



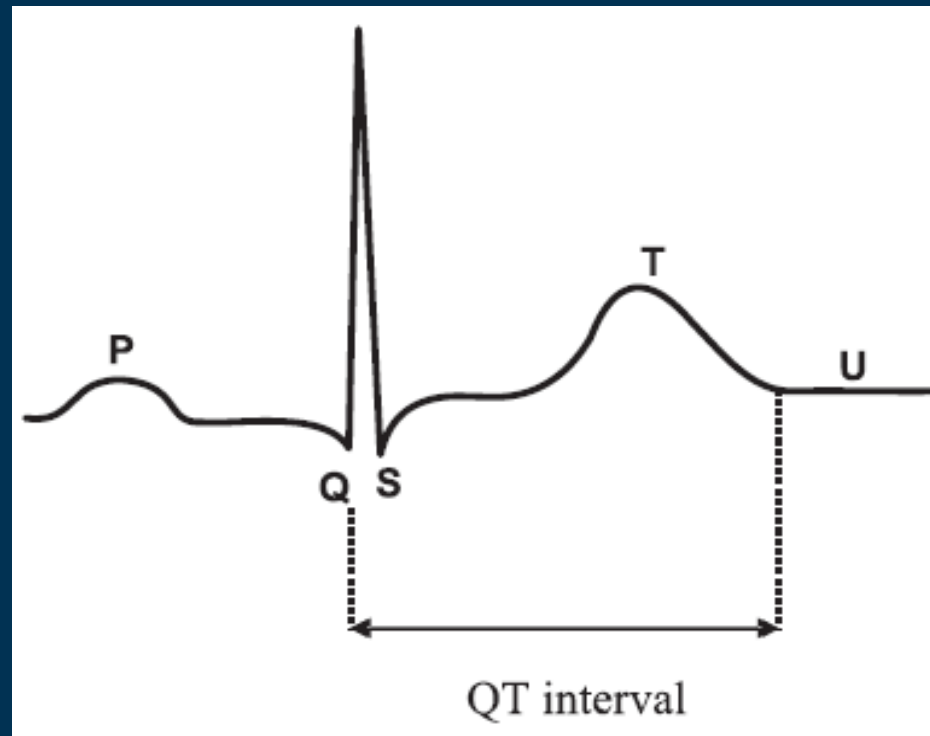
QT Prolongation Secondary to Drug Interactions – What to do?

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[Objectives]

- Describe how one measures the QT interval
- List what influences the QT interval
- Identify why prolonged QT is a problem
- Describe how medications affect the QT interval
- Outline how to assess a drug-drug interaction that may result in QT prolongation

[QT interval]



Can J Cardiol 2005;21:857-64

[Rate correction formula]

- Recommended: linear regression formula
- Bazett's formula
 - Overestimates QTc at higher heart rates
 - Underestimates QTc at slow heart rates

$$QTc \text{ (msec)} = QT \text{ (msec)} / \text{square root RR interval (sec)}$$

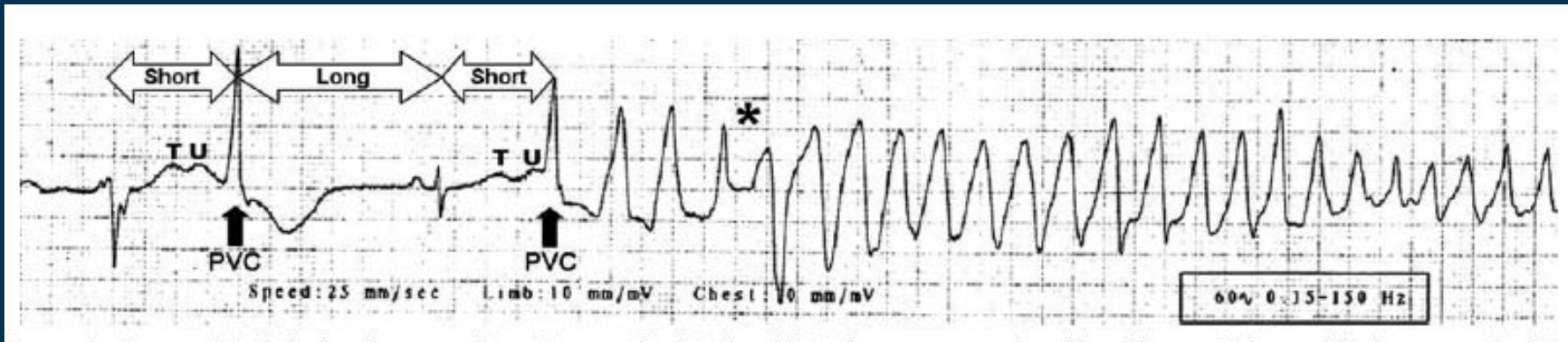
[QTc prolongation]

QTc prolongation (> 99th percentile)

- > 480 msec females
- > 470 msec males
- > 500 msec highly abnormal

- Other considerations
 - Wide QRS/pacemaker
 - A fib

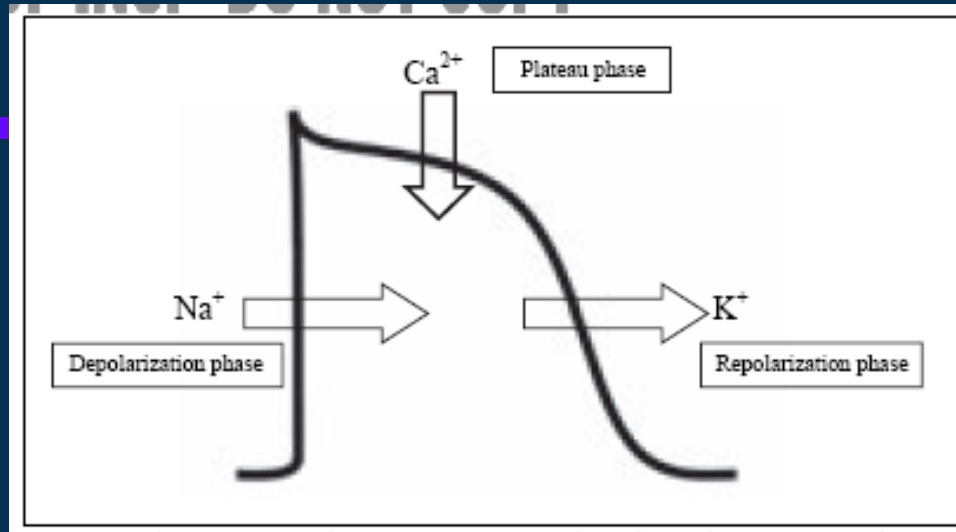
Torsade de pointes



Short-long-short ventricular cycle length initiation

[Treatment]

- Non-sustained
 - Magnesium 2 g IV
 - Repeat Mg
 - Increase heart rate
 - Temp pacer
 - Isoproterenol
 - Potassium
 - Maintain 4.5 – 5 mmol/L
 - Remove offending drug



I_K = Delayed rectifier current

I_{Kr} = Rapidly activating (major current responsible for repolarization in humans)

I_{Ks} = slowly activating

[QT prolongation - drug]

- I_{Kr} blockade
- www.qtdrugs.org
 - Lists associated with QT prolongation
 - List associated with but unlikely to cause QT prolongation

- » [Drug Lists by Risk Groups](#)
- » [Browse Drug List by Brand and Generic Names](#)

Pub Med Search on:

- » [Drug Name, QT & Torsades](#)

- » [Printable Drug Lists](#)

- » [Drug Lists Updates](#)

- » [Why are drugs put on the lists?](#)

[Herbal Remedies](#) ▶

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Drugs that Prolong the QT Interval and/or Induce Torsades de Pointes Ventricular Arrhythmia

Drug-induced ventricular tachycardia associated with prolongation of the QT interval is a well-recognized form of drug toxicity termed Torsades de Pointes (TdP). Because the evidence for risk is variable between the many drugs associated with TdP, we have divided the drugs into four groups. Each of the following four lists of drugs relate to their relative risk of inducing Torsades de Pointes or prolonged QT.

1

[View List](#) ▶ [Sort by Brand](#) ▶ [Sort by Generic](#) ▶

Drugs with Risk of Torsades de Pointes

Drugs that are generally accepted by the Scientific Advisory Board of the AZCERT to have a risk of causing Torsades de Pointes.

2

[View List](#) ▶ [Sort by Brand](#) ▶ [Sort by Generic](#) ▶

Drugs with Possible Risk of Torsades de Pointes

Drugs that in some reports have been associated with Torsades de Pointes and/or QT prolongation but at this time lack substantial evidence for causing Torsades de Pointes.

3

[View List](#) ▶ [Sort by Brand](#) ▶ [Sort by Generic](#) ▶

Drugs to be Avoided by Congenital Long QT Patients

Drugs to be avoided for use in patients with diagnosed or suspected congenital long QT syndrome. (Drugs on Lists 1, 2 and 4 should also be avoided by patients with QT syndrome.)

4

[View List](#) ▶ [Sort by Brand](#) ▶ [Sort by Generic](#) ▶

Drugs Unlikely to Cause Torsades de Pointes

Drugs that, in some reports, have been weakly associated with Torsades de Pointes and/or QT prolongation but that are unlikely to be a risk for Torsades de Pointes when used



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Center for Education and
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Drugs
With Risk

Drugs with
Possible Risk

Drugs With
Conditional Risk

Drugs with Conditional Risk of Torsades de Pointes

Drugs that, in some reports, have been weakly associated with torsades de pointes and/or QT prolongation but that are unlikely to be a risk for torsades de pointes when used in usual recommended dosages and in patients without other risk factors (e.g., concomitant QT prolonging drugs, bradycardia, electrolyte disturbances, congenital long QT syndrome, concomitant drugs that inhibit metabolism).

[TdP]

- QT prolongation \neq arrhythmogenicity
 - Amiodarone
- Dose related
 - Quinidine
- Dispersion of repolarization
 - Repolarization reserve

[Drugs]

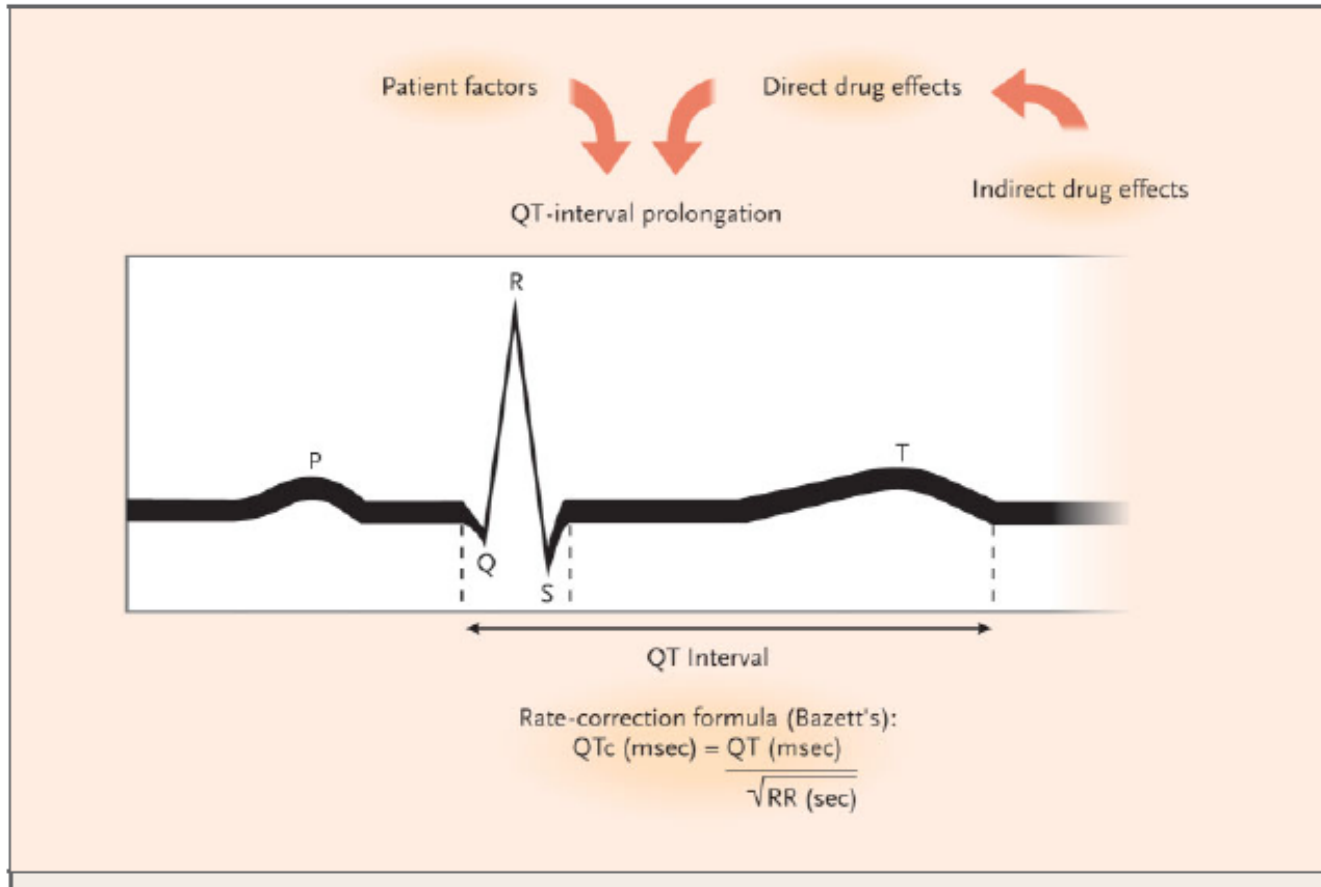
Direct Effects

- Disopyramide, procainamide, quinidine, amiodarone, sotalol, dofetilide, ibutilide, bretylium
- Clarithromycin, chlorpromazine, domperidone, erythromycin, haloperidol (IV), methadone

[Drug-induced TdP]

- Moxifloxacin 1:100,000 to 1:1,000,000
- Cisapride 0.001%
- Antiarrhythmics 1 – 10%
 - Sotalol 5.4%
 - Ibutilide 4.3%
 - Quinidine 8%

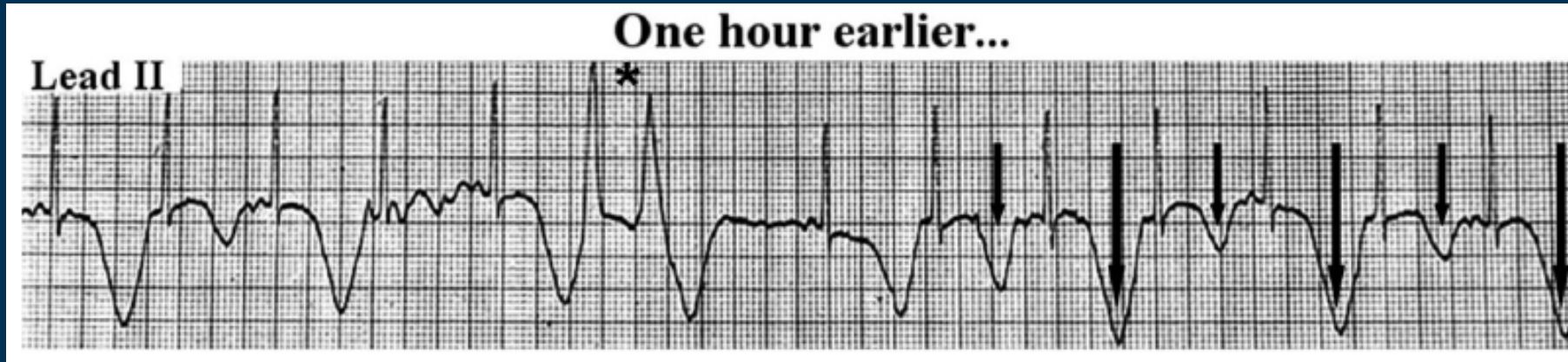
[QT interval + ?]



Risk Factors

- QTc > 500 msec
- QT prolonging drugs
- > 1 QT prolonging drugs
- CHF
- MI
- Advanced age
- Bradycardia
- Female sex
- Hypokalemia
- Hypomagnesemia
- Hypocalcemia
- Tx with diuretics
- Impaired drug metabolism
- Occult congenital LQTS

High risk feature: T wave alternans



Who to monitor

- AHA recommendation for ECG monitoring
 - Initiation of a drug known to cause TdP
 - Overdose from potentially proarrhythmic agent
 - New-onset bradyarrhythmia
 - Severe hypokalemia or hypomagnesemia
- Document QTc at baseline and 8 – 12 hrs after initiation, increased dose or overdose of QT prolonging drugs
- How long – depends on t_{1/2} of drug

[Approach to therapy]

QTc prolonging drug ordered

QTc measurement

Assessment of Risk Factors

Assessment of alternatives

Examples

Drug ordered	Haloperidol 5 mg IV prn	Moxiflox daily	Amio 200 mg daily
QT measured	460 msec	450 msec	480 msec
Risk Factors	ICU No drugs	Methadone 40 mg HR 76	72 yo Clarithro 250 mg daily
Alternative	Midazolam Loxapine		Azithro

[Decision]

- Alternatives
- Risk factors
- Risk vs benefit
- Monitoring