Early Repolarization: Culprit or Innocent Bystander

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Vic Froelicher, MD
Early Repolarization: Culprit or Innocent Bystander

Nikhil A. Jain
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Are these Phenotypes dangerous?

PVCs, silent ST depression, early repolarization/ J waves, QRS end slurring/notching
ECG Added to Stanford Athletes Annual Pre-participation Exam 2007
Global Early Repolarization with J waves

Born: 10/02/1986
Age: 20 Y
Sex: Male
Height: 72.0 in
Weight: 200.6 lb
BP: / / mmHg

HR 46 /min
Axis 49°
P 49°
QRS 66°
T 50°

Intervals
RR 1281 ms
P 110 ms
QO 146 ms
QRS 102 ms
QT 404 ms
QTc 357 ms

Interpretation
SINUS BRADYCARDIA
OTHERWISE NORMAL ECG

5.73 UNCONFIRMED REPORT

Validated by Dr Vic Froelicher / 08/16/2007 13:10:36

Who needs more studies to participate?
### ST Elevation Lateral Leads (1mm, any)  
658 Collegiate Athletes

<table>
<thead>
<tr>
<th>Resting HR</th>
<th>Athletes</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males (55%)</td>
<td>Females (45%)</td>
</tr>
<tr>
<td></td>
<td>Afro-American (12%)</td>
<td>Others (88%)</td>
</tr>
<tr>
<td>&lt;55 bpm</td>
<td>53%</td>
<td>31%</td>
</tr>
<tr>
<td>55-70</td>
<td>55%</td>
<td>30%</td>
</tr>
<tr>
<td>&gt;70 bpm</td>
<td>67%</td>
<td>32%</td>
</tr>
<tr>
<td>Total</td>
<td>56%</td>
<td>31%</td>
</tr>
</tbody>
</table>

Males > Females, African-Americans > others, no effect resting HR
ST Elevation on Resting ECG

1. Acute (Dynamic)
   1. Ischemia (localizes, arrhythmogenic)
      1. Variant Angina
   2. ST Elevation MI

2. Chronic (Stable)
   1. Early Repolarization – changes with heart rate
   2. Pericarditis
   3. Over Q waves associated with LV aneurysms
   4. Spinal Cord Injury and mental patients
   5. Brugada Patterns (V123) – but syndrome dynamic
ER Benign?

Sudden Cardiac Arrest Associated with Early Repolarization

Michel Haïssaguerre, M.D., Nicolas Derval, M.D., Frederic Sacher, M.D., Laurence Jesel, M.D., Isabel Deisenhofer, M.D., Luc de Roy, M.D.,

Long-Term Outcome Associated with Early Repolarization on Electrocardiography

Jani T. Tikkanen, B.S., Olli Anttonen, M.D., M. Juhani Junttila, M.D., Arto Välimaa, M.D., Eero Kankaanranta, M.D., Henrik A. Bigger, M.D.
Based on a unique population of 202 individuals (mean age 36 yrs) with ventricular tachycardia and no other evidence for heart disease.

Two surprising observations were made in this important study:

1. 18 subjects with ECG tracings at the time before VF or VT, dynamic ST elevation similar to that seen with coronary spasm was noted and,

2. Higher prevalence of inferior/lateral notching/slurring on their resting ECGs than in controls (31% vs 5%).
Community epidemiological study (N=10,864, 44±8 yrs) that considered baseline characteristics and utilized visually interpreted ECGs including manual measurements of ST elevation in the inferior and lateral leads with CV death as the outcome.

They found no hazard associated with ER in the lateral leads but roughly an adjusted hazard of 2 for inferior lead ER. The subjects with inferior ER had a higher prevalence of Minnesota Code ECG findings associated with coronary artery disease and the example they provide exhibits ST elevation occurring over inferior Q waves.
The amplitude of J-point elevation had to be at least 1 mm (0.1 mV) above the baseline level, either as QRS slurring (a smooth transition from the QRS segment to the ST segment) or notching (a positive J deflection inscribed on the S wave) in the inferior lead (II, III, and aVF), lateral lead (I, aVL, and V4 to V6), or both.
Methods

ERP was assessed manually in all ECGs using paper prints. The criteria for detection of ERP were exactly as recently described by Haïssaguerre and colleagues. Briefly, classification as ERP required a J-point elevation >0.1 mV in 2 adjacent leads with either slurring or notching morphology. Presence or absence of ST-elevation in addition to J-point elevation was not taken into account and nonspecific intraventricular conduction delay was excluded from analysis.

Methods and Findings: Electrocardiograms of 1,945 participants aged 35–74 y, representing a source population of 6,213 individuals, were analyzed applying a case-cohort design. Mean follow-up was 19 years. Prevalence of ERP was 13.1% in our study. ERP was associated with cardiac and all-cause mortality, most pronounced in those of younger age and male sex; a clear ERP-age interaction was detected (p = 0.005). Age-stratified analyses showed hazard ratios (HRs) for cardiac mortality of 2 for both sexes. An inferior localization of ERP further increased ERP-attributable cardiac mortality to HRs of 3 for both sexes.

Conclusions: They found a high prevalence of ERP (13%) in their population-based cohort of middle-aged individuals. ERP was associated with about a 2- to 4-fold increased risk of cardiac mortality in individuals between 35 and 54 y.

An inferior localization of ERP was associated with a particularly increased risk.
Figure 1: Baseline Electrocardiograms from Four Case Subjects.
In each panel, early repolarization is evident in the varying patterns of QRS slurring or notching in inferolateral leads (arrows). Panel D shows a beat-to-beat fluctuation in this pattern.
Figure 2. Baseline Electrocardiograms of Two Male Subjects with J-Point Elevation of More Than 0.2 mV in the Inferior Leads.

In two subjects with J-point elevation of more than 0.2 mV in the inferior leads, Subject 1 has a slurred elevation (arrows) and Subject 2 has a notched elevation (arrows). Both subjects died from arrhythmia during the follow-up period.
Help from the Literature

PubMed search from 1990 onwards yielded the following:

- “Early repolarization”: 893 hits
- “J-point wave”: 228 hits
- “J-wave”: 106 hits
- “J-point elevation”: 110 hits
- “J deflection”: 87 hits
- “J-point deflection”: 16 hits
Definition: Early Repolarization (1951-1976)

1. ST Elevation at the J junction of the QRS complex (0.5 mm or more [≥0.05 mv])
2. Distinct notch (J wave) or slur on the down slope of the R wave
3. Concavity of the ST segment
4. Tall, upright T waves
5. V345 more common than II,aVF

Most common in the young and Afro-Americans
Cellular Physiology Studies (circa 2000)

Antzelevitch, Yan, Genning, Boineau JP

- Action potential studies, mapping suggesting that J wave and R wave slurring are early repolarization and not late depolarization.
- They co-opt the terms early repolarization and J-point!
- Do they change the measurement of QRS duration???
1. Distinct notch (J wave) or slur on the down slope of the R wave
2. ST Elevation of 1 mm or more (maybe); Set at onset slur or peak J wave
3. Concavity of the ST segment
4. Tall, upright T waves
5. V3-45 more common than II, aVF
In the current studies, it is difficult to tell or compare what was done methodologically because of inconsistent terminology for ST elevation and how the level was set (J-point, J junction, J wave peak, top of the slur or notch are all possibilities). In the examples provided in the studies, the ST segment often is isoelectric but other times is elevated.

No matter how compelling theories based on action potential studies are, the term “early repolarization” is well established and causes too much confusion if co-opted for another phenomena.
Definitions

- **ST Elevation** – 1 mm (0.1 mv, 100 microv) elevation from isoelectric line at J point (same as QRS end, ST beginning or ST0 [zero]) in lateral and/or inferior leads
- **J-wave** – distinct positive excursion at the end of the QRS complex. If QRS ends with R wave, J-wave in downslope of R wave; (if ending in S wave, J-wave in upstroke of S wave?)
- **J-wave Syndromes** – hypothetical merge of Early Repol with Osborn wave, Brugada, ischemia
Definition Confusion

- Contiguous/adjacent versus any lead in an area group (Lateral=I,aVL, V456; Inferior=III,aVF,II)
  - Originally for reproducibility (only 2.5 sec, respiratory variation)
  - Computer analysis based on 10 seconds of average data
  - Wider area of involvement??

- J-point = peak of the J wave, beginning of slur or end of the QRS? And what is the end of the QRS?
  - The ECG and Exercise community always called the end of the QRS complex the J-point or QRS end or ST0
Definition: Early Repolarization (but with more concave ST segment and positive T wave)

ST level set at j-junction (j-point) where the QRS complex meets the ST segment, not at the top of the notch or peak of the J wave
Definition: J-waves (can be with or without [like here] ST elevation)

On R-wave

After S-wave
Definition: Slurring/notching
Other Pertinent ER Papers

- ER Normal Variant ECG: Correlate and Consequences. Klatsky et al. (Kaiser Perm Oakland) AJM 2003;115:171. From 73,088 adults (mean age 46) from voluntary Health screen 2,000 ECGs coded: BL 0.5 mm (15%), Definite 1.0 mm (33%); more likely to be male, less than 40 yo, bradycardic, Afro American and physically active. Hypothesis that STE would lead to hospitalizations and diagnoses not supported.

- J-Point Elevation of Primary VF and matched controls. Rosso et al. (UCSF and Israel) JACC 2008;52:1231. 45 patients with Idiopathic VF, 124 matched controls and 121 athletes. STEL the same in both groups (33% vs 24%)

- Ability of QRS notching to distinguish malignant vs benign ER. Merchant et al. (Boston) AJC 2009; 104:1402. 39 patients with idiopathic VT/VF, 23% with 1.0 mm STEL

- J-wave, Slurring and STEL in Athletes with Cardiac arrest. Cappoto et al. Circ AE 2010;3;305. 21 SCD athletes and 365 healthy athletes, J-wave height/STEL= 0.05mV, STEL 10% vs 22%
Is Early Repolarization in Idiopathic VT/VF Different?

- J-Point Elevation of Primary VF and matched controls. Rosso et al. (UCSF and Israel) JACC 2008;52:1231.
  - 45 patients with Idiopathic VF, 124 matched controls and 121 athletes. J “point” elevation (=J wave) in inferior leads (27 vs 8%), I and AVL (13% vs 1%), V456 7% both, athletes in between.
  - STEL and QRS slurring the same in both groups (33% vs 24%)

- Ability of QRS notching to distinguish malignant vs benign ER. Merchant et al. (Boston) AJC 2009; 104:1402.
  - 39 patients with idiopathic VT/VF, 23% with 0.10 mV STEL (slurred or notched)
  - 200 normals with STEL, Notching (J-wave) more prevalent in Idiopathic VF (44 vs 5%).

- J-wave, Slurring and STEL in Athletes with Cardiac arrest. Cappoto et al. Circ AE 2010;3;305.
  - 21 SCD athletes and 365 healthy athletes, J-wave height/STEL= 0.05mV, J-wave/slurring 29% vs 8%, STEL 10% vs 22%
Antzelevitch and Yan (J wave Syndromes: [Early Repol, Osborn wave, Brugada, ischemia] in Heart Rhythm 2010;7:549)

Three Early Repolarization (ER) subtypes:

- **Type 1** - ER pattern in the lateral precordial leads, prevalent among healthy male athletes and “is rarely seen in VF survivors(?)”;

- **Type 2** - ER pattern in the inferior/lateral leads associated with moderate risk; and

- **Type 3** - which displays an ER pattern in the inferior, lateral, and right precordial leads (anterior) and is associated with the highest level of risk for development of malignant arrhythmias and is often associated with ventricular fibrillation storms.
45,829 ECGs obtained from March 1987 to December 1999 at the Palo Alto Veterans Affairs Health Care Center for clinical indications on inpatients and outpatients; death status as of 2002 with cause of death from CPRS.

Exclusions: Inpatients (n = 12,319), paced rhythms (n = 290), Wolff Parkinson White syndrome (n = 42), atrial fibrillation/flutter (n = 1,253), acute myocardial infarctions (n = 29), heart rates >100 bpm (n = 2,799), and QRS durations >120 ms (n= 3,141) were excluded from the study leaving a target cohort of 29,281 patients.

25,544 were male (87%, 55 ± 14 years of age) and 3,737 were females (13%, 56 ± 17 years of age); 13% were African American, 6% Hispanic, and 81% Caucasian and other.

After 7.6 yrs FU, 6,739 deaths (1,995 CV, 30%)
Methods

- Computer analysis of the ECGs was completed with human confirmation of all computer generated reports. Since J-waves are not recognized by current ECG computer programs, these were coded visually.
  - ST elevation was considered 0.1 mv or more of elevation at the end of the QRS complex. J-wave - definite positive excursion at the end of the QRS complex before the J-point or QRS end. If the QRS complex ended with an R wave, the J-wave was noted in the down slope of the R wave; if ending in an S wave, it was noted on the upstroke of the S wave.

- The criterion requiring two contiguous leads in any area lead group (inferior: II, III and AVF, lateral: I, aVL, V4-V6, anterior: V1-V3) was applied.

- Sub-groups: No ST elevation, inferior lead only, lateral lead only, inferior or lateral lead, inferior and lateral lead, and global elevation (inferior, lateral, and anterior elevation).
Inferior or lateral ST elevation was present in 664 (2.3%) patients: 185 (0.6%) in inferior leads and 479 (1.6%) in lateral leads, with elevations in both areas in 163 patients (0.6%) patients. Global elevation was present in 0.4% and J waves were present in 11% without and 75% with ST elevation.

Patients with lateral ST elevation alone or with any other pattern including lateral ST elevation were significantly younger, had a lower heart rate, a lower prevalence of any ECG abnormality other than LVH and a higher prevalence of African Americans.

The inferior lead only elevation group differed from all others with ST elevation by being older, having a higher heart rate, lower prevalence of males and exhibiting more ECG abnormalities, particularly inferior Q waves (13.5%).

Those w/o STEL had a lower prevalence of J-waves (11.2%) than any of the STE groups, which ranged from 71% to 84%.
ST Elevation ≥ 1 mm Lateral Leads
ST Elevation $\geq 1$ mm Inferior Leads

![Graph showing survival over years with a decreasing survival rate.]
ST Elevation ≥ 1 mm Inferior or Lateral Leads with J-Wave
Global ST Elevation ≥ 1 mm (N=117)
Cox Hazards

- Adjustment was first for age, gender and Afro-American ethnicity and second adding resting heart rate, BMI and ECG abnormalities.

- Age, gender, resting HR and ECG abnormalities (LVH, MC for CAD, Q waves) were significant in the Cox Models but not race and BMI.

- The most striking finding is the decreased risk associated with the lateral lead only ST elevation alone or with any other pattern including lateral ST elevation. While the significance disappears with adjustment, the trend remains for both outcomes. This is consistent in the groups with global elevation and those with accompanying J-waves.

- There was a significant adjusted or unadjusted hazard of 2X found for inferior lead elevation only in non-African Americans.
Conclusions from Our Data

- In this outpatient clinical population using modern computer technology, there was no association of lateral patterns of ST elevation, J-waves or global elevation with cardiac or all cause mortality.
- Inferior ST Elevation had a multivariate adjusted HR of 2 for CV death in non-African Americans.
- Our results do not support a clinical reason for considering Global or Lateral Lead STEL or J-wave classification to be associated with CV risk.
- 2 mm of STEL in the lateral or inferior leads is rare.
Data Analysis

• Resolution of the main hypothesis

• Reading the tea leaves
# ST Elevation Lateral Leads

(1mm, any; Veterans)

<table>
<thead>
<tr>
<th>Heart Rate</th>
<th>&lt;25 yo (n=628)</th>
<th>25-35 (n=1941)</th>
<th>35-45 (n=5704)</th>
<th>&gt;45 yo (n=20168)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males (n=422)</td>
<td>Females (n=206)</td>
<td>Males (n=1617)</td>
<td>Females (n=324)</td>
</tr>
<tr>
<td></td>
<td>AA Other</td>
<td>AA Other</td>
<td>AA Other</td>
<td>AA Other</td>
</tr>
<tr>
<td>&lt;55bpm</td>
<td>53% 5%</td>
<td>44% 30%</td>
<td>33% 14%</td>
<td>11% 5%</td>
</tr>
<tr>
<td>55-70</td>
<td>47% 4%</td>
<td>37% 12%</td>
<td>27% 6%</td>
<td>9% 2%</td>
</tr>
<tr>
<td>70-85</td>
<td>44% 12%</td>
<td>31% 7%</td>
<td>19% 4%</td>
<td>8% 1%</td>
</tr>
<tr>
<td>&gt;85bpm</td>
<td>100% 8%</td>
<td>14% 3%</td>
<td>9% 3%</td>
<td>6% 1%</td>
</tr>
<tr>
<td>Total</td>
<td>50% 24%</td>
<td>34% 13%</td>
<td>22% 5%</td>
<td>9.5% 2%</td>
</tr>
</tbody>
</table>

*Total: Females = 1% vs Males = 5.6%*
## ST Elevation Lateral Leads (1mm, any; males)

<table>
<thead>
<tr>
<th>HR (bpm)</th>
<th>&lt;25 years</th>
<th>25-35</th>
<th>35-45</th>
<th>&gt;45 years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Afro-American</td>
<td>Other</td>
<td>AA</td>
<td>Other</td>
<td>AA</td>
</tr>
<tr>
<td>&lt;55 bpm</td>
<td>38%</td>
<td>32%</td>
<td>19%</td>
<td>5%</td>
<td>11%</td>
</tr>
<tr>
<td>55-70</td>
<td>25%</td>
<td>18%</td>
<td>10%</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>70-85</td>
<td>16%</td>
<td>13%</td>
<td>7%</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>&gt;85 bpm</td>
<td>11%</td>
<td>5%</td>
<td>4%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Total</td>
<td>26%</td>
<td>18%</td>
<td>9%</td>
<td>3%</td>
<td>6%</td>
</tr>
</tbody>
</table>
### ST Elevation Lateral Leads (1mm, any)

<table>
<thead>
<tr>
<th>HR (bpm)</th>
<th>Male Athletes (N=353, 17 to 26 y/o)</th>
<th>Male Veterans (&lt; 25 y/o N=422)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Afro American</td>
<td>Other</td>
</tr>
<tr>
<td>&lt;55 bpm</td>
<td>7/15= 47%</td>
<td>36/118= 30.5%</td>
</tr>
<tr>
<td>55-70</td>
<td>12/22= 54.5%</td>
<td>44/154= 28.5%</td>
</tr>
<tr>
<td>70-100 bpm</td>
<td>4/6= 67%</td>
<td>12/38= 32%</td>
</tr>
<tr>
<td>Total</td>
<td>23/43= 53%</td>
<td>92/310= 30%</td>
</tr>
</tbody>
</table>
ST Elevation in Anterior Leads of 353 Male athletes
Is there Clinical Relevance?
ER vs Pathology

- Heart rate (low, not high)
- Age (young, not old)
- Gender (male, not female)
- ST level (<0.2 mV, not more)
- Ethnicity (Afro American, not other)
- Athletic status (yes, not sedentary)
What’s Next?

- Develop Software to detect J-waves and R wave downward slurring
- Apply Software to digital VA DB and evaluate hazard of the new “ER”
The End (at last!)

- Thanks to all who have worked on the DB
- Thanks to the summer volunteers
- Thanks for your attention
- Questions?
Considerations

- Visual vs Computer analysis
- Ethnicity and Sport
- Contiguous vs any lead in an area
- QRS prolongation and STEL particularly in IdioVF/VT
- J-point: end of QRS vs peak of J-wave?
Potential Abstracts

- Racial STEL pattern differences (T wave inversion)
- Anterior STEL
- Comparison of Athletes to young clinical controls
- J wave prevalence and prognosis
- QRS prolongation and STEL
- Max normal STEL