Anesthesia Management of the Patient with Long QT Syndrome

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Objectives

- Briefly discuss the historical background of LQTS
- Present a current definition of Long Q-T Syndrome
- Compare the pathophysiology of the two major forms of congenital (c) LQTS
- Describe the clinical manifestations of the two forms of c-LQTS
- Discuss current diagnosis and treatment options c-Long QT syndrome
- Describe the pathophysiology and management of torsades de pointes
- Discuss the general anesthetic consideration and intraoperative management of the patient with LQTS
- Outline a proposed peri-operative plan of care for the patient with Long QT syndrome.

Disclaimers

- None

GOAL

la substantifique moëlle

A concrete plan of approach with the at-risk patient

Background

LQTS – A Long Road

Background

- 1856: Friedrich *Meissner* in Leipzig town in German reports:
  - Deaf child drops dead after teacher yelled at her
  - When reported parents said two deaf siblings also died suddenly during emotional events
  - NO ECG then
- 1957: Anton Jervell and Fred Lange-Nielsen describe:
  - 4 in 10 children in Norwegian family were deaf & had recurrent syncope
  - 3 died before age of 10
  - Dramatic QT prolongation on ECG was noted
  - Inheritance appeared to be autosomal recessive

Background

- 1963 Cesarino Romano of Italy and
- 1964 Owen Connor Ward of Ireland
- Independently reported similar clinical syndrome:
  - Sudden death during exercise and emotional events
  - Autosomal dominant inheritance
  - No hearing loss

Attempted Definition

Arrhythmogenic disorder Characterized by:

Prolongation of the QT interval on ECG

- Pre-disposes to Polymorphic Ventricular tachycardia
  - Syncope
  - cardiac arrest
  - death

Long Q-T Syndrome – Two types

Congenital, inherited (primary)

- Due to genetic mutations of cardiac ion channels

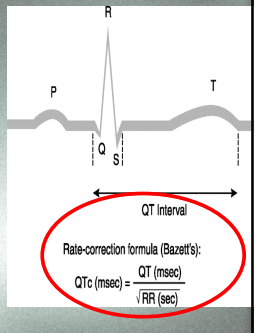
Acquired (secondary)

- Adverse response to medications
- Metabolic or physiologic abnormalities

QT Interval Physiology

QT Interval Physiology

- Measured from the start of the QRS complex to the completion of the T Wave
- Measured in Leads II, V5 and V6
- Derived from 3-5 cardiac cycles (HR)
- Varies with HR
  - Prolongs with bradycardia
  - Shortens with increased HR



QT Interval Physiology

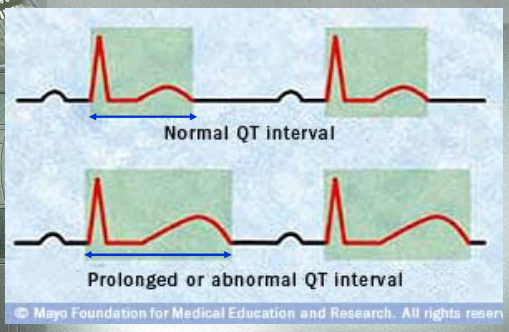
Normal is ≤ 420

QTc is prolonged when

> 440 msec in men

> 450 msec in women

QT Interval Physiology



Congenital LQTS

Should We Care?

The Faces of LQTS

- Incidence : 1:1100 – 3000 (Developed World)
- U.S. 1:7000 persons affected
  - causing 2000-3000 sudden deaths in children and young adults yearly
- One of the most common causes of autopsy negative, sudden unexplained death.
- ~ 60-70% of new cases diagnosed in females than males but with lesser cardiac event
- In females cardiac events have been correlated to menses – unexplained
- >400 I.D genetic mutations assoc. with LQTS
- ~ 30% of phenotypically affected subjects have no mutation identified on genetic analysis
- ~70% of those affected are silent carriers

LQTS
A Generic term

Phenotypic description of a group of disorders:

- QT interval prolongation - ECG
- Polymorphic ventricular tachycardia (torsades de pointes -TdP)
- Reported gene mutations lead to excess intracellular positive ions.
- Generally referring to Congenital LQTS

Congenital LQTS

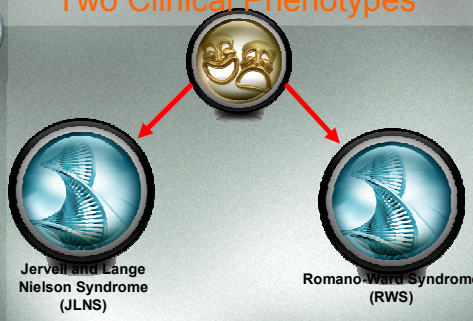
Sub-type	Frequency	Gene	Mutation Effect	ECG finding
LQTS 1	30-35%	KVLQT1	$\downarrow K^+$ Efflux	Broad, late-inset, T wave
LQTS 2	25-30%	HERG	$\downarrow K^+$ Efflux	Widely-split, low-amplitude, T wave
LQTS 3	5-10%	SCN5A	Prolonged Na^+ influx	Biphasic or peaked, late-onset, T wave
LQTS 4	1-2%	ANKB	Build-up of Na^+ within cell and Ca^{2+} outside of cell	Variable Qt interval prolongation
LQTS 5	1%	Mink	$\downarrow K^+$ Efflux	Not defined
LQTS 6	rare	MiRP1	$\downarrow K^+$ Efflux	Not defined
LQTS 7	rare	KCNJ2	$\downarrow K^+$ Efflux	Modest prolongation of Qt interval
LQTS 8	rare	CACNA 1C	Prolonged Ca^{2+} influx	Exaggerated Qt interval prolongation
LQTS 9	rare	CAV3	Prolonged Na^+ influx	Not defined
LQTS 10	Extremely rare, found in 1 family	SCN4 β	Prolonged Na^+ influx	Not defined

Congenital LQTS

Characterized by:

- Palpitations
- Recurrent syncope
- Cardiac arrest
- Seizure-like episodes
- Only 60% are symptomatic at time of diagnosis

Two Clinical Phenotypes



Congenital LQTS

Jervel and Lange-Nielson Syndrome

- Autosomal Recessive
- Associated with Profound Bilateral Sensorineural (cause is CN VIII or centers in brain) hearing loss (Homo Vs Heterozygous)
- Runs a more malignant course
- Assoc. with SIDS/SCD

Congenital LQTS

Romano-Ward Syndrome

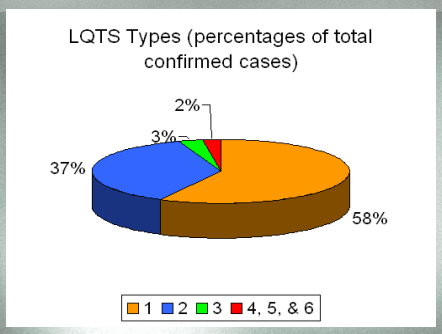
- Autosomal dominant with variable penetrance (genetic expression varies)
- More common form of LQTS
- Only has cardiac manifestations
- 50% never show symptoms
- Death is 1st indication in 10-15% of cases

Congenital LQTS

Genotypes

- Six genetic variations assoc. with congenital LQTS
- LQT-1 and LQT-5 assoc. with JNLS
- LQT 1-6 assoc. with RWS
- LQT-1 LQT2 and LQT 3 account for over 90% of cases of congenital LQTS

Congenital LQTS



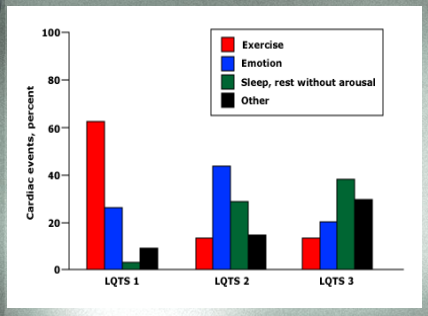
Congenital LQTS

Risk is genotype-dependent

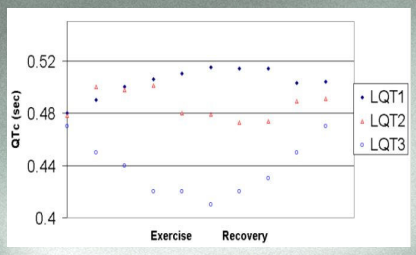
Congenital LQTS

- LQT-1 = ↑ ↑ risk with adrenergic stimuli from emotional stress and exercise (?swimming)
  - AKA “catecholamine dependent”
- LQT-2 = ↑ Auditory stimuli but not exercise
- LQT-3 = Bradycardia from sleep and rest
  - AKA “Pause dependent”

Congenital LQTS



Congenital LQTS

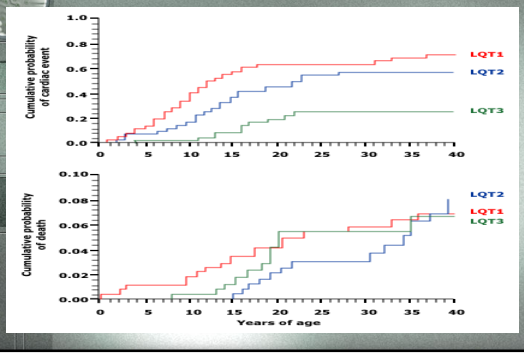


Courtesy of Ipej.org

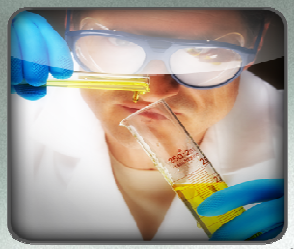
Congenital LQTS

- Median ages for 1st cardiac event:
  - LQT1 = 9
  - LQT2 = 12
  - LQT3 = 16
- Patients with JLNS likely to have their 1st cardiac event at a younger age
  - If untreated, mortality is 20% in year after initial event and 50% within ten years

Congenital LQTS

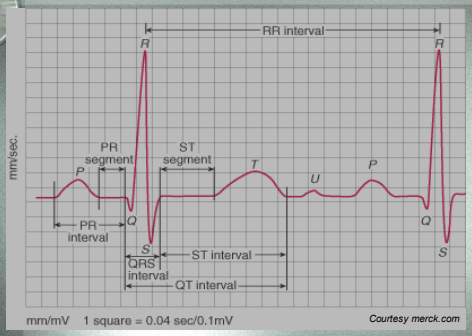


Congenital LQTS



Diagnosis

QT Interval Revisited



Congenital LQTS

Diagnosis

TABLE 2 Schwartz Score for the Diagnosis of Long QT Syndrome (1993)

Variable	Points
Electrocardiogram	
QTc ms* ≥480	3
460-470	2
450 (males)	1
Torsade de pointes	2
T wave alternans	1
T wave notches in 3 leads	1
Bradycardia†	0.5
Clinical history	
Syncope	
With stress	2
Without stress	1
Congenital deafness	0.5
Family history‡	
Family members with confirmed LQTS§	1
Unexplained sudden death in first-order family members <30 years	0.5

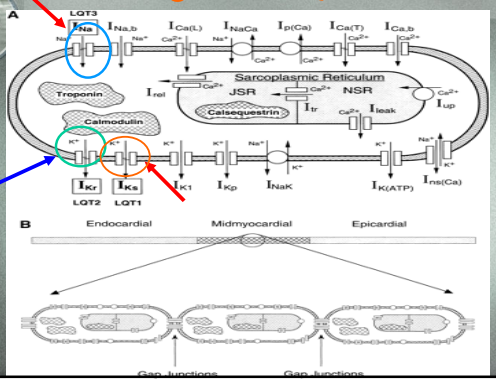
*QTc calculated with the formula of Bazett (QTc=QT/ RR).
†Resting heart rate below the second percentile for age.
‡The same family member cannot be considered twice.
§Schwartz score ≥4: <1 point: low probability; 2-3 points: intermediate probability; ≥4 points: high probability.

LQTS

Genetico-Molecular Physiology

Channelopathies

Congenital LQTS



Congenital LQTS

Treatment

- Primary goal is to avoid torsades de pointes
- Avoid triggers such as strenuous exercise (swimming and running)
- Check and correct electrolytes in clinical settings
- Consult cardiologist or cardiac electropysiologist
- Consider genetic counseling for confirmed LQTS

Congenital LQTS

- LQT-1 & LQT-2
  - β-blockade is the gold standard of treatment
  - Propranolol is drug of choice
    - daily dose of 2-3mg/kg = 210mg for 70kg patient
    - Prevents cardiac events in 70% of patients
    - Nadolol, Atenolol and Metoprolol all show equal effectiveness
- LQT-3
  - Na channel blockers Flecanide (75 to 150 mg twice daily orally) and Mexilitine

Congenital LQTS

Pacemakers and ICDs

- Symptomatic patients despite β-blockade
- Could be used with β-blockers
- Pacemaker especially beneficial to LQT-3 patients due to pause-bradycardia induced Tdp.

Congenital LQTS

Left cervicothoracic sympathetic ganglionectomy

- Removal of the first 4 or 5 left thoracic ganaglia and total left stellate ganglion
- In patients with frequent ICD triggers while on beta blockade
- More effective in LQT-1 patients
- Does not eliminate risk
- Not superior to ICD

Congenital LQTS

Gene-specific therapy

- Under investigation
- Experimental models have not changed traditional treatment approaches

Acquired/Secondary LQTS

Acquired LQTS (a-LQTS)

- Caused by external or iatrogenic factors
- Drugs are the most common cause of a-LQTS
- Aprox. 50 FDA approved drugs are culprits
- Principal ion channel resp. for a-LQTS is the I_{Kr} (HERG)
  - Same implicated in LQTS-2
  - Probable physiologic relationship btw LQTS-2 and drug-induced LQT syndrome

Acquired/Secondary LQTS

Peri-op related drugs implicated

- Amiodarone
- Procainamide
- Haloperidol
- Droperidol
- Ondansetron
- Granisetron
- Chloral Hydrate

Acquired/Secondary LQTS

Other Drugs

- Nicardipine
- Geodon (Ziprasidone)
- Fosphenytoin
- Salmeterol
- Methadone
- Sotalol
- Macrolide antibiotics (erythromycin)
- Dobutamine
- Epinephrine

Acquired/Secondary LQTS

Other Drugs

- Dopamine
- Isoprotenerol
- Norepinephrine
- Phenylephrine
- Albuterol
- Levalbuterol
- Metoprotenerol
- Terbutaline

CRNA

NO BENIGN PROVIDER

Acquired/Secondary LQTS

Anesthesia related drugs

- Midazolam has not been shown to prolong QT interval
- Propofol produces an insignificant QT prolongation compared to Thiopental
  - Another study – shortens QT interval
  - Preferred agent for maintenance (TIVA)
- Vecuronium and Cisatracurium show no QT interval prolongation
- Succynlcholine consistently prolonged QT interval

Acquired/Secondary LQTS

Anesthesia related drugs

- Reversals:
  - neostigmine-atropine,
  - edrophonioum-atropine,
  - neostigmine-glycopyrrolate
    - All Prolong the QT interval
- Droperidol 0.75mg IV and Zofran 4mg IV produced similar QT prolongation
- Droperidol 0.625mg did not produce a significant prolongation of the QT interval, compared to saline placebo (separate study).

Volatile Agents

- Sevoflurane, Isoflurane and Desflurane at 1 MAC all prolong the QT interval
- Halothane significantly shortens QT interval
  - But Halothane also sensitizes cardiac myoctyes to catecholamines
  - Should be avoided in susceptible patients

Anesthesia related drugs
Volatile Agents

Agents have all been administered safely with peri-operative beta blockade, in patients with known LQTS

Regional Anesthesia

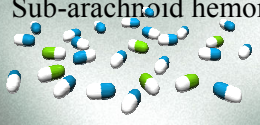
Study in ASA I and II male patients undergoing elective surgery under spinal anesthesia

Showed significant QT prolongation after onset of blockade

Cozanitis DA, Sawicka W, Wujtewicz MA, Kawecka A, Lasek J, Wujtewicz M. Influence of spinal anesthesia on corrected QT interval. Reg Anesth Pain Med. 2005 Nov-Dec;30(6):548-52

Acquired/Secondary LQTS

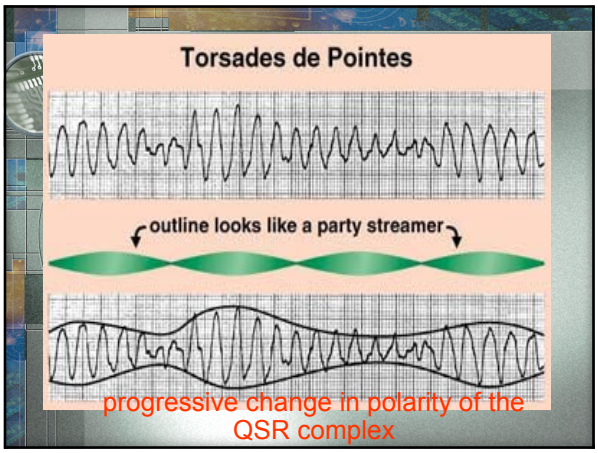
- Pre-existing cardiac conditions facilitate drug-induced a-LQTS:
  - Ventricular hypertrophy
  - Myocardial ischemia
  - Myocardial fibrosis
- Sub-arachnoid hemorrhage



Other conditions assoc. with LQTS

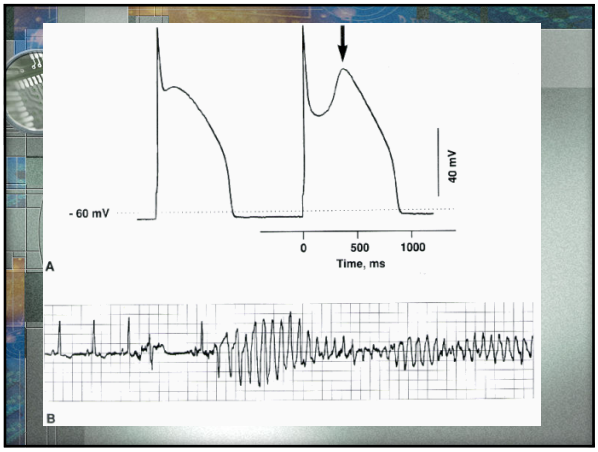
- Timothy Syndrome
  - Autosomal dominant inheritance with
    - Structural heart defects, QT prolongation, Syndactyly and autism
- Anderson-Tawil Syndrome
  - Autosomal dominant inheritance assoc. with LQTS
  - AKA LQT syndrome 7
  - Assoc with physical abnormalities of the head, face, and limbs
- Brugada Syndrome
  - Inherited defect in Na+ channels, associated with several ECG patterns

Torsades de…?

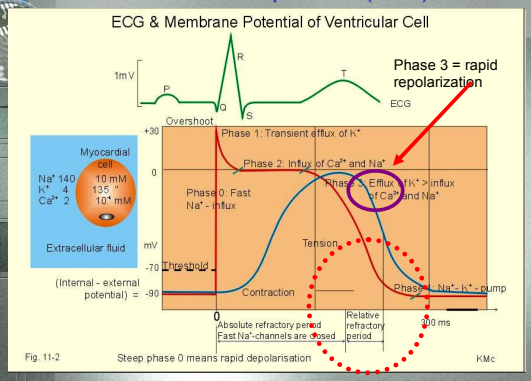


Torsades de Pointes

- Triggered by:
  - Decreased outward K^+ currents
  - Reactivation of calcium channels (key to EAD maintenance)
  - Reactivation of delayed Na^+ channels
  - All result in early-after depolarization
    - Delayed repolarization
    - Oscillation of membrane potential
  - TdP usually Preceded by a pause in most LQTS cases

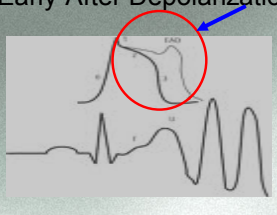


Torsades de pointes (TdP)



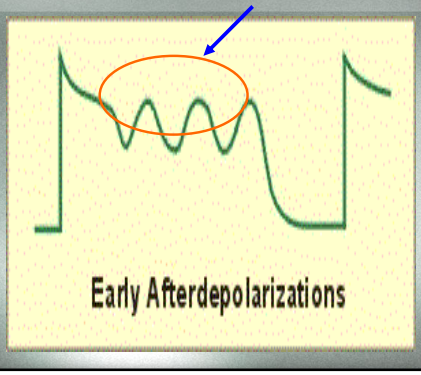
Torsades de Pointes

Early-After Depolarization

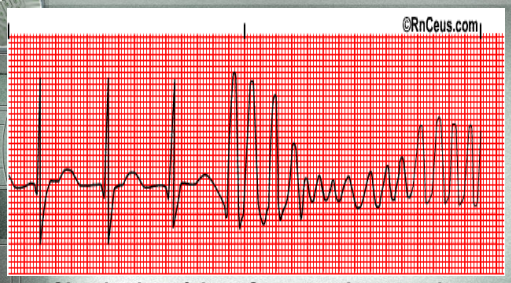


EADs that reach threshold could propagate an action potential

Torsades de Pointes

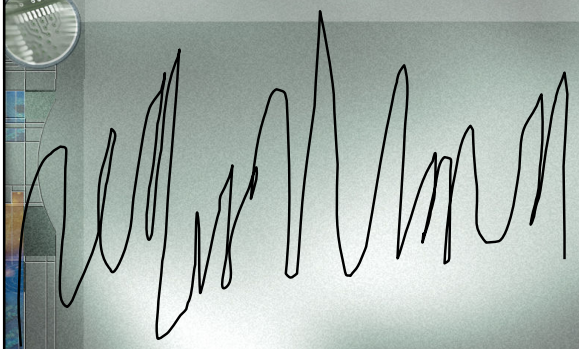


Torsades de pointes (TdP)



Classic short & long Sequence between the R-to-R interval

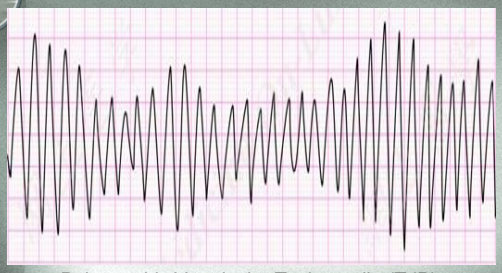
Torsades de Pointes



Torsades de Pointes

- Typical TdP morphology may not be seen in
  - Single lead monitoring
  - Short runs of torsades
- Early events usually short-lived
- Reading could also be affected by
  - Patient movement
  - Faulty lead placement
  - Bovie interference
  - Static electricity

Torsades de Pointes



Polymorphic Ventricular Tachycardia (TdP)

Torsades de Pointes

Treatment

- Can be self-limiting or life-threatening
- May result in sudden cardiac death
- Short-term treatment for both congenital and acquired LQTS similar
  - Beta-1 adrenergic stimulation is contraindicated in catecholamine-dependent congenital phenotype

Torsades de Pointes

Short-term treatment

- Discontinuation of offending agent
  - Terminate use of known triggers
  - Predisposing conditions such as bradycardia and electrolyte imbalances should be identified and corrected
- Defibrillation
  - Ventricular fibrillation requires direct current (DC) defibrillation
  - Is the last resort in stable patients because of known TdP recurrences following cardioversion
- Suppression of EADs
  - Magnesium sulfate is first line of treatment
    - It decreases calcium influx, lowering amplitude of EADs

Torsades de Pointes
TREATMENT

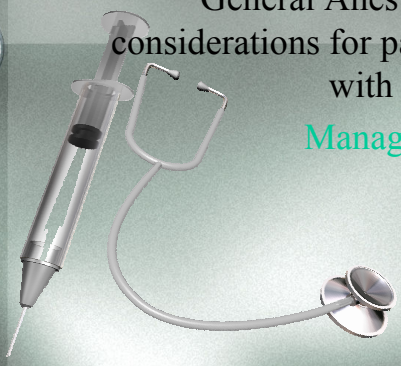
- Magnesium sulfate
  - 2-4gm IV initially in 30-60 seconds
  - Repeat 2nd dose in 5-15 minutes
  - Effective even in patients with normal Mg+ levels
  - Or infusion of 3-20mg/min over 7-48 hours
  - Magnesium sulfate decreases calcium influx, decreasing EAD amplitudes
- Some recommend high normal potassium values
- Lidocaine has an initial beneficial effect but TdP recurs in all cases
- Mexiletine may also be used to suppress TdP.
- Isoproterenol can also be used to accelerate heart rate and override electrical pacing (keeping HR >90 bpm)
  - contraindicated in catecholamine-dependent congenital LQTS
  - Used as interim treatment until overriding pacing can be started.

Torsades de Pointes
TREATMENT

Temporary transvenous pacing

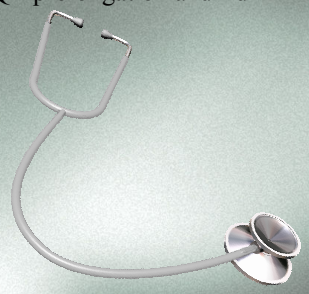
- Effective in both forms of LQTS
  - It facilitates repolarizing potassium currents
  - It prevents long pauses, suppressing EADs and decreasing the QT interval
  - Atrial pacing is preferred mode
    - It preserves the atrial contribution to ventricular filling
    - It results in a narrower QRS complex and hence a shorter QT
    - Pacing should be instituted at a rate of 90-110 bpm until the QT interval is normalized.

General Anesthestic considerations for patients with LQTS
Management



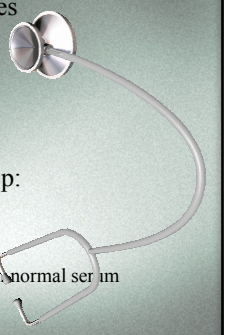
Anesthesia Management

- Avoid triggers of QT prolongation and TdP
- Provide Peri-op
  - Anxiolysis
  - β-blockade
  - Analgesia
- Maintain
  - Normothermia
  - Normoxia
  - Euglycemia
  - Normocarbia



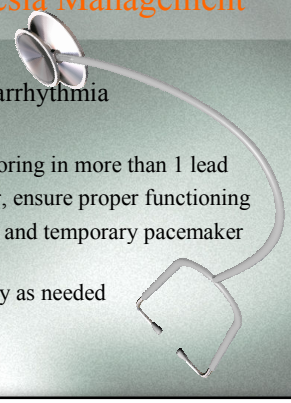
Anesthesia Management

- Avoid hemodynamic extremes
  - Bradycardia
  - Tachycardia
  - Hypotension
  - Hypertension
- Correct serum electrolytes esp:
  - Potassium
  - Magnesium
    - Prophylaxis beneficial even with normal serum concentrations



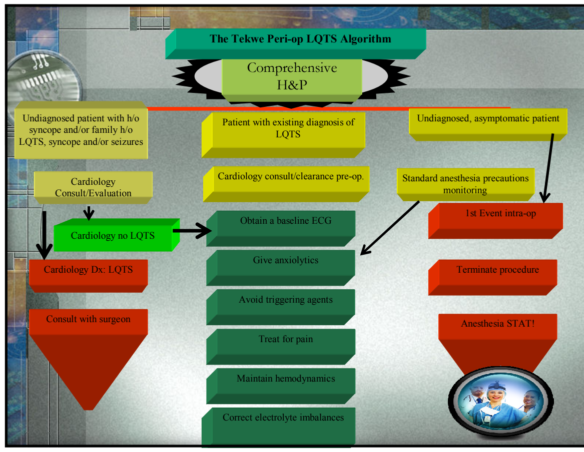
Anesthesia Management

- Prevent and treat arrhythmia
  - Cont. ECG monitoring in more than 1 lead
  - If ICD/pacemaker, ensure proper functioning
  - Have defibrillator and temporary pacemaker available
  - Consult cardiology as needed



The Dogs Bark….

…..and the Caravan Goes by!


The Tekwe Peri-op LQTS Algorithm
Comprehensive H&P
Undiagnosed patient with h/o syncope and/or family h/o LQTS, syncope and/or seizures
Patient with existing diagnosis of LQTS
Undiagnosed, asymptomatic patient
Cardiology Consult/Evaluation
Cardiology consult/clearance pre-op.
Standard anesthesia precautions monitoring
Cardiology no LQTS
Obtain a baseline ECG
1st Event intra-op
Cardiology Dx: LQTS
Give anxiolytics
Terminate procedure
Avoid triggering agents
Consult with surgeon
Treat for pain
Anesthesia STAT!
Maintain hemodynamics
Correct electrolyte imbalances

References

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