The impact of clinical and genetic findings on the management of young Brugada Syndrome patients

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Brugada Syndrome

Diagnosis and ECG pattern

- **ECG pattern of Brugada Syndrome**

- **Diagnosis**
  - Type 1 ECG pattern
  - At least in one right precordial lead
  - Spontaneous or drug-induced

- **Clinical data**
  - Low prevalence: 0.02 %
  - Ventricular arrhythmia and SCD
  - Lack of data

Brugada Syndrome, Mizusawa & Wilde, Circ EP, 2012
Diagnosis and Management of Patients with Inherited Primary Arrhythmia Syndromes, Priori S., HR, 2013

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**Study design**

- **Study design**
  - Multicentric, European
  - Retrospective

- **Inclusion Criteria**
  - ≤ 18 year of age at diagnosis
  - Spontaneous Type 1 ECG pattern
    - OR
  - Drug-induced Type 1 ECG pattern
    - Ajmaline: 1mg/kg
    - Flécaïnide: 2mg/kg

- **Collected Data**
  - Clinical: symptom at diagnosis, past medical history, familial history, ...
  - ECG: baseline and during drug-challenge
  - Genetic: SCN5A mutations
  - Therapeutic: hydroquinidine, ICD, ...

Symptoms were defined as syncope, SCD or ventricular arrhythmia

- **Objectives**
  - Describe the pediatric Brugada Syndrome clinical presentation
  - Identify prognostic factors for risk stratification
• 106 patients from 16 tertiary European hospitals

<table>
<thead>
<tr>
<th>Population</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>58 (55)</td>
</tr>
<tr>
<td>Age at diagnosis, y</td>
<td>11.1 ± 5.7</td>
</tr>
<tr>
<td>Follow-up, mo</td>
<td>54 [15-99]</td>
</tr>
<tr>
<td>Spont. Type 1 ECG Pattern, n</td>
<td>36 (34)</td>
</tr>
<tr>
<td>SCN5A mutation, n (n=75)</td>
<td>58 (77)</td>
</tr>
<tr>
<td>Familial history of SCD, n (%)</td>
<td>46 (43)</td>
</tr>
</tbody>
</table>
Collected Data

Drug challenges, symptoms and follow-up

- **Sodium blocker challenges**
  - **Ajmaline**: n=42; 14.3 ± 3.7 ans
  - **Flecaïnide**: n=27; 13.4 ± 4.5 ans
  - 33 challenges below age 15
  - 2 non-sustained ventricular tachycardia during challenges

- **Symptoms at diagnosis**
  - **Symptomatic**: n=21
    - 15 syncopes
    - 4 aSCD and 2 VT
  - **Asymptomatic**: n=80
    - 63 familial screening
    - 13 incidental

- **Follow-up**
  - 15 life threatening events among 10 patients:
    - 3 deaths
    - 2 ventricular fibrillation and tachycardia
    - 5 ventricular tachycardia only
    - ¼ triggered by fever
  - 6 syncope without documented arrhythmia
  - 4 supra ventricular tachycardia

- **Hydroquinidine/ICD/SCN5A**
  - 8 of 11 free of events on hydroquinidine
  - 9 (41%) of the 22 ICD implanted experienced serious ICD-related complications
  - No event in the 17 SCN5A negative

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Predictive factors of arrhythmic events

**Symptoms and spontaneous type 1 ECG pattern**

<table>
<thead>
<tr>
<th></th>
<th>LTA events (n=10)</th>
<th>No LTA event (n=96)</th>
<th>HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>6 (60)</td>
<td>52 (54)</td>
<td>0.79</td>
<td>0.72</td>
</tr>
<tr>
<td>Sympto. at diag., n</td>
<td>7 (70)</td>
<td>14 (15)</td>
<td>9.65</td>
<td>0.001</td>
</tr>
<tr>
<td>(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spont. Type 1 (%)</td>
<td>8 (80)</td>
<td>28 (29)</td>
<td>9.1</td>
<td>0.005</td>
</tr>
<tr>
<td>Familial SCD, n (%)</td>
<td>3 (30)</td>
<td>43 (45)</td>
<td>2.12</td>
<td>0.28</td>
</tr>
<tr>
<td>SCN5A mut., n (%)</td>
<td>9 (90)</td>
<td>49 (51)</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>

Spontaneous type 1 ECG pattern and symptoms at diagnosis are predictive of a shorter time to first life threatening arrhythmic event
Predictive factors of arrhythmic events

**Cumulative risk stratification**

- Symptoms **AND** Spontaneous type 1 ECG pattern  ➔ **HIGH RISK**
- Asymptomatic **AND** drug-induced type 1 ECG pattern  ➔ **LOW RISK**
- Others clinical situations  ➔ Intermediate risk?

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>12</th>
<th>24</th>
<th>60</th>
<th>96</th>
<th>120</th>
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</thead>
<tbody>
<tr>
<td>S+/E+ = Sympto. &amp; Spont. Type 1</td>
<td>14</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>S+/E- = Sympto. &amp; Drug induced</td>
<td>7</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>S-/E+ = Asympto. &amp; Spont. Type 1</td>
<td>22</td>
<td>22</td>
<td>13</td>
<td>11</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>S-/E- = Asympto. &amp; Drug induced</td>
<td>63</td>
<td>63</td>
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<td>63</td>
</tr>
</tbody>
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Discussion

• **Questionable drug challenges?**
  – Not really useful before age 15 if no symptoms
  – Not too early (false negative) and incidence increase after childhood

• **Fever: a trigger for arrhythmic events**
  – Parents need to be advised to treat it!
  – Record a standard ECG if a BrS child come to hospital with fever
  – Monitor until it returns to its usual baseline

• **SCN5A mutations**
  – High prevalence in index patients
  – No arrhythmic event in genotype negative patients + 9/10 with events were genotype positive patients
  – Could be useful for risk stratification?

• **Therapeutic**
  – ICD: useful against sudden death but high devices related complications
  – Quidinidine: could be useful but not demonstrated yet
Introduction

Methods

Results

Discussion

Conclusion

Brugada Syndrome in the Young

• Spontaneous type 1 ECG pattern and symptoms at diagnosis are predictive of a shorter time to first arrhythmic event in the young.

• Arrhythmic risk is high in patients with both symptoms and spontaneous type 1 and they need to be considered for ICD or quinidine therapy.

• Regular clinical follow-up seems to be sufficient for patients with drug-induced type 1 without any symptom.

• Consider hydroquinidine in other situations?

• Fever remains the most important trigger and need to be treated.
Merci de votre attention
Management of the Young with a known BrS in the Family

**Spontaneous type 1 ECG pattern**

*Or earlier review at physician discretion
† Potentially cardiac arrhythmias related symptoms, excluding vaso-vagal syncope
‡ If allowed by current local regulations
§ Ajmaline 1mg/Kg or flecaïnide 2mg/Kg

- **Pathogenic variant in first degree relatives**
  - No
  - Yes

  **Every year**
  - Control ECG + 12 leads 24h Holter
  - Genetic testing if genotype positive relatives

  **Symptoms**
  - Consider ICD or quinidine

**Symptoms†**

- No
- Yes (Consider if no contra-indication)

**Pharmacologic challenge§**

- Positive
- Negative

- **Every 2-3 years**
  - ECG + 12 leads 24h Holter
  - Consider quinidine

- **Every year**
  - ECG +12 leads 24h Holter
  - Consider quinidine

- **Every 5 years**
  - ECG + 12 leads 24h Holter

**Positive**

- **Age 15**
  - Pharmacologic challenge§

**Negative**

- **Prone to BrS**
  - Every 2-3 years
  - ECG + 12 leads 24h Holter

**Not prone to BrS**

- Every year
  - ECG + 12 leads 24h Holter