QTc Risk Clinical Decision Support: Risk For Sudden Cardiac Death:
Prolonged QTc and Torsades de Pointes

Thank you for your interest in this educational program.

In our second educational module, we will discuss prolonged QTc intervals and torsades de pointes as risk factors for sudden cardiac death.

Torsades de pointes is extremely rare in the absence of risk factors. An analysis of one-hundred and forty-four (144) published articles, describing two-hundred and forty-nine (249) patients with drug-induced torsade de pointes was published in the early 2000s. At the time, this encompassed every known published case of drug-induced torsades de pointes, and nearly one hundred percent (100%) of these patients had at least one (1) risk factor and nearly three-quarters of these patients had two (2) or more risk factors.

The information emphasizes the fact that torsades de pointes is very uncommon in the absence of risk factors. It's one of the adverse effects that is very dependent on the presence of risk factors.

RISK FACTORS FOR TORSADES DE POINTES ILLUSTRATED VIA A CASE STUDY

This module utilizes a case study to illustrate some risk factors of torsades de pointes.

PATIENT CASE - DAY 1

This case study is based on a drug-induced torsades de pointes case published fifteen years ago. In this case, the patient was a sixty-five year old female, who presented with weakness, diminished urine production and diarrhea. She was admitted with the diagnoses of acute kidney injury and a urinary tract infection.

Her history of present illness is that she was discharged from the hospital eight days prior to this presentation after being treated for osteomyelitis of the left hip, at which time she was treated with vancomycin and ciprofloxacin. Her past medical history included hypertension, coronary artery disease, systemic lupus erythematosus, and she had an allergy to penicillin which is pertinent to this case.

PATIENT CASE - LABS ON ADMISSION

Selected laboratory values on admission showed her serum sodium concentration was normal, but she was markedly hypokalemic with serum potassium of 2.9, her magnesium was borderline hypomagnesemic at 1.4. As mentioned before she has an acute kidney injury as manifested by serum creatinine seven point nine (7.9) and a BUN of thirty four.

PATIENT CASE - MEDICATIONS INITIATED ON ADMISSION

Medications on admission included intravenous potassium chloride to attempt to correct the hypokalemia. She was administered hydroxyzine 200 mg orally twice daily, metoprolol 100 mg orally twice daily, 150 mg of ranitidine orally twice daily, 200 mg of hydroxychloroquine orally twice daily, and 250 mg of levofloxacin orally once daily for the management of the UTI.

PATIENT CASE - DAY 3

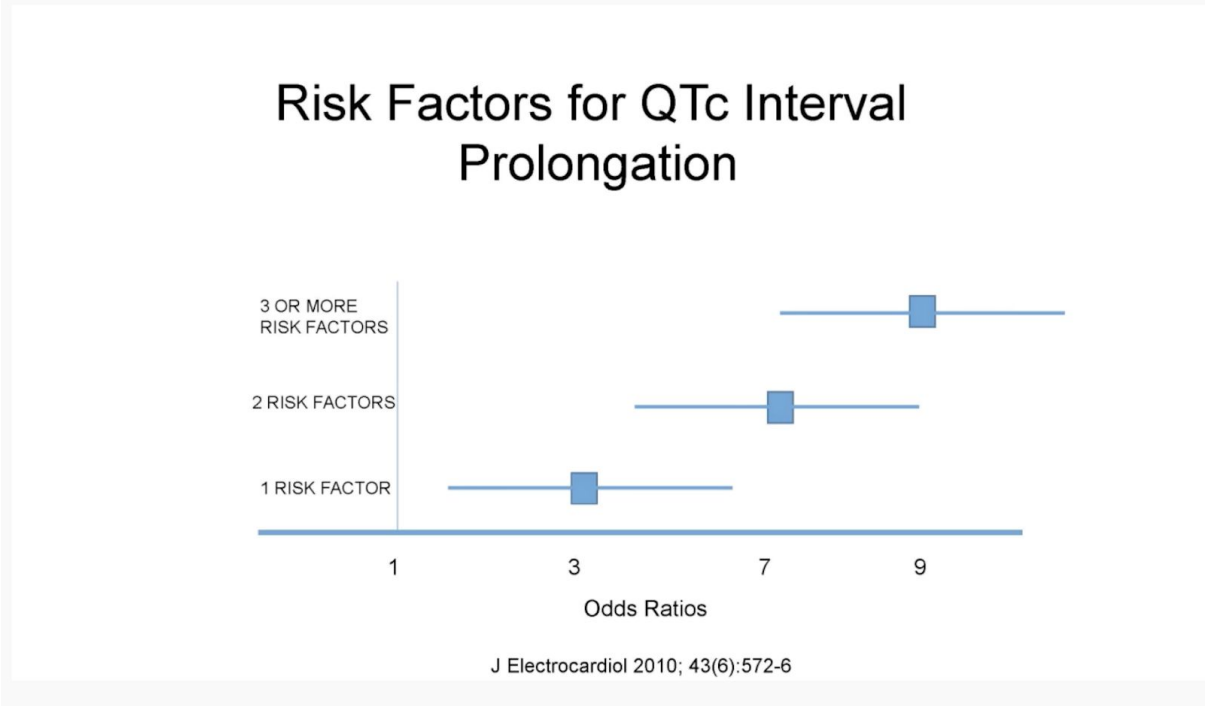
Everything proceeded as expected until an electrocardiogram (ECG) on the morning of day three of hospitalization revealed a QTc interval of 605 ms which is markedly prolonged based on normal measurements in the range of 360-440 ms. At 12:50 pm the patient was found unresponsive and placed on a telemetry monitor — a continuous ECG monitor — which revealed the ECG (shown above) which showed twisting of the points or torsades de pointes.

To manage the torsades de pointes, the patient received two grams of magnesium sulfate intravenously. The arrhythmia terminated and the patient regained consciousness. She was then placed on telemetry and had recurrent episodes that required defibrillation. Fortunately defibrillation was successful at resuscitating the patient and she was discharged after a prolonged hospital stay.

RISK FACTORS FOR DRUG-INDUCED PROLONGED QTc

As mentioned previously, risk factors are very important for development of QT prolongation and torsade de pointes. For this discussion, we will focus on the risk factors identified by Tisdale: 1) an admitting corrected QT interval (QTc) of more than four hundred and fifty (450) milliseconds. 2) Women are at higher risk — female sex is an independent risk factor for QTc and torsade de pointes. 3) Older age generally defined as older than 65 years of age or 68 years of age depending on the study. We used an age over 68 years. 4) Electrolyte abnormalities — particularly hypokalemia and hypomagnesemia 5) heart failure with reduced ejection fraction 6) being on a loop diuretic is an independent risk factor 7) acute myocardial infarction 8) being on at least one QT-interval -prolonging medication, and additionally 9) being on two (2) or more QT prolonging medications.

RISK FACTORS FOR QTc INTERVAL PROLONGATION AND TORSADES DE POINTES



Narrator: This slide shows data from a paper published in the *Journal of Electrocardiology* in 2010. This shows that the presence of additional risk factors increases the odds for developing QT-prolongation. For a patient who had one risk factor the odds for QT prolongation was about 3, the odds ratio for patient with 2 risk factors, the odds ratio for developing QTc prolongation increased to a little over 7, and for a patient with 3 or more risk factors for QTc prolongation, the odds ratio for QT prolongation increased to about 9. This data shows that stacking risk factors on top of one another markedly increases the odds for developing QTc interval prolongation.

WHAT FACTORS DID THIS PATIENT CASE HAVE THAT CONTRIBUTED TO TORSADES DE POINTES?

What risk factors did the patient in this case study display that contributed to the development of torsades de pointes:

1) She was 65 years old — not over 68 — as mentioned, some of the risk factor studies show over 65 years of age to be a risk factor.

2) She was female, which increases risk.

3) She has some pertinent abnormal laboratory findings, specifically electrolyte abnormality, particularly the fact that she was markedly hypokalemic and was at least borderline hypomagnesemic.

Additionally, she was taking the QT-prolonging medication levofloxacin. The dosing prescribed for her was 250 milligrams every 24 hours, and so there
was an attempt to adjust the dose for her acute kidney injury. However the dose was not adequately adjusted for the degree of her acute kidney injury, for her serum creatinine 7.9 and resulting very low creatinine-clearance, the dose actually for this patient should have been 250 milligrams every 48 hours. So there was a dose adjustment made, but the dose adjustment was inadequate for her degree of acute kidney injury.

CIRCULATION CARDIOVASCULAR QUALITY AND OUTCOMES

QTc CDS
CLINICAL DECISION SUPPORT

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 QTc interval prolongation

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

Studies were conducted a few years ago, published in the journal **Circulation: Cardiovascular Quality and Outcomes** with the objective of developing and validating a risk score to identify hospitalized patients who are at the highest risk of QTc interval prolongation.

RISK FACTORS FOR QTc INTERVAL PROLONGATION

QTc CDS
CLINICAL DECISION SUPPORT

Risk Factors for QTc Interval Prolongation

Variable	Odds Ratio (95% CI)	Points
One QTc – prolonging drug	2.8 (2.0-4.0)	3
Heart failure	2.7 (1.6-5.0)	3
Sepsis	2.7 (1.5-4.8)	3
≥2 QTc – prolonging drugs	2.6 (1.9-5.6)	3
Acute MI	2.4 (1.6-3.9)	2
Admission QTc ≥450 ms	2.3 (1.6-3.2)	2
Serum K^+ ≤3.5 mEq/L	2.1 (1.5-2.9)	2
Loop diuretic	1.4 (1.0-2.0)	1
Female sex	1.5 (1.1-2.0)	1
Age ≥68 years	1.3 (1.0-1.9)	1

Moderate Risk: Score: 7-11

High Risk: Score >11

Maximum Risk Score: 21

CI = confidence Interval; K^+ = potassium; and MI = myocardial infarction

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

The study presented here found a number of independent risk factors for QTc interval prolongation — some of which have been reported, some of which have not — and determined odds ratios for each independent risk factor. Points were then assigned based on the odds ratios. Displayed here, they are listed in descending order of odds ratio. The maximum risk score is 21. The threshold values for different levels of risk for QT interval prolongation are presented here and will be covered again in Module 3.

To complete this module, please continue to the knowledge test section of this module's webpage for a short quiz that will test your knowledge of the presented information before advancing to Module Three:

MODULE TWO KNOWLEDGE TEST

Thank you for your time and for your interest in this educational program
"QTc Risk Clinical Decision Support: A Primer For Healthcare Providers"