Channelopathy characterized by:

- **Genetic mutations**: Na\(^+\) channel in 15-30% of pts; Ca\(^{++}\) channel, K\(^+\) channel, GPD1L

**Brugada syndrome: diagnosis**

- **Diagnostic ECG**: typical ECG alterations (V\(_1\)-V\(_2\))
- **Risk of sudden death**
- **NO structural heart disease**
  - J point ≥ 2mm
  - Coved type ST segment elevation
  - Negative T wave

---

**Diagnosis**

- J point ≥ 2mm
- Coved type ST segment elevation
- Negative T wave
LOOP RECORDER
ICD
HIDROQUINIDINE
EPS
12L-HOLTER
F-UP
ABLATION
LOOP RECORDER
HIDROQUINIDINE
Brugada Piedmont Registry

826 pts → 12 diagnosed after Sudden Death

**total 814 pts** 2001-2016

### Symptoms at presentation

- **Asymptomatic** 608 (75%)
- **Syncope** 195 (24%)
- **neurally mediated** 77 (9%)
- **unexplained**
- **aSD** 11 (1.4%)

**Locations**
- Torino
- Asti
- Vercelli
- Orbassano
- Rivoli
- Cuneo
- Novara
- Savigliano

**Unexplained events**
- 118 (15%)
- 1 (1%)
A 45 years old man: traumatic syncope, which occurred after awakening at 6.30 a.m, while he was in the bathroom, with doubtful prodromes

1st ECG: sinus rhythm, normal conduction, non-significant ST-T alterations
Head-up tilt test (HUTT)

Tilt test was negative but

ST segment in V1-V2 with a type 2 Brugada pattern was recorded
Pt with syncope + suspect Brugada ECG (type 2)

Which investigations are reasonable/recommended?

ECG with V1-V2 at 2nd and 3rd intercostal space (ICS)
ECG was recorded with V1-V2 at a higher intercostal space →

in this case it remained doubtful, still not diagnostic
Which investigations are reasonable/recommended?

Pt with syncope + suspect Brugada ECG pattern (type 2) →

ECG with V1-V2 at 2nd and 3rd intercostal space →

type 2 Brugada ECG →

Drug challenge with sodium channel blockers
Pharmacological challenge with Na\(^+\)-channel blockers was performed...

**Basal ECG**

- V1
- V2
- V3
- V4

**Ajmaline infusion (1mg/kg in 5 min)**

- V1
- V2
- V1 - II space
- V2 - II space
What do guidelines recommend?

What does literature report?

Summary...

✓ 45 years old man
✓ syncope of uncertain origin
✓ Drug induced type 1 Brugada ECG pattern
Natural History of Brugada Syndrome
Insights for Risk Stratification and Management

Silvia G. Priori, MD, PhD; Carlo Napolitano, MD, PhD; Maurizio Gasparini, MD; Carlo Pappone, MD; Paolo Della Bella, MD; Umberto Giordano, MD; Raffaella Bloise, MD; Carla Giustetto, MD; Roberto De Nardis, MD; Massimiliano Grillo, MD; Elena Ronchetti, PhD; Giovanna Faggiano, MD; Janni Nastoli, BS

Circulation 2002;105:1342

HR 6.4 for risk of cardiac arrest

Italian Registry
200 pts

No syncope, nor type 1

Syncope + induced type 1

Asymptomatic spontaneous type 1

Syncope + spontaneous type 1
1312 patients from 14 prospective observational studies
12-lead 24-hour Holter monitoring: intermittent spontaneous type 1 Brugada pattern
Summary…

✓ 45 years old man
✓ syncope of uncertain origin
✓ drug induced type 1 Brugada ECG pattern and
✓ spontaneous type 1 documented at f-up

What do guidelines recommend?
What does literature report?
2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

ICD implantation should be considered in patients with a spontaneous diagnostic type 1 ECG pattern and history of syncope.

ICD implantation may be considered in patients with a diagnosis of Brugada syndrome who develop VF during PVS with two or three extrastimuli at two sites.
Role of EP-study in Brugada pts (overall population)

Probst et al, FINGER Registry, Circulation 2010;121: 635

P = 0.05
Programmed Ventricular Stimulation for Risk Stratification in the Brugada Syndrome
A Pooled Analysis

Sroubek J et al. Circulation 2016;133:622-630
Annual incidence of cardiac arrest among 1312 individuals included in the analysis

<table>
<thead>
<tr>
<th></th>
<th>Spontaneous Type 1 ECG Pattern</th>
<th>Drug-Induced Type 1 ECG Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syncope at presentation</td>
<td>34/1056 (3.22 (2.23–4.50))</td>
<td>10/693 (1.44 (0.69–2.65))</td>
</tr>
<tr>
<td>Events, n/person-y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>3.22 (2.23–4.50)</td>
<td>1.44 (0.69–2.65)</td>
</tr>
<tr>
<td>Induced arrhythmia</td>
<td>5.60 (2.98–9.58)</td>
<td>1.96 (0.40–5.73)</td>
</tr>
<tr>
<td>No induced arrhythmia</td>
<td>2.55 (1.58–3.89)</td>
<td>1.29 (0.52–2.67)</td>
</tr>
<tr>
<td>Asymptomatic at presentation</td>
<td>17/1630 (1.04 (0.61–1.67))</td>
<td>4/1506 (0.27 (0.07–0.68))</td>
</tr>
<tr>
<td>Events, n/person-y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>1.04 (0.61–1.67)</td>
<td>0.27 (0.07–0.68)</td>
</tr>
<tr>
<td>Induced arrhythmia</td>
<td>1.70 (0.73–3.35)</td>
<td>0.45 (0.01–2.49)</td>
</tr>
<tr>
<td>No induced arrhythmia</td>
<td>0.78 (0.36–1.47)</td>
<td>0.23 (0.05–0.68)</td>
</tr>
</tbody>
</table>

Incidence rates expressed as annual percentages, (95% confidence intervals). Induced arrhythmia defined as that occurring with single or double extrastimuli.

Sroubek J et al. Circulation 2016;133:622-630
Etiological diagnosis, prognostic significance and role of electrophysiological study in patients with Brugada ECG and syncope

Carla Giustetto, Natascia Cerrato, Enrico Ruffino, Elena Gribaudo, Chiara Scrocco, Lorella Barbonaglia, Francesca Bianchi, Miriam Bortnik, Guido Rossetti, Paula Carvalho, Riccardo Riccardi, Davide Castagno, Matteo Anselmino, Laura Bergamasco, Fiorenzo Gaita

Int. J. of Cardiology 2017; 241:188–193

Arrhythmic events in neurally mediated syncope versus unexplained

<table>
<thead>
<tr>
<th>Group</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>118</td>
<td>97</td>
<td>78</td>
<td>64</td>
<td>50</td>
<td>39</td>
<td>33</td>
<td>28</td>
<td>23</td>
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<td>18</td>
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<tr>
<td>G2</td>
<td>77</td>
<td>68</td>
<td>59</td>
<td>49</td>
<td>42</td>
<td>37</td>
<td>30</td>
<td>26</td>
<td>19</td>
<td>12</td>
<td>9</td>
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</tr>
</tbody>
</table>

f-up 62 months

p < 0.001

Neurally mediated

2 (0.3% person-year)

Unexplained

6 (1.8% person-year)
Etiological diagnosis, prognostic significance and role of electrophysiological study in patients with Brugada ECG and syncope

Role of PVS in unexplained syncope

Best predictors of ventricular events at follow-up:
- unexplained syncope
- spontaneous type 1
- Inducibility at PVS

<table>
<thead>
<tr>
<th>pos EPS</th>
<th>26</th>
<th>23</th>
<th>22</th>
<th>20</th>
<th>17</th>
<th>15</th>
<th>14</th>
<th>13</th>
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<tr>
<td>neg EPS</td>
<td>31</td>
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<td>14</td>
<td>14</td>
<td>10</td>
<td>8</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

27% 5.2% per year 0 events
19 years old man, asymptomatic for syncope, no history of SD.
ECG for sport eligibility: suspicious for Brugada pattern

What should we do?
Brugada Piedmont Registry 684 patients

12 Lead - 24 hour Holter 251 patients

- Spontaneous type 1 at basal ECG (group 1): 70%
- Drug-induced type 1 (group 2): 30%

Group 1:
- Persistent type 1: 12%
- Intermittent type 1: 57%
- No type 1: 31%

Group 2:
- Persistent type 1: 80%
- Intermittent type 1: 20%
12-lead Holter ECG: NO spontaneous type 1
Asymptomatic 19 years old pt evaluated for sport eligibility

Basal ECG

Positive ajmaline test
Augmented ST-Segment Elevation During Recovery From Exercise Predicts Cardiac Events in Patients With Brugada Syndrome

Hisaki Makimoto, MD,* Eiichiro Nakagawa, MD, PhD,† Hiroshi Takaki, MD, PhD,* Yuko Yamada MD,* Hideo Okamura, MD,* Takashi Noda, MD, PhD,* Kazuhiro Satomi, MD, PhD,* Kazuhiro Suyama, MD, PhD,* Naohiko Aihara, MD,* Takashi Kurita, MD, PhD;‡ Shiro Kamakura, MD, PhD,* Wataru Shimizu, MD, PhD*

Exercise test

93 Brugada pts

yes 37%

no 63%

102 controls

augmentation of ST-segment elevation at early recovery?

none
pre-exercise test

Peak exercise
Which investigations are reasonable/recommended?

Asymptomatic pt
+
suspect Brugada ECG pattern (type 2)

Negative 12-lead-Holter monitoring

Type 1 Brugada ECG at exercise test

programmed ventricular stimulation
Brugada Registry of the Piedmont region: arrhythmic events at follow-up

Mean follow-up of 62 ± 48 months

Freedom from arrhythmic events vs time (years)

<table>
<thead>
<tr>
<th>Group</th>
<th>Time (years)</th>
<th>Events</th>
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<tbody>
<tr>
<td>G1</td>
<td>0-2</td>
<td>118</td>
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<td>110</td>
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<td></td>
<td>70</td>
</tr>
</tbody>
</table>

Unexplained syncope vs asymptomatic

Unexplained: 9% (1.8% person-year)
Asymptomatic: 2% (0.3% person-year)
Neurally-mediated: 1% (0.2% person-year)

Asympt, p <0.0001
Meta-Analysis on Risk Stratification of Asymptomatic Individuals With the Brugada Phenotype

Konstantinos P. Letsas, MD, Tong Liu, MD, PhD, Qingmiao Shao, MD, Panagiotis Korantzopoulos, MD, PhD, Georgios Giannopoulos, MD, Konstantinos Vlachos, MD, Stamatis Georgopoulos, MD, Athanasios Trikas, MD, Michael Efremidis, MD, Spyridon Deftereos, MD, and Antonios Sideris, MD

Am J Cardiol 2015;116:98e103

14 prospective observational studies  
mean f-up 20 - 77 months

3,536 asymptomatic subjects (2,820 men) \( \rightarrow \) 1,398 with spontaneous type 1 ECG

Asymptomatic pts with spontaneous type 1 ECG exhibit an increased risk of arrhythmic events
Inducible ventricular arrhythmias at PVS were predictive of arrhythmic events.
In summary:

1. **aSD**
   - ICD
   - if still arrhythmic events or ICD refusal: add HQ/ablation

2. **unexplained SYNCOPE**
   - PVS +
   - ICD
   - PVS -
     - loop recorder

3. **neurally mediated SYNCOPE / ASYMPTOMATIC**
   - Spontaneous type 1 ECG
   - Drug-induced type 1
   - 12 lead Holter: Spontaneous type 1
   - YES
   - NO
     - F-up
Thank you for your attention!