ECG restitution of the beat-to-beat QT-TQ intervals in humans

Anthony A. Fossa, PhD.
Research Fellow
Global Clinical Technology, Pfizer Inc.
ECG Restitution

• Ability of the heart to recover from one beat to the next.
• Examines the relationship between action potential duration (QT interval) and diastolic interval (TQ interval) through the ECG.
• Replaces the traditional invasive electrophysiology procedure
• As QT/TQ ratio increases between beats this may be associated with increase arrhythmia vulnerability due to re-entry
QT prolongation during tachycardia dramatically impairs restitution (increase QT/TQ ratio >1)

Normal = RR 1000 ms (60 BPM)

QT (430 ms) TQ (570 ms) QT (430 ms)

70 ms QT prolongation (RR = 1000 ms)

QT Prolongation plus Tachycardia

RR = 400 ms (150 BPM)

QT (320 ms) TQ (80 ms) QT (320 ms)

RR = 400 ms

TQ (10 ms) QT (390 ms)
Methods in normals and TdP

Normals subjects (from two studies)
- Baseline values and autonomic challenges
  - standing, burst exercise, isoproterenol and phenylephrine
- Baseline and oral sotalol challenge
  - 160 (n=38) or 320 (n=19) mg

TdP Case Study
- 66 yo female CAD: Holter after sotalol (2 mg/kg, iv) prior to TdP

Restitution Parameters
- Lower TQ 5th quantile: boundary of lower 5% of beats
- % Beats with QT/TQ > 1: Reflects relative time spent in on steep portion of restitution relationship
- Upper 98% quantile of QT/TQ ratio: reflects degree and magnitude of steepness in restitution relationship for beats that may pose the greatest risk
ECG restitution at ambulatory and resting baselines in normal subjects (n = 6)

- 20 hr Ambulatory
- 2 hr Nocturnal
- 2 hr Awake supine

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<th></th>
<th>Ambulatory</th>
<th>Nocturnal</th>
<th>Awake</th>
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<tbody>
<tr>
<td>Median TQ</td>
<td>531</td>
<td>660</td>
<td>685</td>
</tr>
<tr>
<td>Lower 5% TQ Quantile</td>
<td>327</td>
<td>420</td>
<td>440</td>
</tr>
<tr>
<td>% QT/TQ Ratio &gt; 1</td>
<td>11.9</td>
<td>4.5</td>
<td>4.3</td>
</tr>
<tr>
<td>Upper 98% QT/TQ ratio</td>
<td>1.3</td>
<td>1.2</td>
<td>1.1</td>
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Restitution steepness increases with sympathetic-mediated tachycardia.
Isoproterenol Challenge

Human Iso-Epi  Human Iso Infusion.x  TIME = 33 min

Department of General Pharmacology
Pfizer, Inc - Groton, CT
Sotalol improves restitution despite QT prolongation

Comparison of Cmax period to time-matched baseline

- RR: ↑ 235 ms
- QT: ↑ 101 ms
- TQ: ↑ 134 ms
- QTc: ↑ 52 ms

- TQ 5th Quantile: ↑ 115 ms
- QT/TQ 98th Quant: ↓ 15%
- %QT/TQ beats >1: ↓ 30%
Restitution is impaired prior to TdP

Comparison to Cmax period from normals

RR: ↓ 172 ms
QT: ↑ 53 ms
TQ: ↓ 225 ms
QTc: ↑ 95 ms

TQ 5th Quantile: ↓ 126 ms
QT/TQ 98th Quant: ↑ 58%
%QT/TQ beats >1: ↑ 722%
ECG Restitution Summary

- Can be obtained through digitized Holter recordings
- May be used to assess changes in autonomic state in conjunction with QT prolongation
- If boundaries can be defined, could delineate normal from abnormal repolarization status.
Other Contributors

• Pfizer
  – Theresa Dombi
  – Bridget Martell
  – Joy Sieklucki

• Daiichi-Sankyo
  – Nenad Sarapa

• AMPS
  – Fabio Badilini

• U. Rochester Med. Ctr.
  – Jean-Philippe Couderc
  – Wojciech Zareba

• LMU Munchen, Germany
  – Stefan Kaab
  – Martin Hinterseer

• iCardiac
  – Meijian Zhou