Evaluation of the Young Patient with Unexplained Cardiac Arrest

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University of Iowa Children’s Hospital
Carver College of Medicine
Physician’s Perspective

• Clues for event etiology?
• Diagnostic tests?
• Best treatment strategy?

Parents’ Perspective

• Is my child okay?
• What happened?
• Can we prevent it from happening again?
• What about our other children, ourselves?
Sudden Cardiac Arrest in Children

1. Background and Etiology of SCA
2. Diagnostic Evaluation
   • Clues from History
   • Specific tests: Pros and Cons
3. Proposed Algorithm for Work-up
SCA Definition

- Sudden unexpected collapse within 1 hour of symptom-onset (witnessed)

or

- Subjects were to have been observed alive and symptom-free within 24 hours of the event.

(World Health Association criteria)

Incidence of Sudden Death

Population-Based Analysis of Sudden Death in Children: The Oregon Sudden Unexpected Death Study

Sumeet S. Chugh, Kyndaron Reinier, Seshadri Balaji, Audrey Uy-Evanado, Cathy Vickers, Ronald Mariani, Karen Gunson, and Jonathan Jui

Heart Institute, Cedars-Sinai Medical Center, Los Angeles CA; and the Departments of Emergency Medicine, Pediatrics and Pathology, Oregon Health and Science University, Portland OR

- 7.5 / 100,000 children under 18
- 96.0/ 100,000 children; for those <1 yr
- 76% of pediatric SCA cases occurred < 1 yr
- Pediatric cases constituted 2.8% of all SCAs
- Compared to 1 – 20 / 100,000
• General pediatric population 1 in 20,000–50,000
• Apparently normal child 1– 1.5 in 100,000
• Tetralogy of Fallot repair <1 in 700
• Wolff-Parkinson-White syndrome 1 in 670
• Senning & Mustard operation 1 in 180
• Hypertrophic obstructive cardiomyopathy 1 in 167
• Long QT syndrome 1 in 111
• Brugada syndrome 1 in 10
• Arrhythmogenic right ventricular dysplasia 1 in 50


• Survival for all pediatric OHCA was 6.4%
  – 3.3% infants (<1 yr)
  – 9.1% children (1 – 11)
  – 8.9% adolescents (11 – 19 yr)
  – 4.5% for adults
• Prevention is key

(Donoghue, Ann Emerg Med, 2005)
Etiologies of Pediatric SCA

Acquired

Structural & Functional

Pediatric SCA

Primary Electrical

Arrhythmia!

Structural & Functional...

Hypertrophic cardiomyopathy
Arrhythmogenic right ventricular dysplasia
Coronary artery (CA) abnormalities
- CA arising from the opposite sinus of Valsalva
- Single CA ostia
- Hypoplastic CA syndrome
Williams syndrome with coronary ostial stenosis
Kawasaki syndrome
Primary pulmonary hypertension
Myocarditis/dilated cardiomyopathy
Restrictive cardiomyopathy
Marfan’s syndrome with aortic dissection
Aortic valve stenosis

(Berger, Pediatr Clin N Am 2004)
Primary Electrical…

Long QT syndromes
  - Romano Ward
  - Jervell Lange Nielsen
  - Acquired

Brugada syndrome

Wolff-Parkinson-White syndrome

Primary or idiopathic VT/VF

Catecholamine-exercise VT

Heart block
  - Congenital
  - Acquired

(Berger, Pediatr Clin N Am 2004)

Acquired…

Commotio cordis

Drug abuse
  - Stimulants, Cocaine,
  - Inhalants, gasoline, glue,
  - typewriter correction fluid,
  - nitrites (amyl, butyl), emetine

Secondary pulmonary artery hypertension
  (Eisenmengers syndrome)

Atherosclerotic coronary artery disease

(Berger, Pediatr Clin N Am 2004)
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Evaluation

- Event History
- Pt History
- Family History
- Physical Exam
- Special Tests
Evaluation – Event History

- Recent illness?
- Medications?
- Activity?
  - exertion, sleep
- Symptoms?
  - chest pain, palpitations, SOB
- Was an arrhythmia documented?
- Was CPR given?

Evaluation – Patient History

- Syncope?
- Palpitations?
- Chest pain?
- Change in stamina?
- Acute/chronic medications?
  - Prescribed
  - Recreational
Evaluation – Family History

- Syncope, seizures?
- Congenital deafness?
- Unexplained death?
  - Drowning,
  - Car accident
- Autosomal dominant!!

Genetic - Structural & Functional...

Hypertrophic cardiomyopathy
Arrhythmogenic right ventricular dysplasia
Coronary artery (CA) abnormalities
  - CA arising from the opposite sinus of Valsalva
  - Single CA ostia
  - Hypoplastic CA syndrome
Williams syndrome with coronary ostial stenosis
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(Berger, Pediatr Clin N Am 2004)
Genetic - Primary Electrical...

Long QT syndromes
  Romano Ward
  Jervell Lange Nielsen
  Acquired

Brugada syndrome
  Wolff-Parkinson-White syndrome
  Primary or idiopathic VT/VF
  Catecholamine-exercise VT

Heart block
  Congenital
  Acquired

Physical Exam

• Marfanoid features
• Auscultation
  – Murmurs/gallop
  – Increased P2
• Signs of CHF

(Berger, Pediatr Clin N Am 2004)
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Diagnostic & Confirmatory Tests

- ECG
- Ex. Treadmill Test
- Holter
- Signal Ave ECG
- Provocative Study
- Cardiac MRI

- Genetic Testing
- Cardiac CT
- EP Study
- Implantable Loop Recorder
ECG Utility

**May Identify:**
- HCM
- ARVC
- Dilated cardiomyopathy
- WPW
- Conduction diseases
- Long/short QT syndrome
- Valvular Heart Disease
- Myocarditis
- Aortic rupture
- Congenital heart disease

**May/Will Not Identify:**
- CPVT
- Brugada
- Commotio cordis
- Marfan’s disease
- Congenital anomalies of coronary arteries
## ECG Findings

<table>
<thead>
<tr>
<th>Disease</th>
<th>QRS</th>
<th>ST segment</th>
<th>t-wave</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCM</td>
<td>↑ voltage LVH</td>
<td>Down sloping</td>
<td>Inverted mid-L leads</td>
</tr>
<tr>
<td>ARVD</td>
<td>Prolonged QRS</td>
<td>Up sloping</td>
<td>Inverted V2 – V4</td>
</tr>
<tr>
<td>ARVD</td>
<td>Epsilon waves</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LQTS</td>
<td>Normal</td>
<td>Normal</td>
<td>Prolonged/short Variable morph</td>
</tr>
<tr>
<td>WPW</td>
<td>Delta wave</td>
<td>2º changes</td>
<td>2º changes</td>
</tr>
<tr>
<td>Brugada syndrome</td>
<td>Pseudo-RBBB (V1 – V3)</td>
<td>Coved</td>
<td>Inverted V2 – V4</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>LVH changes</td>
<td>Normal</td>
<td>2º changes</td>
</tr>
<tr>
<td>Coronary anomalies</td>
<td>Normal</td>
<td>Normal?</td>
<td>Normal?</td>
</tr>
</tbody>
</table>

### ECG - HCM

![ECG Image](image-url)
Echocardiogram

LV thickening

- **21 – 22 mm typical**, but can vary widely
- “Gray Area” = **13 – 15 mm**, but can occur in well-trained athletes
- May be normal in children, but develop pathologic hypertrophy in the future
- Regular, serial echos recommended for children suspected of HCM until grown

(Bader, Pediatr Clin N Am .2004)
Echocardiogram - ARVC

Major Criteria
• Regional RV akinesia, dyskinesia or aneurysm, PLUS 1 below (end diastole):
  – PLAX RVOT ≥32mm
  – PSAX RVOT ≥36mm
  – Or fractional area change ≤33%

Minor Criteria
• Regional RV akinesia, dyskinesia, PLUS 1 below:
  – PLAX RVOT ≥29 to <32mm
  – PSAX RVOT ≥32 to <36mm
  – Or fractional area change >33% to ≤40%

Echocardiogram – CA Disease

(Frommelt, Pediatr Clin N Am 2004)
Holter Diagnostic Testing

- AV block
- WPW: intermittent pre-excitation
- LQTS: t-wave alternans
- HCM: ventricular arrhythmias
- ARVD: PVC’s, ventricular tachycardia
Treadmill testing

Exercise Treadmill - HCM

- Abnormal systolic BP response = failure to \( \uparrow \) systolic > 25 mmHg above resting
- Detected in 25% of pts with HCM
- Positive predictive accuracy for sudden death is ~15%
- Relative risk ~ 1.8
Exercise Treadmill - CPVT

- Ventricular ectopy or VT occur at rates 70-160 bpm
- Sensitivity ~ 80%

Exercise Treadmill - WPW

- Abrupt loss of pre-excitation ~ 15% (Bershader Heart Rhythm 2007)
  - inter-rater reliability inconsistent
  - abrupt loss of pre-excitation generally predicted longer APERP, but not always!!
- Abrupt loss of pre-excitation not necessarily predictor of low risk
- No prospective studies on WPW risk stratification based on exercise testing

(Adapted from Jezoir, Chest, 2005)
Exercise Treadmill - LQTS

**QT Interval**
- LQT1: most prolonged during exercise and recovery
- LQT2: longest at low exercise HR
- LQT3: longest at rest

(Adapted from Hekalla, Europace, 2010)

**Tpe interval**
- LQT1: nearly unchanged during exercise
- LQT2: shortened
- LQT3: shortened

Exercise Treadmill

(Adapted from Kimball, Pediatric Card, 2002)
Signal Average ECG

Signal Averaged ECG

(Indik, Ind Pacing Electro J 2003)
Provocative Study

Provocative Drugs

Role of Adrenaline and Procainamide Infusion
- Unmask latent primary electrical Dx
- Identify asymptomatic family members at-risk for Dx

Can aid in Diagnosis (Krahn, et al., 2005)
- Adrenaline 0.05 ↑ 0.10, 0.20, 0.30, and 0.40 μgm /kg/min at 5-minute intervals
- 30-minute washout period
- 15 mg/kg procainamide (max dose 1 g) infused over 30 minutes
- 56% CPVT
- 11% Brugada syndrome
- 33% Unexplained - idiopathic ventricular fibrillation

(Krahn, Circ, 2005)
Provocative Drugs

(Vyas, J Electrocardiology, 2006)

MRI

(QT > 30 milliseconds
sensitivity 92%
specificity 86%
PPV 75%
NPV 96%
MRI – Apical Hypertrophy

(Moon, Heart, 2004)

MRI Criteria - ARVC

- Regional RV akinesia, dyskinesia or aneurysm; or
- Dyssynchronous RV contraction
- Major: Above PLUS 1 below:
  - Ratio of RV end-diastolic volume to BSA $\geq 110$ (M) or $\geq 100$ (F) mL/m$^2$
  - RV ejection fraction $\leq 40$
- Minor: Above PLUS 1 below:
  - Ratio of RV end-diastolic volume to BSA $\geq 100$ to $<110$ (M) or $\geq 90$ to $<100$ (F) mL/m$^2$
  - RV EF $>40\%$ to $\leq 45\%$
Genetic Testing

(Tester JACC 2007; Tester Mayo Clinic Proc 2007)
Electrophysiology Testing

EP Study

WPW
- Used 1º for risk stratification
- Shortest pre-excited R-R interval more predictive than APERP

Brugada Syndrome
- May be used for risk stratification of asymptomatic patients who have spontaneously abnormal ECG

ARVC
- Little data in children
- Voltage mapping may aid in diagnosis; identifying VT characteristics
Implantable Loop Recorder (ILR)

- Pts without CHD, LQTS, or a family Hx of SUD were more likely to have a diagnosis confirmed by ILR

(AI Dhahri, PACE, 2009)
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**Diagnostic Algorithm – Usual Suspects**

- **Abnormal ECG, Normal Echo**
  - Possible Dx: WPW
  - Possible F/U tests:
    - Signal Ave ECG

- **Abnormal**
  - Possible Dx: ARVC

- **Normal ECG**
  - Possible Dx: Long QT synd
  - Provocative +/- EP study

- **Normal Echo**

- **Abnormal Echo**
  - Possible Dx: HCM or DCM
  - Possible Dx: ARVC

- **Normal**
  - Ex Treadmill Test

- **Abnormal**
  - Possible Dx: CPVT
  - Possible Dx: Long QT synd
  - F/U or Confirmatory tests:
    - ILR
    - MRI, Cardiac CT
    - Genetic Testing
    - Ex Treadmill Test
Revised Task Force Criteria

Minor Criteria:
• Late potentials in ≥1 of 3 parameters in the absence of a QRS duration of ≥110 ms
• Filtered QRS duration (fQRS) ≥114 ms
• Duration of terminal QRS <40 μV (low-amp signal duration) ≥38 ms
• RMS voltage of terminal 40 ms ≤20 μV
• Terminal activation duration of QRS ≥55 ms measured from the nadir of the S wave to the end of the QRS, including R’ in V1, V2, or V3, in the absence of complete right bundle-branch block

(Cox, Circ Arryth Electrophys, 2010)
Signal Averaged ECG - Normals

Signal-averaged electrocardiography values according to age, using a 40-Hz high-pass bidirectional filter

<table>
<thead>
<tr>
<th></th>
<th>&lt;1 yr</th>
<th>1–5 yr</th>
<th>6–9 yr</th>
<th>10–14 yr</th>
<th>≥15 yr</th>
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</thead>
<tbody>
<tr>
<td>FQRS</td>
<td>&lt;92</td>
<td>&lt;111</td>
<td>&lt;114</td>
<td>&lt;116</td>
<td>&lt;120 M, &lt;112 W</td>
</tr>
<tr>
<td>RMS40</td>
<td>&gt;125</td>
<td>&gt;40</td>
<td>&gt;23</td>
<td>&gt;21</td>
<td>&gt;21</td>
</tr>
<tr>
<td>LAS40</td>
<td>&lt;22</td>
<td>&lt;30</td>
<td>&lt;39</td>
<td>&lt;31</td>
<td>&lt;36</td>
</tr>
</tbody>
</table>

Abbreviations: FQRS, filtered QRS; M, men; W, women.

Adapted from Fallah-Najmabadi, Am J Cardiol. 1996)

Signal Averaged ECG

• Late potentials present ~ 50% - 80% of ARVC cases (Yoshioka, Am J Cardiol 2000)

• Filtered QRS duration ≥ 110 ms identified pts who had ARVD and were inducible by EP study (Nasir, Pacing Clin Electrophysiol 2003)
  – 91% sensitivity
  – 90% specificity

The University of Iowa
**Exercise Treadmill - CPVT**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Number of patients (female/male)</th>
<th>Age at onset (years)</th>
<th>Age at diagnosis (years)</th>
<th>Follow-up time (years)</th>
<th>Heart rate at rest (bpm)</th>
<th>Threshold frequency (bpm)</th>
<th>Onset of ventricular premature complexes</th>
<th>Onset of ventricular tachycardia</th>
<th>Mortality among the probands</th>
<th>Genetic defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lenhardt et al. 1993</td>
<td>21/9/12</td>
<td>3-16</td>
<td>3.5-16.5</td>
<td>2-16</td>
<td>42-73</td>
<td>105-150</td>
<td>NA</td>
<td>2/21</td>
<td>NA</td>
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<tr>
<td>Lahnt et al. 2001</td>
<td>13/9/4</td>
<td>3.5-12</td>
<td>0.25-25</td>
<td>1.5</td>
<td>47-90</td>
<td>90-123</td>
<td>90-123</td>
<td>0</td>
<td>Chromosome 1p13-21 (recessive)</td>
<td>Ryr2 gene mutation</td>
</tr>
<tr>
<td>Pifar et al. 2002</td>
<td>30/17/13</td>
<td>2-38</td>
<td>15±10</td>
<td>4±2.5</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Ryr2 gene mutation</td>
</tr>
<tr>
<td>Senni et al. 2003</td>
<td>29/16/13</td>
<td>2-30</td>
<td>NA</td>
<td>6±8-4.9</td>
<td>50±11</td>
<td>NA</td>
<td>70-214</td>
<td>7/29</td>
<td>NA</td>
<td>Ryr2 gene mutation</td>
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<tr>
<td>Formis et al. 2005</td>
<td>12/9/3</td>
<td>4-51</td>
<td>NA</td>
<td>2-28</td>
<td>43±73</td>
<td>NA</td>
<td>90-150</td>
<td>1/12</td>
<td>Ryr2 gene mutations</td>
<td>Ryr2 gene mutation</td>
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<tr>
<td>Ciferri et al. 2009</td>
<td>16/3/11</td>
<td>4-3-12</td>
<td>3-13</td>
<td>1-9</td>
<td>45-49</td>
<td>70-140</td>
<td>145-180</td>
<td>4/16</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

**ILR**

<table>
<thead>
<tr>
<th>Test</th>
<th># of Pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>U-lead ECG</td>
<td>8-19</td>
</tr>
<tr>
<td>Ambulatory ECG monitoring</td>
<td>2-15</td>
</tr>
<tr>
<td>Exercise stress</td>
<td>2-10</td>
</tr>
<tr>
<td>Tilt table</td>
<td>4-5</td>
</tr>
<tr>
<td>Upright challenge</td>
<td>4-6</td>
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<tr>
<td>Electrophysiologic study</td>
<td>2-6</td>
</tr>
</tbody>
</table>

(Frangini, PACE, 2008)
## Signal Averaged ECG - Normals

<table>
<thead>
<tr>
<th>SAECG Parameter</th>
<th>Age Group¹</th>
<th>Criteria² (adult)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filtered QRS (ms)</td>
<td>&lt; 1 yr</td>
<td>1-5 yr</td>
</tr>
<tr>
<td></td>
<td>&lt;92</td>
<td>&lt;111</td>
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<tr>
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(¹Fallah-Najmabadi, Am J Cardiol. 1996)
(²Cox, Circ Arryth Electrophys. 2010)