Understanding ECG Features in ARVD, Long QT and Brugada Syndrome

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Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is a progressive disease of predominantly the right ventricle, characterized by ventricular tachycardia that can lead to sudden cardiac death in children and young adults.
ECG in ARVD

ECG in sinus rhythm

1) Prolonged QRS duration \( \geq 110 \) msec in leads V1-V3.
2) Epsilon wave.
3) T wave inversion in right precordial leads.
4) Low-voltage QRS amplitude.
ARVD (ARVC)

ECG in sinus rhythm

1) QRS in V1 $\geq 110$ msec

2) epsilon wave

3) T wave inversion
ECG in ARVD

ECG in sinus rhythm

1) Prolonged QRS duration ≥ 110 msec in leads V1-V3.
2) Epsilon wave.
3) T wave inversion in right precordial leads.
4) Low-voltage QRS amplitude.
ECG in ARVD

ECG in sinus rhythm

1) **Prolonged QRS duration ≥ 110 msec in leads V1-V3.**

Prolonged QRS duration ≥ 110 msec in lead V1 was reported to carry a sensitivity of 55% and a specificity of 100% in a series of patients whose initial manifestation was sustained ventricular tachycardia. Generally, QRS duration is more prolonged in lead V1 compared to that in leads I and V6. Complete or incomplete right bundle branch block is also a common finding.
**ECG in ARVD**

**ECG in sinus rhythm**

1) Prolonged QRS duration ≥ 110 msec in leads V1-V3.

2) Epsilon wave.

3) T wave inversion in right precordial leads.

4) Low-voltage QRS amplitude.
ECG in ARVD

ECG in sinus rhythm

2) Epsilon wave.

Epsilon wave, an abnormal deflection resulting from delayed right ventricular activation is noticed at the end of the QRS complex in up to 30% of patients.
ECG in ARVD

ECG in sinus rhythm

1) Prolonged QRS duration $\geq 110$ msec in leads V1-V3.
2) Epsilon wave.
3) T wave inversion in right precordial leads.
4) Low-voltage QRS amplitude.
ECG in ARVD

ECG in sinus rhythm

3) T wave inversion in right precordial leads.

T wave inversion in right precordial leads is frequently seen in about 60% of patients with T wave abnormalities in leads V1 to V3 and remains the most suggestive indicator of ARVD.
ECG in ARVD

ECG in sinus rhythm

1) Prolonged QRS duration ≥ 110 msec in lead V1–V3.
2) Epsilon wave.
3) T wave inversion in right precordial leads.
4) Low-voltage QRS amplitude.
4) Low-voltage QRS amplitude.

Low-voltage QRS amplitude indicates a widespread myocardial process.
ARVD (ARVC) - severe case -

ECG in sinus rhythm

1) QRS in V1 ≥ 110 msec

2) epsilon wave

3) T wave inversion

4) low-voltage
ECG in ARVD

Signal-averaged ECG

Abnormal signal-averaged ECGs are often found in patients with ARVD. The fibrofatty replacement characteristic of ARVD interrupts the electrical continuity of myocardial fibers, which accounts for conduction delay. Signal-averaged ECG have a sensitivity of 57% and a specificity of 95%.
ECG in ARVD

Signal-averaged ECG

Late potentials
ECG in ARVD

ECG of arrhythmias

Left bundle branch block (LBBB) type ventricular tachycardia.

Frequent ventricular extrasystole (more than 1000/24 hours)
ARVD (ARVC)

Ventricular premature contraction: VPC

LBBB type
ARVD (ARVC)

ventricular tachycardia: VT

LBBB type
## ARVD - Diagnostic Criteria -

### I Global and/or regional dysfunction and structural alterations
- **MAJOR**
  - Severe dilatation and reduction of right ventricular ejection fraction with no (or only mild) LV impairment
  - Localised right ventricular aneurysms (akinetoric or dyskinetic areas with diastolic bulging)
  - Severe segmental dilatation of the right ventricle
- **MINOR**
  - Mild global right ventricular dilatation and/or ejection fraction reduction with normal left ventricle
  - Mild segmental dilatation of the right ventricle
  - Regional right ventricular hypokinesia

### II Tissue characterisation of walls
- **MAJOR**
  - Fibrofatty replacement of myocardium on endomyocardial biopsy

### III Repolarisation abnormalities
- **MINOR**
  - Inverted T waves in right precordial leads (V2 and V3)
    - (people aged more than 12 yr; in absence of right bundle branch block)

### IV Depolarisation/conduction abnormalities
- **MAJOR**
  - Epsilon waves or localised prolongation (> 1 10 ms) of the QRS complex in right precordial leads (V1-V3)
- **MINOR**
  - Late potentials (signal averaged ECG)

### V Arrhythmias
- **MINOR**
  - Left bundle branch block type ventricular tachycardia
    - (sustained and non-sustained) (ECG, Holter, exercise testing).
  - Frequent ventricular extrasystoles (more than 1000/24 h) (Holter)

### VI Family history
- **MAJOR**
  - Familial disease confirmed at necropsy or surgery
- **MINOR**
  - Familial history of premature sudden death (<35 yr) due to suspected right ventricular dysplasia.
  - Familial history (clinical diagnosis based on present criteria)

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2 major criteria or
1 major + 2 minor criteria or
4 minor criteria

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McKenna et al.
Br Heart J.
Case
A 47-year-old female

ECG

1) QRS in V1 $\geq$ 110 ms

2) epsilon wave

3) T wave inversion

4) low-voltage

LBBB type
Signal averaged ECG

Late potentials

UCG

RV dilatation

RV

LV

Ao

LA

RV

LV
The long QT syndrome (LQTS) is characterized by a prolonged QT interval in the electrocardiogram (ECG), syncope, and sudden cardiac death due to ventricular tachyarrhythmias, typically torsades de pointes. Two major phenotypic variants have been originally described. One is autosomal dominant (Romano Ward syndrome) and the other is rare autosomal recessive (Jervell and Lange-Nielsen syndrome) also presenting with sensorineural deafness. Sporadic LQTS patients have also been clinically described.
Measurement of the QT Interval of an ECG

\[ QTc = \frac{QT}{\sqrt{RR}} \]

Bazett's formula
Fig. 3. Schematic representation of the sixteen possible combinations between T and U waves. Full curves: T and U waves separate. Dotted curves: T and U waves partially merged. The vertical lines indicate the end of the T wave. The arrows point to the notch or kink between T and U.
## Criteria for diagnosis of LQTS

<table>
<thead>
<tr>
<th>Score</th>
<th>Probability of LQTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1 point</td>
<td>Low probability of LQTS</td>
</tr>
<tr>
<td>2 to 3 points</td>
<td>Intermediate probability of LQTS</td>
</tr>
<tr>
<td>≥4 points</td>
<td>High probability of LQTS</td>
</tr>
</tbody>
</table>

≤1 point, low probability of LQTS

2 to 3 points, intermediate probability of LQTS

≥4 points, high probability of LQTS

Schwartz et al.  
*Circulation.*  
1993;88:782-4
<table>
<thead>
<tr>
<th>Disease</th>
<th>Gene</th>
<th>Ion channel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Romano-Ward syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LQT1</td>
<td>KCNQ1 (KVLQT1)</td>
<td>$I_{Ks}$</td>
</tr>
<tr>
<td>LQT2</td>
<td>KCNH2 (HERG)</td>
<td>$I_{Kr}$</td>
</tr>
<tr>
<td>LQT3</td>
<td>SCN5A</td>
<td>$I_{Na}$</td>
</tr>
<tr>
<td>LQT4</td>
<td>ANK2 (ankyrin B)</td>
<td>Na- K ATPase</td>
</tr>
<tr>
<td>LQT5</td>
<td>KCNE1 (minK)</td>
<td>$I_{Ks}$</td>
</tr>
<tr>
<td>LQT6</td>
<td>KCNE2 (MiRP)</td>
<td>$I_{Kr}$</td>
</tr>
<tr>
<td>LQT9</td>
<td>CAV3 (caveolin- 3)</td>
<td>$I_{Na}$</td>
</tr>
<tr>
<td>LQT10</td>
<td>SCN4B</td>
<td>$I_{Na}$</td>
</tr>
<tr>
<td>Javell &amp; Lange-Nielsen syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>JLN1</td>
<td>KCNQ1</td>
<td>$I_{Ks}$</td>
</tr>
<tr>
<td>JLN2</td>
<td>KCNE1</td>
<td>$I_{Ks}$</td>
</tr>
<tr>
<td>Andersen-Tawil syndrome (LQT7)</td>
<td>KCNJ2</td>
<td>$I_{K1}$ (Kir2.1)</td>
</tr>
<tr>
<td>Timothy Syndrome (LQT8)</td>
<td>CACNA1c</td>
<td>$I_{Ca-L}$</td>
</tr>
</tbody>
</table>
ECG recordings in three patients with LQTS

<table>
<thead>
<tr>
<th>LQT3</th>
<th>LQT2</th>
<th>LQT1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosome 3</td>
<td>Chromosome 7</td>
<td>Chromosome 11</td>
</tr>
</tbody>
</table>

- **II**
  - late-onset T waves

- **aVF**
  - low-amplitude T waves

- **V5**
  - early onset of broad-based T waves

LQT ECG type

- LQT1  Broad-based T wave
- LQT2  Low-amplitude bifid T wave
- LQT3  Late-onset T wave
- ATS   Manifest U wave
LQT1
KCNQ1, V254M

Broad-based T wave

Late-onset normal-appearing T-wave
LQT2

KCNH2, G47C

Low-amplitude bifid T wave
LQT3
SCN5A, E1784K
Late-onset T wave
Andersen-Tawil syndrome

KCNJ2, T75M

Manifest U wave
ECG showed marked QT prolongation, T-wave alternans, and episodes of *Torsades de pointes*.

Nakamura et al.  
*J Am Coll Cardiol.* 2007;50:1808-9
Exercise

LQT1

<table>
<thead>
<tr>
<th>a) Control</th>
<th>b) Post exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>III</td>
<td>III</td>
</tr>
</tbody>
</table>

Auditory stimulus

LQT2

TdP
Brugada syndrome is a clinical entity characterized by ST-segment elevation in right precordial leads (V1-V3) and episodes of ventricular tachyarrhythmia in the absence of structural heart disease.
1. Male predominant (M:F>20:1)
2. The incidence of Brugada syndrome is higher in Asian countries.
3. Cardiac sudden death due to VF often occurs at night.
   a. 4% of all sudden deaths (SD)
   b. 20-50% of SD in patients with structurally normal hearts
   c. A family history of unexplained sudden death is present in approximately 20% of cases.
4. Mutation of the SCN5A gene, the gene encoding the sodium channel, accounts for about 20% of Brugada syndrome cases.
**ST segment abnormalities in lead V1 to V3**

<table>
<thead>
<tr>
<th></th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>J point</strong></td>
<td>≥ 2 mm</td>
<td>≥ 2 mm</td>
<td>≥ 2 mm</td>
</tr>
<tr>
<td><strong>T wave</strong></td>
<td>negative</td>
<td>positive or biphasic</td>
<td>positive</td>
</tr>
<tr>
<td><strong>ST-T configuration</strong></td>
<td>coved type</td>
<td>saddleback</td>
<td>saddleback</td>
</tr>
<tr>
<td><strong>ST segment (terminal portion)</strong></td>
<td>gradually descending</td>
<td>elevated ≥ 1 mm</td>
<td>elevated &lt; 1 mm</td>
</tr>
</tbody>
</table>

Wilde et al. Circulation 2002:106;2514
Brugada syndrome is definitively diagnosed:

- Type 1 ECG > 1 right precordial lead (V1-3) with or without Na+ channel blocker

  +

  - Ventricular fibrillation
  - Polymorphic ventricular tachycardia
  - Family history of sudden cardiac death (<45 y.o.)
  - Coved-type ECGs in family member
  - Inducibility of VT with programmed electrical stimulation
  - Syncope
  - Nocturnal agonal respiration

Heart Rhythm 2005 Consensus Report
Dynamic changes of ST segment

71 y.o. Male

Jan '91

May '96
(VF attack)

June '96

July '96

V1

V2

V3
Sodium channel blockers amplify or unmask ST segment elevation

Control

Na channel blocker (pilsicainide)

V1
ST level 0.12
ST level 0.30
(mV)

V2
ST level 0.70
ST level 1.65
(mV)

39 y.o. Male
PVC and initiation of VF in Brugada syndrome
<table>
<thead>
<tr>
<th>Type</th>
<th>Locus on Chromosome</th>
<th>Gene</th>
<th>Protein</th>
<th>Affected Current</th>
<th>Effect on channel function</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BS1</td>
<td>3p21</td>
<td>SCN5A</td>
<td>Nav1.5</td>
<td>$I_{Na}$</td>
<td>Loss of function</td>
<td>20</td>
</tr>
<tr>
<td>BS2</td>
<td>3p24</td>
<td>GPD1-L</td>
<td>GPD1-L protein</td>
<td>$I_{Na}$</td>
<td>Loss of function</td>
<td></td>
</tr>
<tr>
<td>BS3</td>
<td>12p13.3</td>
<td>CACNA1C</td>
<td>Cav1.2</td>
<td>$I_{Ca-L}$</td>
<td>Loss of function</td>
<td></td>
</tr>
<tr>
<td>BS4</td>
<td>10p12.33</td>
<td>CACNB2b</td>
<td>Cavβ2b</td>
<td>$I_{Ca-L}$</td>
<td>Loss of function</td>
<td></td>
</tr>
<tr>
<td>BS5</td>
<td>19q13.1</td>
<td>SCN1B</td>
<td>Navβ1</td>
<td>$I_{Na}$</td>
<td>Loss of function</td>
<td></td>
</tr>
<tr>
<td>BS6</td>
<td>11q13-14</td>
<td>KCNE3</td>
<td>MiRP2</td>
<td>$I_{to}$</td>
<td>Gain of function</td>
<td></td>
</tr>
</tbody>
</table>
SCN5A Mutation (-)  
51 y.o. Male, VF(+)  

SCN5A Mutation (+)  
33 y.o. Male, VF(+)  

V1  

V2  

V3
Genotype and Phenotype relationship

Wilde et al. JACC 2002;40:350