Anesthesia for Patients with The Long QT Syndrome

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Eternal optimism
No conflicts of interest
Risk Factors for SCD in Young People

Structural Congenital Heart Disease
Congenital Coronary Anomalies
Acute Myocarditis
Hypertrophic and other Cardiomyopathies
Wolff-Parkinson-White Syndrome (WPW)

Channelopathies: Long QT syndrome
Objectives: Long QT Syndrome

Understand the electrophysiology leading to sudden unexplained cardiac death in patients with cardiac channelopathies.

Define which types of commonly administered anesthetic medications are safe and which exacerbate the Long QT Syndrome.

Outline an approach to anesthesia in these patients.

Compare and contrast other forms of cardiac channelopathies.
It is Estimated that 10-35% of Sudden Unexplained Cardiac Death (SUCD): Due to Cardiac Channelopathies

What Are Cardiac Channelopathies?

Clinical Syndromes → Changes in Heart Electrical System

Myocardial Ion Channels → Na⁺ K⁺ Ca²⁺
- Genetic
- Acquired

Altered Ion Channel Protein Permeability → ECG Changes, Life-Threatening, Pro-Arrhythmic, SUCD
Why Are the Cardiac Channelopathies Important?

Lethal Cardiac Arrhythmias in Patients With These Syndromes are Treatable

Risks of Anesthetic Drugs and Adjuvants on ECG Markers of Torsadogenicity.

Staikou C et al. BJA 112(2) 217-30 2014
Recent Case Study

3 year old 15 kg boy collapsed on the playground at school. CPR was promptly initiated.

AED used to cardiovert ventricular fibrillation.

Presented to us: further work up revealed prolonged QT interval.

Underwent internal defibrillator pacemaker insertion.
Objective 1

Understand the electrophysiology leading to sudden unexplained cardiac death in patients with cardiac channelopathies.
Cardiac Channelopathy

- Excess intracellular surplus of positive ions

- Delays ventricular repolarization

- (Prolongs the QT interval)

- Causes early after depolarizations, particularly in the subendocardium.

- Heterogeneous depolarization:
  - Torsades de pointes
Cardiac Channelopathies

The Long QT Syndrome
The Short QT Syndrome
The Brugada Syndrome
Catecholaminergic Polymorphic VT

Sick Sinus Syndrome
Cardiac Conduction Disease
Familial Atrial Fibrillation

Grant AO. Cardiac Ion Channels. Circ Arrhythm Electrophysiol 2009: 2: 185-194
NY City Office of Chief Medical Examiner

274 Autopsy Negative SUD  2008 - 2012
6 Major Channelopathy Genes since 2008
(KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, RyR2)

141 infants
13.5% Channelopathy

133 non-infants
19.5% Channelopathy

Long QT Syndrome

Most episodes of torsades de pointes, end abruptly in LQTS

4-5% of cardiac arrests fatal

Despite this, LQTS

Accounts for ± 1000 deaths each year in the United States.

Majority in children and young adults.

The Long QT Syndrome

Prolonged Ventricular Repolarization (intracellular positive charge)

Predisposes to Torsades de pointes Syncope and Sudden Death.

1:2000 live births annual mortality 1%
14 genetic forms 90-95% LQTS1-3

Majority AD, less than 1% AR
Jervell-Lange-Nielson & Romano-Ward

Deafness
What we need to know about the QT interval

Bradycardia prolongs QT
Tachycardia shortens QT

Bazett \[QT/(RR)^{1/2}\]
Fridericia \[QT/(RR)^{1/3}\]

Framingham \[QT+ 0.154(1-RR)\]
Hodges and Colleagues \[QT-1.75(HR-60)\]

Al-Khatib SM, et al. JAMA April 23/30 2003 (289):16; 2120-2126
## Normal Values QTc

<table>
<thead>
<tr>
<th>QTc Rating</th>
<th>1-5 yrs</th>
<th>Adult Male</th>
<th>Adult Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;440 ms</td>
<td>&lt;430 ms</td>
<td>&lt;450</td>
</tr>
<tr>
<td>Borderline</td>
<td>440 - 460</td>
<td>430 - 450</td>
<td>450 - 470</td>
</tr>
<tr>
<td>Prolonged</td>
<td>&gt;460</td>
<td>&gt;450</td>
<td>&gt;470</td>
</tr>
</tbody>
</table>

Schulein S. Long QT  SAJAA 16(3) 84-87 2010
16 year old 24 hours post-op orthopedic surgery with a Ropivicaine epidural. He is ready to go home.
Transmural Dispersion of Repolarization (TDR)

Myocardial wall repolarization is heterogeneous

(Tp-e) = measure of transmural dispersion of repolarization (TDR)

TDR 40-50 ms

TDR>75 ms LQTS

Associated with TdP

Transmural dispersion of repolarization (TDR)

Epicardial cells have the shortest repolarization period.
Midmyocardial cells (M cells) have the longest repolarisation.

Lower density of K+ channels.

This transmural dispersion of repolarization (TDR) is a normal phenomenon.
In LQTS, TDR can become exaggerated.
Tp-e / QT ratio as an index of arrhythmogenesis

- Tp-e / QT (0.15-0.25)
- 0.28
- TdP is a risk in LQTS

Gupta p et al. Tp-e /QT ratio as an index of arrhythmogenesis Jnl of Electrocardiology 41(2008) 567-574
Risk Stratification LQTS

**Congenital LQTS**
- Syncope
- QTc
- Genotype
- Mutation type

**Drug-induced TdP**
- Older age, females
- Heart disease
- Electrolyte imbalance
- Renal or hepatic dysfunction
- Bradycardia or long pauses
- >1 QT prolonging Med
- Genetic predisposition

Goldenberg I, Moss AJ. Long QT syndrome. *J Am Coll Cardiol.* 2008;51:2291–2300

Risk stratification for the diagnosis of LQTS

<table>
<thead>
<tr>
<th>Syncope</th>
<th>Syncope</th>
<th>QTc interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>With stress</td>
<td>2</td>
<td>≥ 480 msec</td>
</tr>
<tr>
<td>Without stress</td>
<td>1</td>
<td>460-470 msec</td>
</tr>
<tr>
<td>Congenital deafness</td>
<td>0.5</td>
<td>450 msec, men</td>
</tr>
<tr>
<td>Family member with LQTS</td>
<td>1</td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td>SCD in immediate family</td>
<td></td>
<td>T-wave alternans</td>
</tr>
<tr>
<td>&lt;30 yrs</td>
<td>0.5</td>
<td>Notched T-wave in 3 leads</td>
</tr>
<tr>
<td>Low heart rate for age, children</td>
<td>0.5</td>
<td></td>
</tr>
</tbody>
</table>

Probability of LQTS according to total score: low < 1, intermediate 2–3, high > 4.

Testing for LQT1 syndrome

**Exercise:** Lack of QT shortening during exercise

**Epinephrine infusion test:** QTc prolongs >30 ms at an incremental doubling dose of <0.1mcg/kg/min

LQT1 have a compromised slow component of the delayed rectifier potassium current ($I_{Ks}$)

A + test is 76% predictive of LQT1

Does not rule out others forms of LQT

Syndactaly & LQTs 8 Timothy Syndrome

Congenital Deafness & LQTs 1 & 5
Jervell & Lange Nielson Syndrome

The classic presentation of JLNS
Deaf child who experiences syncopal episodes during:
**stress, exercise, or fright.**
50% with JLNS had cardiac events before age three years.
>50% of untreated children with JLNS die prior to age 15 years.

Torsades de Pointes: 50 Years Later, Can We See It Coming?

TdP is the signature arrhythmia of long QT syndrome

Microvolt T wave alternans showing promise in screening for LQTS

Davis Am. Circ Arrhythm Electrophysiol. 2016 Feb;9(2) Editorial


"short-long-short sequence" (SLS) pattern as an initiating mode of *Torsade de Pointes* (TdP).

Not All Acquired LQTS = Torsades de pointes

**Drugs:**

Anti-Arrhythmics: (Class I, III)
Cisapride and Erythromycin, Clindamycin
Organo phosphate poisoning
Antidepressants
Ondansetron, Droperidol, Haloperidol

**Electrolytes:**

Low Calcium, Low Magnesium

**Other:**

SAH, CMO, Myocardial infarction, Starvation Diets, Anorexia Nervosa.

Right sided neck dissection

Viskin S. Long QT Syndromes and torsades de pointes Lancet 1999: 354 1625-1633
Objective 2

Define which types of commonly administered anesthetic medications are safe and which exacerbate the Long QT Syndrome.
CredibleMeds.org

CredibleMeds Filtered QT Drug List

The last revision date: February 21, 2016

13 pages (pdf) all the drugs to be cautious with or avoid
Anesthetic Strategy LQTs

Continue β-blocker
Quiet comfortable Premed
High risk of Torsades MgSO4 @ 30 mg/kg
Propofol Excellent
Dexmedetomidine
Fentanyl

Avoid:
Droperidol
Ondansetron
Catecholamines
Phenylephrine
Hypothermia
Ketamine, Thio, Sux
Caution Sevoflurane
Desflurane

Staikou et al. BJA 108 (5) 730-44 2012
The safety of Modern Anesthesia for Children with Long QT Syndrome

2005-2010. Retrospective. <18 yr old, 8 sites.
103 patients underwent 158 general anesthetics.
51% GA episodes: LQTs & 49% GA: incidental.
76% β-Blockers and 47% sedation on day of surgery.
Tiva: 19%
Gas: 30%
Combination of Tiva & Gas: 51%
Zero: Droperidol use

6.2% TdP neonates, infants in the LQTs related anesthetics

Objective 3

Compare and contrast other forms of cardiac channelopathies.
Sleeper: Attacked by a Nocturnal demon that Squats on his Chest and Suffocates him.

“Choking, gasping, groaning, gurgling, frothing at the mouth, labored breathing without wheezing or stridor, screaming, and other signs of terror.”

In Japan pok-kuri; the Philippines: bangungot or batibat and the Hmong Vietnam call it tsob tsuang. In Thailand, the being to fear is the phi am or 'widow ghost’ who comes to steal away the souls of young men.

Some men defend themselves from phi am by wearing lipstick at night, so that the ghost mistakes them for women and leaves them alone.
Brugada Syndrome (BrS)

Channelopathy with RV conduction delay and ST segment changes. (RVOT)

R precordial ST elevation

Fever may unmask

(coved type ST segment elevation > 0.2 mV and negative T-wave deflection in > 1 lead (V1-V2))

Differential Diagnosis

- R or L BBB, LVH, AMI, Ischemia, Acute myocarditis
- RV ischemia or infarction, Dissecting aortic aneurysm
- Acute PE, Heterocyclic antidepressant overdose
- Duchenne MD, Thiamine deficiency
- Hypercalcemia, Hyperkalemia, Cocaine intoxication
- Marijuana use
- ARVC, LQTS, type 3

References:

- Kloesel b et al. Anesthetic management of patients with Brugada syndrome CJA 2011:58:824-836
Antzelevich’s theory, intrinsic heterogeneity produces the transmural dispersion of repolarization (TDR) between the epicardium and endocardium, which may lead to local pre-excitation termed phase 2 re-entry, triggering VF
Anesthetic Drug Considerations
Brugada

Fentanyl
Thiopentone
Midazolam
Isoflurane, Sevo, N\textsubscript{2}O
Isoproterenol (R\textsubscript{x} ST\textsuperscript{^\wedge})
Vecuronium
Rocuronium
Lidocaine (care)
Amiodarone
Quinidine
Atropine

Contra indicated

Propofol infusions (care)
Bupivicaine
B blockers α agonists
Dexmedetomidine
Neostigmine
Metaclopramide
Procainamide
Flecainide
Epidural block caution
Valsalva
Noradrenaline

www.brugadadrugs.org

Concluding remarks
Survivors of Cardiac Arrest

Approximately 2/3 have an inherited cardiac disease

Channelopathies & SUCD is survived less frequently (28%) than structural inheritable cardiac pathology


We Only See What We Look For And We Only Recognize What We Know!

QT Interval

type 2

type 3

Tp-e/QT
**LQT Syndrome**

- Congenital deafness
- SUCD blood relatives
- Torsades risk
- B Blockers recommended
- Correct any abnormal Electrolytes
- Phenytoin for Torsades
- Stress free anesthetic preferred

**Brugada**

- Isoproterenol recommended
- For ECG related ST changes
- Caution use of Propofol

Crediblemeds.org

Brugadadrugs.org
Placement of Automated External Defibrillators (AEDs) in schools that have students with an identified cardiac need.

Over 415 AED’s in Colorado schools since 2006
Ambulance Drones

- Alec Momont
- Travel 100km/hr
- GPS technology