinical data on 220 of these patients have been published in previous studies (1,13).

ECG definitions

The diagnosis of Brugada syndrome was based on the presence of spontaneous or class I ADD induced coved type I $\geq 2\text{mm}$ ST elevation in $\geq 1$ lead from V1 to V3, the presence of SCN5A mutation and the family history of Brugada syndrome. All available ECGs were screened for the presence of repolarization abnormalities in the inferior and lateral limb leads. All patients who had on at least one ECG $\geq 1\text{mm}$ J point elevation in any limb lead apart from aVR were diagnosed with inferior-lateral repolarization abnormality. The $\geq 1\text{mm}$ inferior-lateral J point abnormalities were further classified into two categories based on the type and magnitude of J point and ST elevation; either Early Repolarization Pattern or Coved Brugada Pattern was
diagnosed. Early Repolarization Pattern was defined as a notched ≥ 1 mm J wave or ≥ 1 mm J point elevation. Notched ≥ 1 mm J wave was defined as a ≥ 1 mm slurring or a positive hump at the QRS complex ST segment transition (Figure 1). The Coved Brugada Pattern was defined as ≥ 2 mm coved ST elevation. The inferior-lateral Early Repolarization Pattern and the Coved Brugada Pattern were further classified as spontaneous or class I AAD induced. During the class I AAD test, the baseline ECG and the ECG during the peak infusion of the class I AAD were considered apart. If inferior-lateral repolarization abnormality was present on the ECG at the end of the class I AAD infusion it was classified as class I AAD provoked repolarization abnormality, irrespective of its presence on the baseline ECG. The ECG repolarization abnormalities were classified by location as inferior (leads II, III, aVF) or lateral (I, aVL). All ECGs were analyzed by three independent investigators for the presence of inferior and lateral repolarization abnormalities. In case of discrepancy the ECG was reanalyzed by at least 2 investigators and consensus was reached about the type of repolarization pattern for the classification.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Class I antiarrhythmic drug test

Class I AAD test was performed to unmask the diagnostic ECG pattern. Most frequently intravenous ajmaline 0.7-1 mg/kg, administered in 5 minutes and less often flecainide 2mg/kg or procainamide 10 mg/kg given over a 10 minutes period were used for this purpose. The test was considered positive for Brugada syndrome if coved type I ECG was documented in ≥ 1 right precordial lead V1-V3.
Statistical analysis

Continuous variables are expressed as mean ±SD. The chi-square and Fisher’s exact tests were used to compare categorical values. Two-sided unpaired Student t test was used to compare continuous variables. The baseline values of the PR and QRS intervals were analyzed using two-way ANOVA considering the presence of Spontaneous Early Repolarization Pattern, inferior-lateral Coved Brugada Pattern and their interaction as factors. The changes in the PR and QRS intervals following class I AAD administration was investigated using repeated measures ANOVA. The comparison of patients with BS with family members without BS for Spontaneous Early Repolarization Pattern controlling for family was performed using the Cochran-Mantel-Haenszel (CMH) test. A p value ≤ 0.05 was considered statistically significant.

Results

Patient population

280 patients with the diagnosis of Brugada syndrome (mean age: 41 ± 18 y, male: 168 pts) were included in the study. The baseline clinical characteristics are shown in Table I. 255 patients underwent genetic testing. SCN5A mutation was identified in 39 patients belonging to 8 families. Four patients were lost to follow up. The mean follow up of the remaining 276 patients was 61.7 ± 47 months.
Incidence of spontaneous or class I AAD provoked inferior-lateral repolarization abnormalities in patients with Brugada syndrome

Of the 280 patients diagnosed with BS, 43 patients (15%) had inferior-lateral ECG repolarization abnormality spontaneously and/or during class I AAD test. The mean age of the 43 patients with inferior-lateral ECG abnormalities was 43±21 years and 27 patients (63%) were males. Of the 43 patients, 32 patients (11% of the whole population of patients with BS) had the inferior-lateral ECG abnormality present spontaneously and 23 patients (8% of the whole population of patients with BS) after class I AAD test. In 12 patients (4%) the inferior-lateral ECG abnormality was present both spontaneously and after class I AAD (Figure 2).

Spontaneous inferior-lateral Early Repolarization Pattern in Brugada syndrome

32 patients (11% of the patients diagnosed with BS) had the inferior-lateral ECG abnormality present spontaneously. All 32 patients had Early Repolarization Pattern (≥ 1 mm J wave) and none of the patients had Coved Brugada Pattern (≥ 2 mm coved ST elevation) spontaneously. In 20 patients (62%) the ECG abnormality was intermittent. Twelve patients (38%) had the repolarization abnormality present only in the lateral leads. Two patients (6%) had the ECG abnormality in both the lateral and inferior leads (Figure 3). The remaining 18 patients (56%) had the ECG abnormality only in the inferior leads. Patients with spontaneous inferior-lateral Early Repolarization Pattern were less likely to be asymptomatic as compared to patients
without these abnormalities (13 of 32 pts vs 156 of 248 pts, p=0.02). Additionally, right precordial spontaneous type I ECG was recorded more frequently among patients with spontaneous inferior-lateral Early Repolarization Pattern (53 of 248 pts vs 12 of 32 pts, p=0.05). Among patients with spontaneous inferior-lateral Early Repolarization Pattern class I AAD provoked more frequently Coved Brugada Pattern in the inferior-lateral leads (7 of 248 pts vs 6 of 32 pts, p=0.001). There was no significant difference between the baseline or class I AAD induced PR and QRS intervals comparing patients with or without spontaneous Early Repolarization Pattern (Table II).

### Class I AAD test provoked inferior-lateral Coved Brugada Pattern in Brugada syndrome

23 patients (8% of the patients with BS) had inferior-lateral repolarization abnormality at the end of the class I AAD test. Thirteen of the 23 patients, 4.6% of patients with BS, had ≥2 mm Coved Brugada Pattern in the inferior-lateral leads provoked by class I AAD administration. The coved ST elevation response was present in the lateral leads in one patient (0.4% of patients with Brugada syndrome) and in the inferior leads in 12 patients (4.3% of patients with Brugada syndrome). Patients with class I AAD test provoked inferior-lateral Coved Brugada Pattern were more likely to have Early Repolarization Pattern on the baseline ECG (6 of 13 pts vs 26 of 267 pts, p=0.001). The baseline PR interval was significantly longer among the thirteen patients with class I AAD provoked inferior-lateral Coved Brugada Pattern as compared to patients without this abnormality (206 ± 48 vs 172 ± 31 ms, p<0.001) (Table II). In contrast, the PR interval prolongation following class I AAD
administration was not significantly different between these two groups. The baseline QRS interval was not significantly different between patients with or without class I AAD provoked inferior-lateral Coved Brugada Pattern. However, following class I AAD administration the QRS interval prolonged significantly more in patients with class I AAD induced inferior-lateral Coved Brugada Pattern (from 108 ± 15 to 178 ± 53 ms vs from 102 ± 19 ms to 131 ± 24 ms, p<0.001). SCN5A mutation was identified with similar frequency among patients with or without inferior-lateral Coved Brugada Pattern (4 of 12 patients vs 35 of 243, p=NS).

Three of the 13 patients (1% of the patient population with the diagnosis of BS) had the class I AAD provoked ≥2 mm coved ST elevation only in the inferior leads and not in the right precordial leads. Therefore, these patients did not meet the current consensus criteria for BS. One of these three patients had Early Repolarization Pattern on the spontaneous ECG, the other two had normal spontaneous ECG. Two of these patients were from the same family with an identified SCN5A mutation. The other family members had the typical type I ECG pattern in the right precordial leads. Both patients presenting with only inferior coved ST elevation from this family were carriers of an SCN5A mutation. The third patient with only inferior class I AAD provoked coved ST elevation was an asymptomatic family member (Figure 4). The proband (her mother) had typical type I ECG pattern in the right precordial leads.

**Class I AAD test provoked inferior-lateral Early Repolarization Pattern in Brugada syndrome**

The remaining 10 of the 23 patients (4% of the BS patient population) had Early Repolarization Pattern present in the inferior-lateral leads at the end of the class
I AAD test. Six (60%) of these patients had Early Repolarization Pattern present also spontaneously prior to class I AAD administration. In these 6 patients the Early Repolarization Pattern did not increase significantly with the class I AAD administration. The PR and QRS intervals did not differ significantly between the patients with and without class I AAD test provoked Early Repolarization Pattern.

**Inferior-lateral Early Repolarization Pattern in family members without Brugada syndrome**

283 family members (age: 35±20 y, male: 140 pts) were diagnosed as not having Brugada syndrome. These healthy young individuals were also screened for the presence of inferior-lateral ECG abnormalities. 24 patients (8.5%) had Early Repolarization Pattern in the inferior-lateral limb leads either spontaneously or after class I AAD challenge. Seventeen patients (6%) had the inferior-lateral Early Repolarization Pattern spontaneously. In 3 patients the abnormality was in the lateral limb leads and in 14 patients in the inferior leads. Seventeen patients (6%) had the inferior-lateral Early Repolarization Pattern after class I AAD administration. Ten (59%) of these patients had inferior-lateral Early Repolarization Pattern also spontaneously. In these 10 patients the Early Repolarization Pattern did not increase significantly after class I AAD administration. There was no significant difference in any clinical parameter between the group of patients with or without inferior-lateral Early Repolarization Pattern. However, the baseline QRS interval was significantly longer among patients with inferior-lateral Early Repolarization Pattern (98 ± 16 vs. 90 ± 13 ms, p=0.03). No events occurred during the follow up in any of the patients with inferior-lateral Early Repolarization Pattern.
A global comparison of all patients with BS to the family members who did not have BS, spontaneous inferior-lateral Early Repolarization Pattern occurred significantly more frequently (11% (32 of 280 pts) vs. 6% (17 of 283 pts), p = 0.03). When considering only patients with BS for whom at least one family member was also tested (193 of the 280 patients) we observed an incidence of 9.8% (19 of 193) of the spontaneous inferior-lateral Early Repolarization Pattern. The difference using the CMH test controlling for family, was no longer significant (9.8% vs. 6%, p=0.158). This later finding might be due to the fact that one third of the patients had no family member tested, thus was excluded from the analysis. Alternatively, Spontaneous Early Repolarization Pattern might have a familial occurrence irrespective of the presence of Brugada syndrome.

Class I AAD induced Early Repolarization Pattern occurred with same frequency among patients with or without BS (4% vs. 6%, p=NS).

Discussion

Coved Brugada pattern in the inferior-lateral ECG leads in Brugada syndrome

The Brugada syndrome was originally reported 15 years ago as a peculiar ECG abnormality accompanied with an increased risk of sudden death. The ECG abnormality was described as right bundle branch block and ST elevation in the right precordial leads (1). Subsequently, large scale population studies revealed that J point and saddle back type ST elevation in the right precordial leads was relatively frequent
in the healthy general population (14-19). In contrast, J point elevation with coved type ST elevation was a very infrequent finding among apparently healthy individuals (14-19). In the meantime, data from international registries revealed that the majority of symptomatic patients had coved type ST elevation (13, 20). These data suggested that the coved type ST elevation carries a higher risk of arrhythmic events. However, the characteristic coved type I ECG has a dynamic nature; during long term follow up in almost all of the patients the ECG normalizes transiently. In patients with baseline saddle back type or normal ECGs class I sodium channel blockers can unmask the diagnostic coved type I pattern (2, 21). Based on these data, in 2002 a consensus panel defined the diagnostic ECG abnormality as spontaneous or class I antiarrhythmic drug induced coved type ST elevation in the presence of at least 2 mm J wave (type I ECG pattern) in the right precordial leads (V1 to V3) (2). Thus, currently, Brugada syndrome is only diagnosed in the presence of coved type I Brugada pattern in the right precordial leads (2, 3).

However, several cases were reported, in whom the coved Brugada pattern was present in the inferior or in one case in the lateral ECG leads (4-7). In all of these reports including altogether 4 patients, either spontaneously or after class I AAD challenge a diagnostic coved type I ECG was also recorded in the right precordial leads. Many of these patients presented with ventricular fibrillation or syncope in the setting of a structurally normal heart. In one of these reports, the patient was a proband with inferior coved ST elevation of a family with identified SCN5A mutation. The SCN5A mutation expression in vitro showed a loss of function type effect on the sodium channel, the same effect as observed in the typical from of Brugada syndrome. The four other family members carrying the same mutation showed the typical form of Brugada syndrome with diagnostic coved type I ECG
pattern in the right precordial leads (4). All these findings suggest that Brugada syndrome has a phenotype variant in which the diagnostic coved ECG manifests not only in the right precordial but also in the inferior leads.

In the current study we systematically investigated the occurrence of ≥ 2 mm coved type ST elevation in the inferior-lateral leads in a large population of patients with Brugada syndrome. In our study population, the coved Brugada pattern did not occur spontaneously in the inferior or lateral leads. This data suggests that the presence of spontaneous coved ST elevation in the inferior-lateral leads is an exceptional finding in BS.

In contrast, class I AAD administration provoked coved Brugada pattern in the inferior or lateral leads in 4.6% of our study population. The localization of the coved Brugada pattern was the lateral leads in only one patient, corresponding to 0.4% of our Brugada patient population. This finding suggests that coved Brugada pattern in the lateral leads is a rather exceptional finding. In contrast, coved Brugada pattern was provoked in the inferior leads in 4.3% of our study population. More importantly, for the first time we report 3 patients (1% of the patient population with BS) in whom the ≥ 2 mm coved ST elevation was only present in the inferior leads. These patients do not meet the current consensus criteria for the diagnosis of Brugada syndrome. Two of these patients had an identified SCN5A mutation and a relative of the third patient had typical BS. These data, together with evidence from previous case reports supports the need to revise the consensus diagnostic criteria. We recommend that patients with class I AAD provoked ≥ 2 mm coved type ST elevation in the inferior leads even without the diagnostic type I ECG in the right precordial leads should be diagnosed as Brugada syndrome.
The pathophysiological mechanism of the inferior or lateral location of the coved type ST elevation is unknown. Currently there are two proposed explanations for the presence of the Brugada type ECG patterns in the right precordial leads; the repolarization disorder and the depolarization disorder theories (22, 23). In our study we report the important finding that BS patients with coved Brugada pattern in the inferior-lateral leads had spontaneously significantly longer PR intervals than patients without inferior-lateral ECG abnormalities. Furthermore, following the administration of a sodium channel blocker the QRS interval prolonged significantly more in patients with the inferior-lateral coved Brugada pattern. These findings favor the importance of conduction slowing in the genesis of the coved inferior-lateral Brugada pattern.

Inferior-lateral early repolarization pattern in Brugada syndrome

Aizawa et al reported several cases of idiopathic ventricular fibrillation in Japanese men that were associated with a notch in the late part of the QRS complex in the inferior leads (11). Subsequently, other similar cases of idiopathic ventricular fibrillation with accentuated J wave with or without ST elevation in the inferior leads were observed (8-11). In 4 patients the administration of a class I AAD augmented the J wave and ST segment elevation (8,9), but it failed to do so in other 4 patients (10, 11). Very recently, Haissaguerre et al reported a multicenter study of 206 patients with idiopathic ventricular fibrillation (12). They found that early repolarization pattern in the inferior or lateral leads was more frequent among patients with idiopathic ventricular fibrillation as in a healthy control group (31% vs. 5%, p<0.001). Early repolarization was defined as ≥ 1 mm elevation of the QRS-ST junction in at least 2 inferior or lateral leads (including V4-V6). The ECG abnormality was
dynamic, but in some cases increase in the J point and ST elevation preceded spontaneous episodes of ventricular fibrillation. The presence of spontaneous or class I AAD test provoked right precordial coved ST segment elevation was an exclusion criteria. However, only 65% of the patient population (84% of the patients with early repolarization pattern) underwent a class I AAD test. The type of antiarrhythmic drug used for the test was not specified. In the tested patients sodium channel blockers did not augment the early repolarization abnormalities (12).

In this study we investigated the presence of inferior-lateral early repolarization pattern in a large population of BS, using a very similar definition as Haissaguerre et al. Our study has several new important findings connected to the study of idiopathic ventricular fibrillation and early repolarization. First, we report that the inferior-lateral early repolarization pattern occurs also relatively frequently in patients with BS, more frequently than in a control group of family members without BS (11% vs. 6%, p=0.03). Secondly, we report that BS has a phenotype variant in which class I AAD provoked coved Brugada pattern appears in the inferior or lateral leads. These patients with Brugada syndrome have frequently early repolarization pattern on the baseline ECG. Our findings suggest that BS should be carefully excluded in patients with inferior-lateral early repolarization pattern and idiopathic ventricular fibrillation. The main difference between the newly described early repolarization disorder and BS seems to be the appearance of coved ST elevation in response to sodium channel blockers in BS either in the inferior-lateral or in the right precordial leads. In our opinion without the performance of class I AAD test, as was the case in 16% of patients reported by Haissaguerre et al, the diagnosis of Brugada syndrome can not be excluded in patients with early repolarization disorder and ventricular fibrillation. Furthermore, the likelihood of diagnosing BS in patients with
early repolarization disorder is also dependent on the type of class I AAD used for the test. It has been reported the flecainide and procainamide are less sensitive than ajmaline (2, 3, and 24). The type of sodium channel blocker used for the class I AAD test has not been reported by Haisaguerre et al. Additionally, in some patients with early repolarization disorder the class I AAD test will provoke ≥ 2 mm coved ST elevation in the inferior-lateral and/or right precordial leads. These patients should be diagnosed with BS and/or as overlapping phenotype of BS with the new early repolarization disorder. In our opinion the diagnosis of Brugada syndrome in these patients has important implications for the clinical management and the family screening. For example, if Brugada syndrome is diagnosed, the patient should not receive sodium channel blockers and his family should be screened with class I AAD test.

We used the family members who tested negative for Brugada syndrome as a control group to examine the incidence of the inferior-lateral early repolarization pattern in a healthy young population. The incidence of spontaneous inferior-lateral early repolarization pattern was 6%. This finding is similar to the 5% incidence reported by Haissaguerre et al. This data suggests that similar to the saddle back ST elevation in the right precordial leads, early repolarization pattern in the inferior-lateral leads occurs also frequently in young healthy individuals. We believe that prior to attributing increased arrhythmia risk to the presence of asymptomatic inferior or lateral early repolarization disorder in the general population, further population studies are necessary.

Limitations
This study was retrospective and included a limited but significant number of patients. We used family members tested for Brugada syndrome as control instead of an independent age and sex matched control group. However, some of these individuals might be silent mutation carriers. Furthermore, we compared the incidence of spontaneous early repolarization pattern between patients with or without Brugada syndrome coming from the same families. It is likely that the presence of spontaneous early repolarization pattern is genetically defined, thus an increased familial occurrence is expected. This might explain the slightly higher incidence of the early repolarization pattern in our control group as compared to the independent control group of Haissaguerre et al (6% vs 5%, respectively). Additionally, this might be a reason why when considering only patients with BS for whom at least one family member was also tested the difference in the incidence of the early repolarization pattern when controlling for family was no longer significant (9.8% vs. 6%, p=0.158).

In the future, further studies are necessary to prove these hypotheses.

Our definition of early repolarization was slightly different from the one used by Haissaguerre et al. We included patients with J wave abnormalities present in one lead instead of 2 leads. However, we did not include patients with early repolarization in the left precordial leads.

Conclusions

In this study we report that 11% of the patients with BS have spontaneous early repolarization pattern in the inferior-lateral leads. This group of patients seemed to have a more severe phenotype. The inferior-lateral early repolarization pattern occurred more frequently in patients with BS than in their family members not having
BS. Class I AAD administration provoked coved Brugada pattern in the inferior-lateral leads in 4.6% of patients with BS. These patients have significantly longer conduction intervals. For the first time we report 3 patients (1% of the study population) in whom the coved Brugada pattern is only present in the inferior leads. We provided evidence that these patients should be diagnosed with BS.

Conflict of interest disclosures: none.

References


Figure 1, Example of spontaneous notched ≥ 1 mm J wave in the inferior leads (arrows) in BS. The patient was a 75 year old proband presenting with aborted sudden death. Notice the diagnostic type I ECG in the right precordial leads and wide QRS complexes (QRS=140 ms).

Figure 2, Example of a 55 years old asymptomatic proband with both spontaneous notched ≥ 1 mm J wave and class I AAD test induced coved type ST elevation in the inferior leads. A, The baseline ECG shows ≥ 1 mm notched J wave in the inferior leads (arrows). Notice the diagnostic type I Brugada ECG pattern in the right precordial leads and the first degree AV block (PR=260 ms). B, during the administration of 0.7 mg/kg ajmaline the diagnostic type I Brugada ECG pattern appeared in the right precordial leads and the test was terminated. Two minutes later the coved ST elevation also appeared in the inferior leads (arrows).

Figure 3, Example of a spontaneous notched J wave in both the inferior and lateral leads. A, The ECG of 53 years old Asian male proband following admission with aborted sudden death shows notched J wave both in the inferior and lateral and even in the precordial leads V3-6 (arrows). B, A follow-up ECG shows in the inferior leads less pronounced J wave (arrows) in the presence of atrial fibrillation and type II saddle back Brugada ECG pattern in the right precordial lead V2. C, The administration of 0.5 mg/kg ajmaline provoked the diagnostic type I ECG pattern in the right precordial leads V1 and V2.
Figure 4. Example of coved ST type elevation appearing only in the inferior leads during class I AAD test. The patient is the 10 years old asymptomatic daughter of a proband with typical Brugada syndrome. A, The baseline ECG was normal. At the end of the 0.7 mg/kg ajmaline infusion in the inferior leads ST alternans (arrows) with contra lateral ST depression in the lateral and precordial leads V2-V5. C, Two minutes after the end of the ajmaline infusion ≥ 2 mm coved type ST elevation appeared in the inferior leads (arrows) with contra lateral ST depression in the right precordial leads.
Table I. Clinical characteristics of patients diagnosed with Brugada syndrome

<table>
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<th>Clinical characteristics</th>
<th>Number of patients (%)</th>
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<tr>
<td>Proband</td>
<td>157 pts (56%)</td>
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<tr>
<td>Positive family history of sudden death &lt;65 y</td>
<td>149 pts (53%)</td>
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<tr>
<td>Clinical presentation</td>
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<tr>
<td>Asymptomatic</td>
<td>169 pts (60%)</td>
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<tr>
<td>Presyncope, palpitation</td>
<td>44 pts (16%)</td>
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<td>Syncope</td>
<td>68 pts (24%)</td>
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<td>Aborted Sudden Death</td>
<td>14 pts (5%)</td>
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<td>Baseline ECG</td>
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<tr>
<td>Type I</td>
<td>65 pts (23%)</td>
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<tr>
<td>Type II</td>
<td>49 pts (18%)</td>
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<tr>
<td>Type III</td>
<td>15 pts (5%)</td>
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<tr>
<td>Normal</td>
<td>151 (54%)</td>
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<tr>
<td>EPS inducible VT/VF* (performed in 238 pts)</td>
<td>61 pts (26%)</td>
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</table>

* EPS = Electrophysiological study, VT/VF = Ventricular tachycardia/ Ventricular fibrillation
Table II, Comparison of spontaneous and class I AAD test induced ECG conduction parameters between patients with and without Spontaneous Early Repolarization Pattern (SERP) and Class I AAD induced inferior lateral coved Brugada Pattern (ICBP).

<table>
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<tr>
<th></th>
<th>Only SERP*</th>
<th>Only ICBP†</th>
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<td></td>
<td>(26 pts)</td>
<td>(7 pts)</td>
<td>(6 pts)</td>
<td>(241 pts)</td>
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<tr>
<td><strong>Baseline (ms)</strong></td>
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<tr>
<td>PR (ms)</td>
<td>174 ± 22</td>
<td>197 ± 33</td>
<td>217 ± 63</td>
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<td>QRS (ms)</td>
<td>105 ± 15</td>
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<td><strong>Following class I AAD administration (ms)</strong></td>
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<tr>
<td>PR (ms)</td>
<td>209 ± 33</td>
<td>247 ± 45</td>
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<td>207 ± 40</td>
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<td>QRS (ms)</td>
<td>135 ± 29</td>
<td>186 ± 57</td>
<td>170 ± 50</td>
<td>130 ± 24</td>
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</table>

* SERP = Spontaneous Early Repolarization Pattern

† ICBP = class I AAD provoked Inferior lateral Coved Brugada Pattern
Figure 2.
Figure 3.
Figure 4.
Inferior and lateral electrocardiographic repolarization abnormalities in Brugada syndrome
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