FRAGMENTED QRS ON THE 12 LEAD ECG: A MARKER OF SUDDEN CARDIAC DEATH

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Background

- Heart disease is the major cause of Death in the US, contributing to >600,000 deaths/year
- SCD contributed to 50% of those deaths, and of those half of them occur in patients with no known heart disease
- Survival after:
  - Out of hospital cardiac arrest is 5.6%
  - Inpatient cardiac arrest: 25.5%
Background

- Severely reduced EF, wide QRS duration, and EF<30 with NSVT are predictor of SCD.
- In most patients predictors of SCD are unknown.
- The number of patients needed to treat to prevent SCD is undesirably high.
- For that, screening the general population for risk stratification of SCD currently cannot be performed.
- Therefore the search for good predictors of SCD is warranted.
Background

• The 12-lead ECG represents both the depolarization and repolarization phases of the heart.

• Major repolarization abnormalities are markers of SCD with low predictive value and include: J point elevation, QT prolongation, T wave alternans, and ST-T wave abnormalities

• Could a depolarization abnormality be a marker of SCD?

• Is fQRS be a marker of SCD?
Background on fQRS

• It is a notching in QRS complex that is not secondary to BBB.

• In one study with 10,904 middle aged patients in Finland,
  • Incidence was reported as 19.7% in the general population.
  • fQRS in lateral leads in patients with CAD was associated with mortality.

• It predicts mortality in patients with acute coronary syndrome and in patients with cardiomyopathy.

• Predictor of arrhythmic events in patients with ischemic and nonischemic cardiomyopathy.

• Meta-analysis has shown that fQRS predicts SCD even in patients with EF>35%.


Background on fQRS

- It has been confirmed on autopsy that fQRS complexes represent “islands” of viable myocardial tissue within myocardial scar.

- These “islands” of myocardium have slow impulse conduction as a result of the partially depolarized and depressed action potential upstroke velocities, which are likely responsible for the inhomogeneous activation of the ventricles.
Background on fQRS

- Therefore, different morphologies of fQRS are caused by shifting of the QRS vector during depolarization in and around the areas of scarred or ischemic myocardium and depend on their extent and location in the ventricle.
Methods

• Identified all patients discharged with CA (2000-2014) at Methodist.

  418 subjects

  166 with SCD

  252 met exclusion criteria

1. Lack of at least one interpretable ECG at any point in time in the EMR.

2. Age <18 at the time of cardiac arrest.

3. Cardiac arrest from a non-cardiac cause or no history of cardiac arrest.
Methods

- 12-lead EKGs were extracted from the charts:
  - prior to cardiac arrest if applicable
  - within 48 hours after cardiac arrest
  - outpatient f/u

- We had 1-3 EKGs per patient
Methods

- All identifiers were removed from the EKGs (CA and healthy controls) prior to review by two blinded-readers.
- The presence or absence of fQRS was documented as well as the major lead territories involved
Methods

- **fQRS** was defined as:
  - Presence of various RSR’ patterns with (QRS<120) w/wo Q wave
  - This includes >1 R’
  - Notching of the R wave or S wave
  - AND present in 2 contiguous leads.
  - Exclude incomplete RBBB, RBBB, LBBB.
    - Exclude if RSR’ in V1 or V2 with QRS>100
    - Exclude if RSR’ in V5, V6, or Lead I with QRS>120
fQRS

- RSR'
- rSr'
- rSR'
- Notched S
- Notched R
- Fragmented QRS
Results

430 subjects

166 with SCD
- 42% VT/VF
- 25% Asystole
- 33% PEA

264 Healthy controls

77% died prior to discharge
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Healthy controls (HC)</th>
<th>SCD</th>
<th>SCD vs. HC</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>148 (56.1%)</td>
<td>103 (62.0%)</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Age at Cardiac Arrest*</td>
<td>61.3 ± 16.1</td>
<td>65.2 ± 15.4</td>
<td>0.0115</td>
<td></td>
</tr>
<tr>
<td>fQRS in ≥2 contiguous ECG leads</td>
<td>59 (22.3%)</td>
<td>95 (57.2%)</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>&gt; 1 Lead Territory in Those with fQRS</td>
<td>1 (1.7%)</td>
<td>16 (16.8%)</td>
<td>0.0035</td>
<td></td>
</tr>
<tr>
<td>O wave in ≥2 contiguous ECG leads</td>
<td>4 (1.5%)</td>
<td>14 (8.4%)</td>
<td>0.0005</td>
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</tr>
<tr>
<td>fQRS and/or Q wave ≥2 contiguous ECG leads</td>
<td>62 (23.5%)</td>
<td>100 (60.2%)</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Number of ECGs</td>
<td>209 (79.2%)</td>
<td>84 (50.6%)</td>
<td>&lt;0.0001*</td>
<td>*</td>
</tr>
<tr>
<td>QRS &gt; 150 in any ECG</td>
<td>5 (1.9%)</td>
<td>36 (21.7%)</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>History of Hypertension</td>
<td>128 (48.5%)</td>
<td>120 (72.3%)</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>History of Hyperlipidemia</td>
<td>63 (23.9%)</td>
<td>79 (47.6%)</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>History of Myocardial infarction</td>
<td>0 (0.0%)</td>
<td>65 (39.2%)</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>History of Cardiomyopathy</td>
<td>0 (0.0%)</td>
<td>69 (41.6%)</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>History of Atrial Arrhythmias</td>
<td>15 (5.7%)</td>
<td>35 (21.1%)</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>History of Pulmonary Disease</td>
<td>24 (9.1%)</td>
<td>42 (25.3%)</td>
<td>&lt;.0001</td>
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<tr>
<td>Family history of CAD</td>
<td>37 (14.0%)</td>
<td>25 (15.1%)</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Family history of SCD</td>
<td>3 (1.1%)</td>
<td>1 (0.6%)</td>
<td>n/a</td>
<td></td>
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<tr>
<td>Beta blocker therapy</td>
<td>45 (17.0%)</td>
<td>77 (46.4%)</td>
<td>&lt;.0001</td>
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</tr>
<tr>
<td>QT prolonging drugs</td>
<td>27 (10.2%)</td>
<td>59 (35.5%)</td>
<td>&lt;.0001</td>
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<tr>
<td>Antiarrhythmic therapy</td>
<td>6 (2.3%)</td>
<td>13 (7.8%)</td>
<td>0.0063</td>
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</tr>
<tr>
<td>Variable</td>
<td>SCD vs. HC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Odds Ratio</td>
<td>95% CI</td>
<td>P-Value</td>
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<tr>
<td>fQRS in any ECG</td>
<td>3.58</td>
<td>2.15-5.96</td>
<td>&lt;.0001</td>
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<td>Q wave in any ECG</td>
<td>5.07</td>
<td>1.43-17.93</td>
<td>0.0118</td>
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<tr>
<td>Male gender vs female</td>
<td>1.15</td>
<td>0.69-1.92</td>
<td>0.5821</td>
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<tr>
<td>Age at Cardiac Arrest *</td>
<td>1.00</td>
<td>0.98-1.01</td>
<td>0.7719</td>
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<tr>
<td>QRS &gt; 150 in any ECG</td>
<td>11.85</td>
<td>4.16-33.77</td>
<td>&lt;.0001</td>
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</tr>
<tr>
<td>Number of ECGs</td>
<td></td>
<td></td>
<td>0.2221</td>
<td></td>
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<tr>
<td>3 vs. 1</td>
<td>1.49</td>
<td>0.20-11.10</td>
<td>0.6955</td>
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<tr>
<td>2 vs. 1</td>
<td>1.65</td>
<td>0.94-2.91</td>
<td>0.0843</td>
<td></td>
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<tr>
<td>History of Hypertension</td>
<td>1.66</td>
<td>0.93-2.98</td>
<td>0.0864</td>
<td></td>
</tr>
<tr>
<td>History of Hyperlipidemia</td>
<td>1.29</td>
<td>0.74-2.25</td>
<td>0.3649</td>
<td></td>
</tr>
<tr>
<td>History of Myocardial infarction**</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>History of Cardiomyopathy**</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>History of Atrial Arrhythmias</td>
<td>1.91</td>
<td>0.80-4.54</td>
<td>0.1454</td>
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<tr>
<td>History of Pulmonary Disease</td>
<td>2.66</td>
<td>1.34-5.27</td>
<td>0.0051</td>
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<tr>
<td>Beta blocker use</td>
<td>1.70</td>
<td>0.95-3.05</td>
<td>0.0750</td>
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<tr>
<td>QT prolonging drug use</td>
<td>3.08</td>
<td>1.61-5.88</td>
<td>0.0007</td>
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<tr>
<td>Antiarrhythmic therapy</td>
<td>0.90</td>
<td>0.25-3.24</td>
<td>0.8773</td>
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</tbody>
</table>
Discussion

• Patients who experienced SCD had a:
  • Significantly higher prevalence of fQRS (57.2%) compared to healthy controls (22.3%)
  • This translated to an OR of 3.58
  • Higher incidence of fQRS in multiple major lead territories (16.8% vs. 1.7%, p =0.0035)

• Prior studies showed that patients with fQRS to have a higher risk of death (RR 1.71, 95% CI 1.02–2.85) and ventricular arrhythmia (RR 2.20, 95% CI 1.05–4.62).
Discussion

- Hospitalized patients with fQRS have a significantly higher risk for ventricular tachycardia/ventricular fibrillation (20.3%) vs. patients without fQRS (7.6%)

- MADIT II sub-study showed that the presence of fQRS (especially identified in inferior leads) was predictive of SCD, SCD or appropriate ICD shock, and all-cause mortality in patients with ischemic cardiomyopathy.
Discussion

Compared to the Finnish study:
• Similar rate of fQRS in a generally healthy population
• Significantly increased rate of fQRS in multiple major lead territories among patients who suffered SCD
Limitations

• Retrospective study.
• Many patients die before a 12-lead ECG is recorded.
• fQRS on a 12-lead ECG requires an optimal low-pass filter setting (100 or 150 Hz) and fragmentation may be missed with a low pass filter setting of 60 Hz or less.
Conclusion

• The use of multiple known ECG markers of abnormal repolarization and depolarization may provide a high predictive value for SCD and be a vital screening tool with incremental value to established risk markers such as reduced LVEF.

• This could be established in a prospective study, which is also difficult to design as SCD occurs in the majority of the patients without prior warning.