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Prevention and Management of Drug-Induced QT Interval Prolongation and Torsades de Pointes

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Disclosures

All planners, presenters, reviewers, and ASHP staff of this session report no financial relationships relevant to this activity.

LEARNING OBJECTIVES

- Given a patient with drug-induced torsades de pointes (TdP), distinguish risk factors for drug-induced QTc interval prolongation and TdP and their contribution to the occurrence of TdP.
- Given a patient with drug-induced TdP, describe how this arrhythmia could have been prevented.
- Assess the influence of emerging predictive analytics (validated QT interval prolongation risk scores, clinical decision support systems) on the risk of drug-induced QT interval prolongation.
- Given a patient with drug-induced TdP, develop a patient-specific treatment regimen.

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Drug-Induced QT Interval Prolongation and Torsades de Pointes — Culprits, Risk Factors, and Consequences

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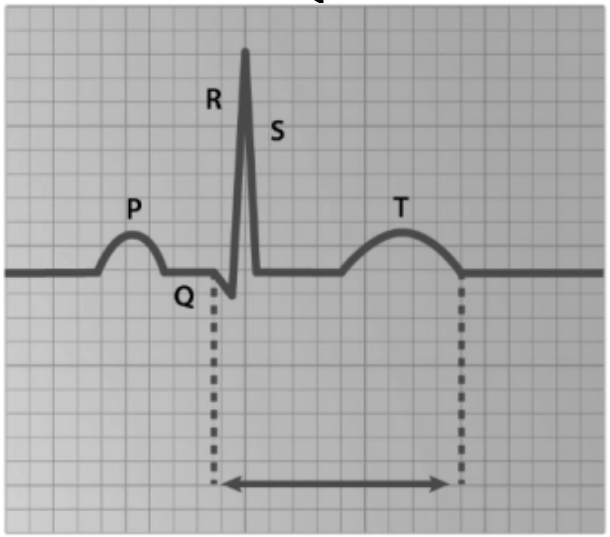
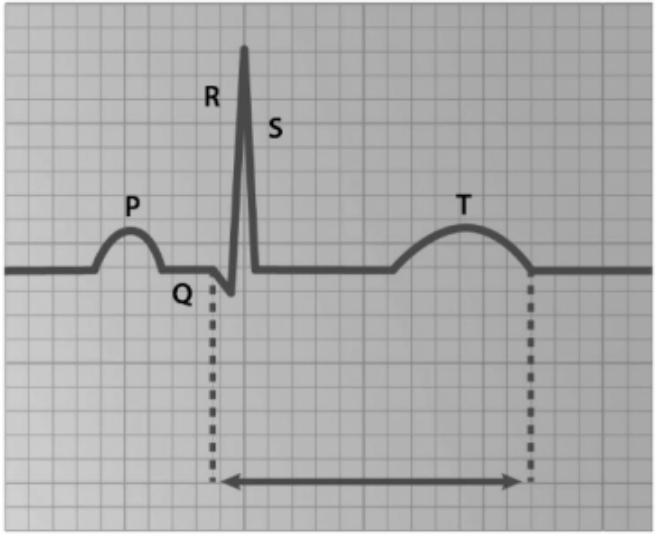
QT Interval Prolongation

Normal QT Interval



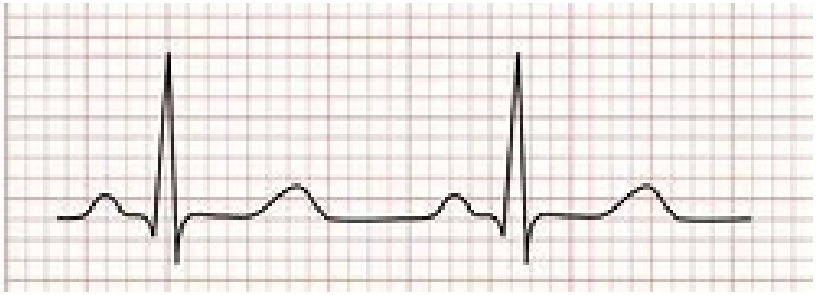
Prolonged QT Interval



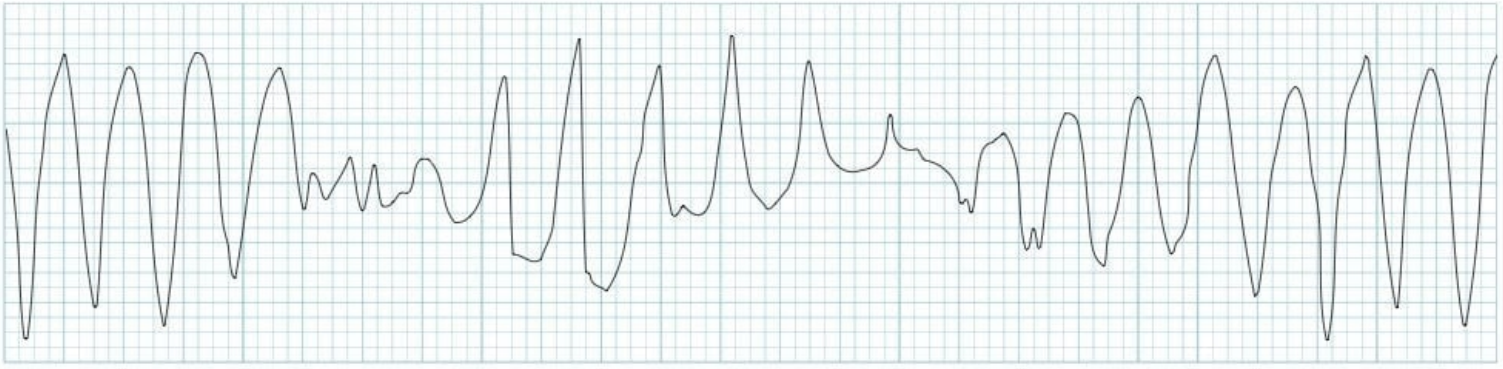
Bazett's Formula= $QT_c = \frac{QT}{\sqrt{RR}}$

TdP

Normal



Torsades



QTc Interval Prolongation

- QTc interval prolongation
  - > 480 ms for females
  - > 470 ms for males
- Increased risk of TdP
  - QTc ≥ 500 ms
  - QTc increases ≥ 60 ms
  - 5-7% for every 10 ms increase

Circ. 2010;121:1047-60

QT Interval Prolongation and TdP

- Congenital long QT syndrome
  - 1 in 2000 births
- 22% of admissions have prolonged QT intervals
  - 51% prescribed QT prolonging drugs
- ~13,000 TdP events in the US annually

Intern Med J. 2012;42:933-40
Can Pharm J (Ott). 2016;149:139-52
Eur Heart J Supplements 2001; 3 (Suppl K): K70–K80

TdP

- Rare outcome
  - Big data needed
  - Rely on QT interval prolongation

- Most often studied in hospitalized patients

Self-Assessment

Ernie is a 52 YOF admitted for heart failure who develops TdP

PMH: Heart failure with reduced ejection fraction, chronic back pain, hypertension, GERD, generalized anxiety
Current meds: Omeprazole, citalopram, lisinopril, tramadol, bisoprolol

Which of the following accurately describes her risk factors for QT interval prolongation?

A Age, citalopram, hypertension
B Hypertension, omeprazole, tramadol
C Bisoprolol, citalopram, heart failure
D Tramadol, heart failure, female

Risk Factors

Risk Factors

- Mechanisms
  - Delayed rectifier potassium current inhibition (I_{KR})
  - Late sodium current enhancement (I_{NaL})
- Modifiable and non-modifiable

Cardiovascular Disease

- Bradycardia
- Stress-related cardiomyopathy
- Acute MI
- Stroke
- Heart failure and reduced ejection fraction

Electrolytes

- Hypokalemia
- Hypomagnesemia
- Hypocalcemia
- Excess licorice
- Apheresis
- Gitelman Syndrome

Endocrine

- Hypothyroidism
- Panhypopituitarism

Autonomic Nervous System

- Pheochromocytoma
- Head-up tilt
- Pure autonomic failure

Emerging Risk Factors

- Environmental
  - Hypothermia
- Inflammatory/Immunity
  - Celiac disease
  - Mechanism
    - CRP, TNF-alpha, IL-6, IL-1

Heart. 2017; 103:1821-9
PloS One. 2014;9:e95994

Other Risk Factors

- Female sex
- Older age
- Genetic
- Propionic acidemia
- Liquid protein diet
- Sickle cell disease
- Drugs

QT Prolonging Drugs

- > 130
- 23% of all outpatients
  - 55% of geriatrics
- 3-fold increased risk of sudden cardiac death

Eur Heart J. 2005;26:2007-12
PLoS One. 2016;11:e0155649
Am J Med. 2003;114:135–41

Crediblemeds Risk Categories

Risk Category	Defined
Known	Prolong QT AND Known TdP risk
Possible	Prolong QT BUT Lack evidence for TdP risk when taken as recommended
Conditional	Known TdP risk BUT Only under certain conditions OR By creating conditions that increase TdP risk
Avoid in LQTS	High TdP risk for congenital LQTS Includes all categories above plus drugs that do not prolong QT but have special risk because of other actions

Newer Drugs of Concern

- Tramadol
- Memantine
- Cimetidine
- Aclarubicin
- Apalutamide
- Abarelix
- Amsacrine
- Maprotiline
- Zuclopenthixol
- Clotiapine
- Lacidipine
- Metolazone
- Propafenone
- Eperisone

Increased Risk of Drug-Induced TdP

- Higher serum concentrations
  - IV administration
  - Inadequate renal dose adjustment
  - Drug interactions
- > 1 QT interval prolonging drug
- Presence of other risk factors

Can Pharm J (Ott). 2016;149:139-52

Drug Induced TdP

- Review of 249 drug-induced TdP events
  - ~100% ≥ 1 risk factor
  - 71% ≥ 2 risk factors

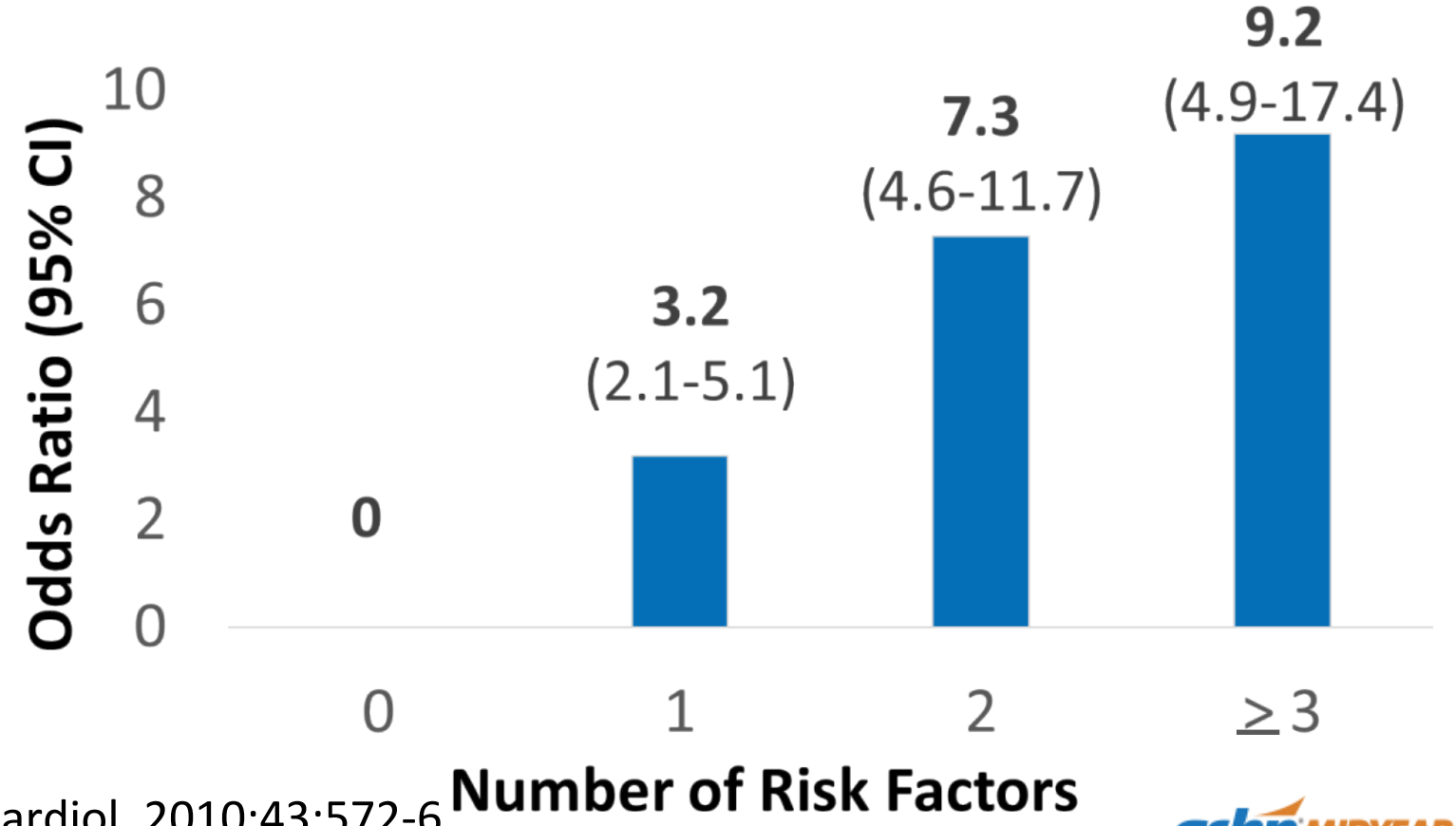
Medicine. 2003;82:282-90

Weighing the Risk

Risk factor	Change in QTc Interval (ms)	
	Inpatients	Outpatients
Baseline QT interval >450ms	N/A	28
Hypokalemia	14.7-24.1	N/A
Hypocalcemia	8.1-20.4	N/A
Female sex	13.9	12
QT prolonging drug	11.1	5
Loop diuretic	10.1	N/A
Older age	>10	3

J Eval Clin Pract. 2017;23:1274-80
Eur J Clin Pharmacol. 2018;74:183-91

Number of Risk Factors Increases TdP Risk



J Electrocardiol. 2010;43:572-6

Case Study

Betty is a 52 YOF admitted for heart failure who develops TdP

PMH: Heart failure with reduced ejection fraction, chronic back pain, hypertension, GERD, generalized anxiety
Current meds: Omeprazole, citalopram, lisinopril, tramadol, bisoprolol

Which of the following accurately describes her risk factors for QT interval prolongation?

A Age, citalopram, hypertension
B Hypertension, omeprazole, tramadol
C Bisoprolol, citalopram, heart failure
D Tramadol, heart failure, female

Which of the following could have decreased the risk of Betty developing TdP?

A Give potassium prophylactically on admission
B Use alternatives to citalopram and tramadol
C Use pantoprazole instead of omeprazole
D Use ranitidine instead of omeprazole

After Discharge: Primary Care Considerations

- Does GERD require a PPI?
- Are alternative PPIs affordable?
- Benefit vs risk of switching/stopping antidepressant?
- Alternatives to tramadol?

KEY TAKEAWAYS

1) **KEY TAKEAWAY**
There are many known and emerging risk factors for drug-induced TdP

2) **KEY TAKEAWAY**
Some drugs and risk factors convey greater risk of TdP than others

3) **KEY TAKEAWAY**
Nearly all instances of drug-induced TdP are associated with at least one other risk factor and the risk can often can be mitigated

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Reducing the Risk of Drug-Induced QT Interval Prolongation and Torsades de Pointes

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Financial Relationships and Disclosures

- No industry relationships or other financial disclosures
- Volunteer (unpaid) member, Advisory Board, QT Drugs list, www.crediblemeds.org

PATIENT CASE

- **Chief complaint**:
  - 65 year-old woman presents to ED with weakness, diminished urine production, and diarrhea
  - Admitted to hospital with:
    - Acute kidney injury
    - Urinary tract infection

Clin Pharmacol Ther 2004;75:242-7.

PATIENT CASE

- **History of Present Illness**:
  - Discharged from hospital 8 days prior to this admission after receiving treatment for osteomyelitis of the left hip
- **Past Medical History**:
  - Hypertension
  - Chronic stable angina
  - Systemic lupus erythematosus
- **Allergies**:
  - Penicillin (reaction not documented)

Clin Pharmacol Ther 2004;75:242-7.

PATIENT CASE

- **Medications Prior to Admission**:
  - Ciprofloxacin 500 mg orally twice daily
  - Vancomycin 1g IV every 8 hours
  - Ranitidine 150 mg orally twice daily
  - Lisinopril 40 mg orally once daily
  - Metoprolol XL 100 mg orally once daily
  - HCTZ 25 mg orally once daily
  - Fexofenadine 60 mg orally twice daily

Clin Pharmacol Ther 2004;75:242-7.

PATIENT CASE

- **Select Laboratory Values on Admission**:
  - Na^{++} = 143 mEq/L
  - K^{+} = 2.9 mEq/L
  - Mg^{++} = 1.4 mg/dL
  - Serum creatinine = 7.9 mg/dL
  - BUN = 34 mg/dL

Clin Pharmacol Ther 2004;75:242-7.

PATIENT CASE

- **Medications Initiated in the Hospital**:
  - Ciprofloxacin and vancomycin discontinued
  - Potassium supplementation
  - Hydroxyzine 200 mg orally twice daily
  - Metoprolol 100 mg orally twice daily
  - Ranitidine 150 mg orally twice daily
  - Clonidine intermittently for hypertensive urgency
  - Hydroxychloroquine 200 mg orally twice daily
  - Levofloxacin 250 mg orally once daily

Clin Pharmacol Ther 2004;75:242-7.

PATIENT CASE

- **On Day #3 of Hospitalization**:
  - ECG in the morning:
    - ❖QTc interval = 605 ms
  - 12:50 pm:
    - ❖Patient found unresponsive
    - ❖Placed on telemetry monitor – **Torsades de pointes**
  - Received MgS04 2g IV:
    - ❖Arrhythmia terminated, patient regained consciousness

Clin Pharmacol Ther 2004;75:242-7.

Which one of the following drugs is the most likely culprit in causing drug-induced torsades de pointes in this patient?

A Clonidine
B Levofloxacin
C Metoprolol
D Ranitidine

PATIENT CASE

- **On Day #3 of Hospitalization**:
  - 2:30 pm
    - ❖Telemetry monitor alarm sounded: **Torsades de pointes**
    - ❖Patient found pulseless
    - ❖TdP terminated spontaneously
    - ❖Patient was intubated and transferred to ICU

Clin Pharmacol Ther 2004;75:242-7.

PATIENT CASE

- **On Day #3 of Hospitalization**:
  - 3:50 pm
    - ❖Telemetry monitor alarm sounded: **Torsades de pointes**
    - ❖Patient found pulseless
    - ❖Patient underwent defibrillation, sinus rhythm restored

Clin Pharmacol Ther 2004;75:242-7.

Which one of the following is therapies is most likely to facilitate termination of TdP in this patient?

A Synchronized direct current cardioversion

B Isoproterenol 2-10 mcg/min continuous IV infusion

C Lidocaine 1-1.5 mg/kg IV, then 3 mg/min IV infusion

D Magnesium sulfate 1-2 g IV over 15 minutes

PATIENT CASE

- **On Day #3 of Hospitalization**:
  - 3:55 pm
    - ❖Telemetry monitor alarm sounded: **Ventricular fibrillation**
    - ❖Patient underwent defibrillation x 3
    - ❖MgSO4 2g IV administered
    - ❖Sinus rhythm restored

Clin Pharmacol Ther 2004;75:242-7.

COULD THIS CASE HAVE BEEN PREVENTED? COULD IT HAVE BEEN PREDICTED?

- **This patient's TdP risk factors:**
  - Female
  - 65 years old
  - Hypokalemia
  - Hypomagnesemia
  - Multiple QT-prolonging drugs
    - ❖ Hydroxychloroquine
    - ❖ Hydroxyzine
    - ❖ Levofloxacin
  - Inadequate dose adjustment of levofloxacin for acute kidney injury

PREDICTIVE ANALYTICS

- Generates predictions using techniques including data mining, modeling, machine learning, and others
- Can be used to develop methods of risk quantification and prediction of QT interval prolongation and/or TdP
- Predictive analytics have also been incorporated into clinical decision support (CDS) tools to alert clinicians regarding patients at increased risk of developing QTc interval prolongation

Pediatr Clin North Am 2016;63:357-366
Pharmacotherapy 2018;38:813-821.

Pro-QTC Score - Mayo Clinic

- Institution-wide computer-based QT alert system was implemented at Mayo Clinic
- System screens all ECGs and alerts clinicians if QTc interval is ≥ 500 ms
- A “pro-QTc” score was developed

Mayo Clin Proc 2013;88:315-325.

Diagnoses/Conditions Included in Mayo Clinic Pro-QTc Risk Score

Acute coronary syndrome	Hypoglycemia	Post-syncope or seizure
Anorexia nervosa/starvation	Intoxication with QT-prolonging drugs	Stroke, SAH, head trauma
Bradycardia (HR < 45 bpm)	Congenital long QT syndrome	Hypokalemia
HFrEF	Pheochromocytoma	Hypomagnesemia
Diabetes mellitus	Kidney dialysis	Hypocalcemia
Female sex	Post-conversion of AF to sinus rhythm	≥ 1 drug from crediblemeds list within ≤ 7 days
Hypertrophic cardiomyopathy	Post-cardiac arrest	

Each factor assigned a score of 1

Mayo Clin Proc 2013;88:315-325.

Mayo Clinic Pro-QTc Risk Score

- 99% of n=470 patients with QTc ≥ 500 ms had ≥ 1 risk factor (excluding female sex)
- In patients with with QTc ≥ 500 ms, mean pro-QTc risk score = 3.1± 16
- Score ≥ 4 predicted mortality
  - Hazard ratio 1.72 (95% CI 1.11-2.66, p< 0.001)
- Components of the risk score significantly associated with death;
  - # of QTc-prolonging medications
  - Electrolyte abnormalities

Mayo Clin Proc 2013;88:315-325.

Circulation
Cardiovascular Quality and Outcomes

American Heart Association®

Development and Validation of a Risk Score to Predict QT Interval Prolongation in Hospitalized Patients

James E. Tisdale, Heather A. Jaynes, Joanna R. Kingery, Noha A. Mourad, Tate N. Trujillo, Brian R. Overholser and Richard J. Kovacs

- **Objective:**
  - Develop and validate a risk score to identify hospitalized patients at highest risk of QT_c interval prolongation

Circ Cardiovasc Qual Outcomes 2013;6:479-487.

Development and Validation of a Risk Score to Predict QTc Interval Prolongation

- Prospective, observational study in n=1200 patient admissions to two 28-bed CCUs over a 1-year period
- Risk score developed in first 900 patients
- Validated in subsequent 300 patients

Circ Cardiovasc Qual Outcomes 2013;6:479-487.

Development and Validation of a Risk Score to Predict QTc Interval Prolongation

Definition of QT Interval Prolongation

- QTc interval ≥ 500 ms at anytime during hospitalization
- Change in QTc interval ≥ 60 ms from value on admission

Circ Cardiovasc Qual Outcomes 2013;6:479-487.

Development and Validation of a Risk Score to Predict QTc Interval Prolongation

Independent Risk Factors for QTc Interval Prolongation

Variable	Odds ratio	p
Age ≥ 68 years	1.3 (1.0-1.9)	0.04
Female sex	1.5 (1.1-2.0)	0.03
Loop diuretic	1.4 (1.0-2.0)	0.007
Serum K^+ ≤ 3.5 mEq/L	2.1 (1.5-2.9)	<0.001
Admitting QTc ≥ 450 ms	2.3 (1.6-3.2)	<0.001
Acute MI	2.4 (1.6-3.9)	<0.001
≥ 2 QTc-prolonging drugs	2.6 (1.9-5.6)	0.02
Sepsis	2.7 (1.5-4.8)	0.002
Heart failure	2.7 (1.6-5.0)	<0.001
One QTc-prolonging drug	2.8 (2.0-4.0)	<0.001

Circ Cardiovasc Qual Outcomes 2013;6:479-487.

Development and Validation of a Risk Score to Predict QTc Interval Prolongation

Calculation of Risk Score for QTc Interval Prolongation

Risk Factor	Points
Age ≥ 68 years	1
Female sex	1
Loop diuretic	1
Serum K+ ≤ 3.5 mEq/L	2
Admitting QTc ≥ 450 ms	2
Acute MI	2
≥ 2 QTc-prolonging drugs	3
Sepsis	3
Heart failure	3
One QTc-prolonging drug	3
Maximum risk score	21

Circ Cardiovasc Qual Outcomes 2013;6:479-487.

Development and Validation of a Risk Score to Predict QTc Interval Prolongation

QTc Interval Risk Score Stratification

Risk score category	Risk score	QTc prolongation in derivation group	QTc prolongation in validation group
Low	< 7	51%	53%
Moderate	7-10	35%	34%
High	≥ 11	14%	13%

ROC AUC (c-statistic) = 0.832

Circ Cardiovasc Qual Outcomes 2013;6:479-487.

Development and Validation of a Risk Score to Predict QTc Interval Prolongation

QTc Interval Risk Score Stratification

Risk category	Sensitivity	Specificity	+ Predictive value	- Predictive value
Moderate	0.67	0.88	0.55	0.88
High	0.74	0.77	0.79	0.76

Circ Cardiovasc Qual Outcomes 2013;6:479-487.

Development and Validation of a Risk Score to Predict QTc Interval Prolongation

- A risk score using easily obtainable clinical risk factors predicts patients at highest risk for QTc interval prolongation during hospitalization
- May be useful for guiding monitoring and treatment decisions

Circ Cardiovasc Qual Outcomes 2013;6:479-487.

RISQ-PATH Score - Belgium

Risk Factor	Points assigned
K+ ≤ 3.5 mEq/L Baseline QTc ≥ 450 ms (males) or 470 ms (females)	6 points each
Age ≥ 65 years Female sex Smoking Ischemic cardiomyopathy Hypertension Arrhythmia Thyroid disturbances Ca^{2+} < 8.6 mg/dL For each “list 1” crediblemeds drug	3 points each
BMI ≥ 30 kg/m^2 Liver failure CRP > 5 mg/L	1 point each
Neurological disorders Diabetes GFR ≤ 30 mL/min For each “list 2” crediblemeds drug	0.5 points each
For each “list 3” crediblemeds drug	0.25 points each
Maximum total	40.5 + sum QT drugs

Int J Clin Pharm 2017;39:424-432.

RISQ-PATH Score - Belgium

Low risk score defined as < 10

Measure	Result
ROC AUC	0.72 (95% CI 0.62-0.81)
Sensitivity	96.2% (78.4-99.8%)
Specificity	32.9% (25.6-41.0%)
Positive predictive value	19.7% (13.4-27.9%)
Negative predictive value	98.0% (88.2-99.9%)

Int J Clin Pharm 2017;39:424-432.

Genetic Variant Risk Score

- Secondary analysis of R, DB, PC crossover trial of 3 QT interval-prolonging drugs with n=15 time-matched QT and plasma drug concentrations
  - Dofetilide
  - Quinidine
  - Ranolazine
  - Placebo
- Genetic analysis of n=22 subjects was performed
- Genetic score comprised n=61 common genetic variants
- Correlated with slope of subject's drug-induced increase in QTc vs drug concentration

Circulation 2017;135:1300-1310.

Genetic Variant Risk Score

- Secondary analysis of R, DB, PC crossover trial of 3 QT interval-prolonging drugs with n=15 time-matched QT and plasma drug concentrations
  - Dofetilide
  - Quinidine
  - Ranolazine
  - Placebo
- Genetic analysis of n=22 subjects was performed
  - n=17 European descent, n=4 African descent, n=1 Asian descent
- Genetic score comprised n=61 common SNPs with previously established effects on QT interval from a large GWAS
- Correlated with slope of subject's drug-induced increase in QTc vs drug concentration

Nat Genet 2014;46:826-836; Circulation 2017;135:1300-1310.

Genetic Variant Risk Score

Subjects of European descent (n=17)

	r (95% CI)	p	r^2
Genetic score vs baseline	0.52 (0.05 to 0.80)	0.03	0.27
Genetic score vs dofetilide QTc slope	0.55 (0.09 to 0.81)	0.02	0.30
Genetic score vs quinidine QTc slope	0.48 (-0.03 to 0.79)	0.06	0.23
Genetic score vs ranolazine slope	0.52 (0.05 to 0.80)	0.03	0.27

Circulation 2017;135:1300-1310.

Genetic Variant Risk Score

Subjects of African descent (n=4)

	r (95% CI)	p	r^2
Genetic score vs baseline	0.97 (0.11 to 1.00)	0.03	0.94
Genetic score vs dofetilide QTc slope	0.97 (0.12 to 1.00)	0.03	0.94
Genetic score vs quinidine QTc slope	0.18 (-0.94 to 0.97)	0.82	0.03
Genetic score vs ranolazine slope	0.55 (-0.87 to 0.99)	0.45	0.30

Circulation 2017;135:1300-1310.

Genetic Variant Risk Score

- Tested risk score in:
  - n=216 patients who had experienced TdP
  - n=771 controls who had not experienced TdP
- Genetic risk score was associated with significantly increased risk of TdP
  - $p=1.3 \times 10^{-7}$
  - $r^2 = 0.12$

Circulation 2017;135:1300-1310.

Incorporation of Predictive Analytics into Clinical Decision Support (CDS) Tools

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Effectiveness of a Clinical Decision Support System for Reducing the Risk of QT Interval Prolongation in Hospitalized Patients

James E. Tisdale, Heather A. Jaynes, Joanna R. Kingery, Brian R. Overholser, Noha A. Mourad, Tate N. Trujillo and Richard J. Kovacs

Circulation Cardiovasc Qual Outcomes 2014;7:381-390.

Incorporation of Predictive Analytics into Clinical Decision Support (CDS) Tools

- A CDS was developed incorporating our validated risk score for QT interval prolongation
- Tested in a pre-post interventional design
- n=3140 consecutive patient admissions to the 2 x 28-bed CCUs at IU Health Methodist Hospital
- Exclusion criteria:
  - Age < 18 years (n=10)
  - ECG rhythm of complete ventricular pacing (n=215)
  - Designation of outpatient in a bed or < 24 hour stay (n=524)
- After applying exclusion criteria, n=2400 patients enrolled

Circulation Cardiovasc Qual Outcomes 2014;7:381-390.

Computer Alert Screen Appearance

Alert text:

Based on the following parameters, this patient is at greater than 80% increased risk of developing QTc prolongation.

NAME: [redacted] RISK SCORE: 12.00

Risk Factor	Result	Points
High risk triggering medication	procainamide	2.00
Concomitant therapy with ≥ 1 higher risk QTc medication	IV amiodarone	5.00
Concomitant therapy with ≥ 1 QTc medication	No Qualifying Orders	0.00
Serum K^+ < 3.5 mEQ/L	4.6 mEQ/L	0.00
Thiazide or loop diuretic active order	No Qualifying Orders	0.00
Serum creatinine	Not applicable	N/A
CrCl < 50 mL/min and active renally eliminated medication	No Active RENAL Medication Orders	0.00
Gender = Female	Male	0.00
Age ≥ 65	62	0.00
Troponin-I > 0.2 ng/mL or diagnosis of acute MI	True	2.00
Diagnosis of Heart Failure	False	0.00
Diagnosis of Sepsis	False	0.00
Current QTc interval > 450 ms	484 ms	3.00

Recommend the following Action Steps based on a **Risk Score** of: 12.00

Score > 11 **High Risk** Evaluate all QTc interval-prolonging meds for possible DC

ADE_SYN_CK_TORSADES_RISK AG1 WP_SYN_TORSADES_HIGH3

Incorporation of Predictive Analytics into Clinical Decision Support (CDS) Tools

Primary Outcome Measures

- Odds of developing QT_c prolongation following intervention
- Odds of receiving a QT prolonging medication in patients at risk for or presenting with QT_c prolongation
- Odds of receiving a non-cardiac QT prolonging medication in patients at risk for or presenting with QT_c prolongation

Circulation Cardiovasc Qual Outcomes 2014;7:381-390.

Incorporation of Predictive Analytics into Clinical Decision Support (CDS) Tools

Results

	Adjusted odds ratio (95% CI)	p
QTc interval > 500 ms or ≥ 60 ms change from admitting value	0.65 (0.56-0.89)	<0.0001
Prescribing of any QTc interval-prolonging drug	0.87 (0.77-1.12)	0.13
Prescribing of any non-cardiac QTc interval-prolonging drug	0.79 (0.63-0.91)	0.03

Circulation Cardiovasc Qual Outcomes 2014;7:381-390.

Incorporation of Predictive Analytics into Clinical Decision Support (CDS) Tools

Limitations

- Conducted in two cardiac care units at one institution – generalizability/external validity?
- Pre-post design – can introduce temporal bias
- Influence of education phase?

Circulation Cardiovasc Qual Outcomes 2014;7:381-390.

Incorporation of Predictive Analytics into Clinical Decision Support (CDS) Tools

Conclusions

- A computerized CDS system incorporating a validated risk score for QT interval prolongation influences the prescribing of QT-prolonging drugs and reduces the risk of QT interval prolongation in hospitalized patients with TdP risk factors

Circulation Cardiovasc Qual Outcomes 2014;7:381-390.

Incorporation of Predictive Analytics into Clinical Decision Support (CDS) Tools

Mayo Clinic CDS Alert

- Notifies clinicians when patient has QTc ≥ 500 ms
- Alert was sent for n=2% of adult patients
  - Resulted in a 13.9% decrease in administration of QTc interval-prolonging medications
- n=5% of pediatric patients had QTc ≥ 500 ms
  - Identified a child with previously undiagnosed congenital LQTS
  - Prescribers changed ~80% of QTc interval-prolonging medications after receiving the alert

Mayo Clin Proc 2013;88:315-325
J Med Syst 2017;41:161
Pediatr Cardiol 2015;36:1350-1356.

Incorporation of Predictive Analytics into Clinical Decision Support (CDS) Tools

Mayo Clinic CDS Alert

- In Emergency Department
  - Alert was activated in 1.2% of patients
  - Identified one patient with previously undiagnosed congenital LQTS
  - Mortality was higher in ED patients identified by the QT alert
    - ❖ 13.0% vs 3.7%, $p<0.001$

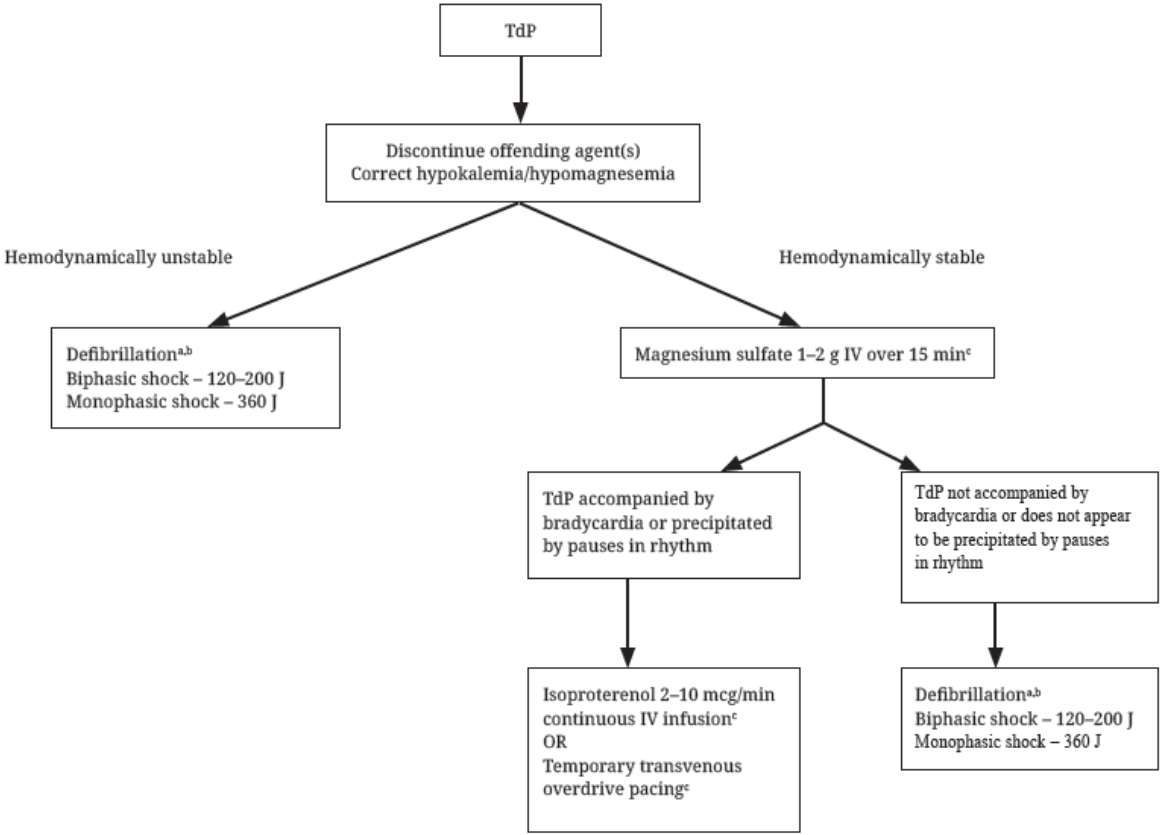
J Emerg Med 2018;54:8-13.

PATIENT CASE

- **Outcome**:
  - Levofloxacin discontinued
  - K^+ and Mg^{2+} replaced aggressively
  - 24 hours later:
    - ❖ QTc = 399 ms
  - No additional episodes of TdP
  - Discharged to home on day 9

Clin Pharmacol Ther 2004;75:242-7.

Management of Torsades de Pointes



Acute Management of Arrhythmias, In: Erstad B, ed. Critical Care Pharmacotherapy. ACCP 2016;1244-1281. Used with permission from the American College of Clinical Pharmacy

Reducing the Risk of Drug-Induced QT Interval Prolongation and Torsades de Pointes

- Know drugs that are associated with QT prolongation and TdP (www.crediblemeds.org)
- Monitor risk factors for QT prolongation and TdP
- Where possible, quantify risk with appropriate risk score
- Where possible – avoid QT-prolonging drugs in patients with risk factors
- Be attentive to drug interactions/dose adjustment for kidney disease where appropriate

Clin Pharmacol Ther 2004;75:242-7.

KEY TAKEAWAYS

1) **KEY TAKEAWAY**
Risk of QTc interval prolongation and torsades de pointes can be quantified with published risk scores, the use of which guide monitoring and treatment decisions in patients taking QTc interval-prolonging drugs

2) **KEY TAKEAWAY**
Drug-induced torsades de pointes should be managed by discontinuing QTc interval-prolonging drugs whenever possible, defibrillation (not synchronized cardioversion) for hemodynamically unstable patients, and administration of intravenous magnesium for hemodynamically stable patients

3) **KEY TAKEAWAY**
Clinical decision support (CDS) tools can be developed to alert clinicians when patients are at risk for QTc interval prolongation, and implementation of CDS alerts have been shown to reduce the risk of QTc interval prolongation

NEW
Limited time only

Chocolate & Crème and Golden Raisin & Crème Torsades

Flaky croissant with French pastry crème