Electrocardiographic Issues in Williams Syndrome

R. Thomas Collins II, MD
Assistant Professor, Pediatrics and Internal Medicine
University of Arkansas for Medical Sciences
Arkansas Children’s Hospital
Director, Multidisciplinary Connective Tissue Clinic
What is an Electrocardiogram?

• Electrocardiograms (ECGs) are displays of the electrical activity of the heart
• A complete ECG will have 12 or 15 leads which measure the directions that the electrical impulses in the heart are traveling
Why Get Electrocardiograms?

- 80% of patients with Williams syndrome (WS) have structural cardiovascular abnormalities (CVA)
- Structural CVA are associated with abnormalities on the electrocardiogram (ECG)
- Patients with WS get ECGs as a screening test (in those without known CVA), or as a way to follow changes seen previously
What Might Be Seen on ECGs?

• Abnormal heart rhythms

• Evidence of enlargement of part of the heart

• Abnormal electrical activity in the heart
Sudden Death in WS

• 25 to 100-fold increase\(^1\)
  • Most often seen in the setting of anesthesia

• Commonly attributed to concomitant SVAS and coronary stenosis\(^2\)

• Can be seen outside of the procedural and anesthetic setting\(^1\)

---

Electricity in the Heartbeat

- Each heartbeat occurs when an electrical current passes into the main pumping chamber of the heart.
Electricity in the Heartbeat

• Each heartbeat occurs when an electrical current passes into the main pumping chamber of the heart

• As soon as the heartbeat occurs, the heart resets for the next beat
Electricity in the Heartbeat

• Each heartbeat occurs when an electrical current passes into the main pumping chamber of the heart
• As soon as the heartbeat occurs, the heart resets for the next beat
• Imagine a lightbulb...
Resetting the Breaker

• Resetting of the breaker in the heart is called repolarization
• It is typically represented by the QTc on the ECG
Prolonged Cardiac Repolarization Increases Sudden Death Risk

• Patients with prolonged QTc are predisposed to recurrent ventricular tachycardia\textsuperscript{1}

• Prolonged QTc is a known cause of sudden cardiac death\textsuperscript{2}

Abnormalities of Cardiac Repolarization in Williams Syndrome

R. Thomas Collins II, MD\textsuperscript{a,c,*}, Peter F. Aziz, MD\textsuperscript{a,c}, Marie M. Gleason, MD\textsuperscript{a,c}, Paige B. Kaplan, MBCh\textsuperscript{b,c}, and Maully J. Shah, MBBS\textsuperscript{a,c}

Retrospective Review

• Two arms
  • WS study arm
    • 499 ECGs from patients with WS in a 270 patient database from the Children’s Hospital of Philadelphia
  • Control arm
    • 1522 normal ECGs selected from over 230,000 ECGs at CHOP
QTc Distribution in Williams vs Controls

- Control QTc 418±17
- Williams QTc 436±27

p<0.0001
Prolonged Repolarization is More Common in Williams Syndrome

- Williams
- Controls

$p<0.0001$ for all samples

Percent Prolonged

QTc

JTC
Mortality Results

- 4 patients died during follow-up
  - 2 of those had prolonged QTc and JTC
  - 1 of the 2 died during non-cardiac surgery and autopsy showed no SVAS or coronary stenosis

- Another patient with prolonged QTc and JTC sustained a cardiac arrest during a procedure and was placed on ECMO.
Conclusions

• Cardiac repolarization is prolonged in WS compared to normal controls.

• Prolonged cardiac repolarization may contribute to the increased risk of sudden death and peri-procedural morbidity in WS.

Collins RT et al. Am J Cardiol 2010;106(7):1029-33. PMID 20854969
Further Study of QTc

• Typically, if a patient has a QTc that is longer than normal, they will undergo a stress test.
• If the QTc gets longer with exercise, then the diagnosis of long QT syndrome is likely.
• Patients with Williams syndrome have difficulty with running on treadmills or peddling exercise bikes vigorously, so that stress tests are not practical.
Relation of Ventricular Ectopic Complexes to QTc Interval on Ambulatory Electrocardiograms in Williams Syndrome

R. Thomas Collins II, MD\textsuperscript{a,b,*}, Peter F. Aziz, MD\textsuperscript{c}, Christopher J. Swearingen, PhD\textsuperscript{a,b}, and Paige B. Kaplan, MBBCh\textsuperscript{d,e}

Ambulatory ECGs (AECGs)

• Partial ECGs that are recorded for 24 hours while patients go about their normal activities
• Gives information on the changes in the heart rate and heart rhythms
• We hypothesized that we could look at the QTc during the maximum heart rate on the AECGs as we would during an exercise test
Goals of the Study

• Characterize the findings from ambulatory ECGs (AECGs) in patients with WS
• Evaluate the effect of heart rate on QTc in patients with WS
• Determine whether the QTc interval on the AECG correlates with ventricular premature complexes (VPCs)
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age at Holter (years)</td>
<td>20.6±8.6</td>
</tr>
<tr>
<td>Gender</td>
<td>30:26 (53% Female)</td>
</tr>
<tr>
<td>Predominate Sinus Rhythm</td>
<td>53/56 (95%)</td>
</tr>
<tr>
<td>Mean Heart Rate (bpm)</td>
<td>85±13</td>
</tr>
<tr>
<td>Maximum Heart Rate (bpm)</td>
<td>143±25</td>
</tr>
</tbody>
</table>
Atrial Rhythm Abnormalities

<table>
<thead>
<tr>
<th>Atrial Ectopy</th>
<th>Result (% of studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial Premature Beats</td>
<td>39/56 (70%)</td>
</tr>
<tr>
<td>Beats per hour</td>
<td>5.8±29.9</td>
</tr>
<tr>
<td>Supraventricular Tachycardia</td>
<td>6/56 (11%)</td>
</tr>
<tr>
<td>Ectopic Atrial Tachycardia</td>
<td>4/6 (67%)</td>
</tr>
</tbody>
</table>
The QTc Increased with the Heart Rate

<table>
<thead>
<tr>
<th></th>
<th>Heart Rate (bpm)</th>
<th>QTc Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum Heart Rate</td>
<td>55±11</td>
<td>425±34</td>
</tr>
<tr>
<td>Heart rate of 100</td>
<td>100±2</td>
<td>447±35</td>
</tr>
<tr>
<td>Maximum Heart Rate</td>
<td>143±25</td>
<td>456±34</td>
</tr>
</tbody>
</table>
Correlation of QTc with Ventricular Premature Complexes

QTc at Minimum Heart Rate

QTc at Maximum Heart Rate
What We Have Learned

• The QTc is prolonged in Williams syndrome
• Prolongation of the QTc correlates with increased abnormal heartbeats
• Prolongation of the QTc in Williams syndrome may contribute to sudden death
What Do We Still Have To Learn

• The cause of QTc prolongation in patients with Williams syndrome
• If treatment of patient with Williams syndrome and QTc prolongation decreases the risk of sudden death
ECG Practice Recommendations

• ECGs annually for patients with a history of structural CVAs
  – More frequently if previously demonstrated abnormalities, or if symptomatic

• ECGs biennially for patients without a history of structural CVAs
  – More frequently if previously demonstrated abnormalities, or if symptomatic
Practice Recommendations

• Initiation of β-blocker therapy in patients with any QTc ≥ 460 msec

• Annual to biennial AECGs in patients with any QTc ≥ 440 msec
  – Frequency determined by degree of QTc prolongation and prior abnormal findings
Genetic Testing for LQTS

- Genetic testing for Long QT Syndrome is not recommended for all patients with WS and a prolonged QTc
  - Only one patient with WS in the literature has been reported to also have a positive genetic test for LQTS
- It may be considered on a case-by-case basis and can be discussed with the primary cardiologist