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Patient Safety Tip of the Week

February 16, 2021

New Methods for QTc Monitoring

Torsade de pointes (TdP) is a form of ventricular tachycardia, often fatal, in which the QRS complexes become "twisted" (changing in amplitude and morphology) but is best known for its occurrence in patients with long QT intervals. (See our earlier columns on the several methods of measuring the QT interval and criteria for QTc prolongation). Though cases of the long QT interval syndrome (LQTS) may be congenital, many are acquired and due to a variety of drugs that we prescribe. The syndrome is more common in females and many have a genetic predisposition. Underlying heart disease, electrolyte abnormalities (eg. hypokalemia, hypomagnesemia, hypocalcemia), renal or hepatic impairment, and bradycardia may be precipitating factors. This list of medications that may prolong the QT interval is substantial and continues to grow. For a full list of drugs that commonly cause prolongation of the QT interval and may lead to Torsade de Pointes, go to the CredibleMeds® website. That extremely valuable site provides frequent updates when new information becomes available about drugs that may prolong the QT interval.

Particularly when we start patients on a medication known to increase the QTc, we would like to be able to monitor trends in the QTc. But that has been impractical and costly in most situations. The need for a convenient and inexpensive way to monitor the QTc was highlighted when some began hyping chloroquine or hydroxychloroquine plus azithromycin for COVID-19 (see our April 7, 2020 Patient Safety Tip of the Week "Patient Safety Tidbits for the COVID-19 Pandemic").

Researchers at the Mayo Clinic (Giudicessi 2021) have now developed an artificial intelligence (AI)-enabled 12-lead electrocardiogram (ECG) algorithm to determine the QTc, and then prospectively test this algorithm on tracings acquired from a smartphone-enabled mobile ECG device.

They used data from over 1.6 million 12-lead ECG's to derive and validate a deep neural network (DNN) to predict the QTc interval. They then prospectively tested the ability of this DNN to detect clinically relevant QTc prolongation (e.g. QTc ≥ 500 ms) on 686 genetic heart disease patients (50% with LQTS) with QTc values obtained from both a 12-lead ECG and a prototype mobile ECG device equivalent to a well-known commercially-available mobile ECG device (the AliveCor KardiaMobile 6L). When

applied to mECG tracings, the DNN's ability to detect a QTc value ≥ 500 ms yielded an area under the curve, sensitivity, and specificity of 0.97, 80.0%, and 94.4%, respectively. The negative predictive value was 99.2% for detecting a QTc value ≥ 500 ms.

Giudicessi and colleagues note that studies from their institution and others have demonstrated that ~1% of all individuals who receive an inpatient or outpatient 12-lead ECG have a QTc ≥ 500 ms and that when this QTc threshold is met or exceeded, there is a 2- to 4-fold increased risk of death. They note that the identification of substantial QTc prolongation provides an important opportunity to identify vulnerable, at-risk hosts and make potentially lifesaving change(s) (i.e. initiation of β-blockers, discontinuation of QTc-prolonging medications, or correction of hypokalemia and hypomagnesemia) needed to mitigate the risk of TdP and sudden cardiac death.

Giudicessi et al. discuss the potential applications of an AI-enabled mobile ECG device approach to QTc assessment and monitoring. That could include universal screening for the early detection of congenital LQTS, plus monitoring patient prescribed QTc prolonging drugs.

Our June 25, 2019 Patient Safety Tip of the Week "Found Dead in a Bed – Part 2" noted many of the QTc prolonging drugs commonly prescribed and also mentioned the importance of **combinations** of such drugs.

While the Giudicessi study focused on specific QTc intervals, don't forget that trends in the QTc interval may also be important. In our June 10, 2014 Patient Safety Tip of the Week "Another Clinical Decision Support Tool to Avoid Torsade de Pointes" we discussed a study by Tisdale et al. (Tisdale 2014) which demonstrated that use of CDSS (clinical decision support systems) and computerized alerts can reduce the risk of QT interval prolongation. Their system would trigger an alert when the QTc interval was >500 ms or there was an increase in QTc of ≥60 ms from baseline. It would be important to see how the metrics of the Giudicessi tool stack up when evaluating **change in QTc from baseline**.

Quite frankly, we see this new tool being **even more valuable in the inpatient sett**ing. There are a number of reasons why this syndrome is more likely to both occur and result in death in hospitalized patients. So, for those patients not being monitored in ICU settings or via remote monitoring, wearing a watch or wearable device capable of trending the QTc interval in real time could help identify patients at risk for Torsade. Hospitalized patients have a whole host of other factors that may help precipitate malignant arrhythmias in vulnerable patients. They tend to have underlying heart disease, electrolyte abnormalities (eg. hypokalemia, hypomagnesemia, hypocalcemia), COPD, renal or hepatic impairment, and bradycardia, all of which may be precipitating factors. More importantly, hospitalized patients may have the sorts of conditions for which we prescribe the drugs that are primarily responsible for prolonging the QT interval (eg. haloperidol, antiarrhythmic agents, etc.). And many of those drugs are given intravenously and in high doses in the hospital as compared to the outpatient arena. Rapid

intravenous infusion of such drugs may be more likely to precipitate TdP than slow infusion.

And think of the application of this tool in patients prescribed psychotropic medications. A whole host of medications commonly prescribed for psychiatric disorders may prolong the QT interval. The new Mayo tool could provide a convenient, inexpensive way to monitor the QTc on either outpatients or those inpatients on behavioral health units who are prescribed such drugs.

This work by Giudicessi and colleagues at the Mayo Clinic may be a real game changer! Mobile ECG devices such as the AliveCor KardiaMobile 6L are relatively inexpensive and easy to use. And, as the quality of ECG tracings from smartwatches has improved, we anticipate the smartwatch may ultimately be a most valuable tool for monitoring QTc intervals in at-risk patients.

Artificial intelligence (AI) and neural networks are being used with increasing frequency in medicine. The same Mayo Clinic researchers also recently published a study (Bos 2021) in which AI-ECG was found to distinguish patients with electrocardiographically "concealed" LQTS from those discharged without a diagnosis of LQTS. About 40% of patients with genetically confirmed LQTS have a normal corrected QT (QTc) at rest. The neural network they developed provided a nearly 80% accurate pregenetic test anticipation of LQTS. The authors suggest this model may aid in the detection of LQTS in patients presenting to an arrhythmia clinic and, with validation, may be the stepping stone to similar tools to be developed for use in the general population.

We refer you back to our June 25, 2019 Patient Safety Tip of the Week "Found Dead in a Bed – Part 2" and our other columns on torsade (listed below) to see what your hospital or healthcare organization should be doing to reduce the risk you'll find a patient "dead in a bed" from torsade de pointes.

Some of our prior columns on QT interval prolongation and Torsade de Pointes:

June 29, 2010 "Torsade de Pointes: Are Your Patients At Risk?"
February 5, 2013 "Antidepressants and QT Interval Prolongation"
April 9, 2013 "Mayo Clinic System Alerts for QT Interval Prolongation"
June 10, 2014 "Another Clinical Decision Support Tool to Avoid Torsade de Pointes"
April 2015 "Anesthesia and QTc Prolongation"
October 10, 2017 "More on Torsade de Pointes"
June 25, 2019 "Found Dead in a Bed – Part 2"
April 7, 2020 "Patient Safety Tidbits for the COVID-19 Pandemic"

References:

CredibleMeds® website
https://crediblemeds.org/

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https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.050231

Tisdale JE, Jaynes HA, Kingery J, et al. Effectiveness of a Clinical Decision Support System for Reducing the Risk of QT Interval Prolongation in Hospitalized Patients. Circulation: Cardiovascular Quality and Outcomes 2014; 7(3): 381-390 Published online before print May 6, 2014
https://www.ahajournals.org/doi/full/10.1161/CIRCOUTCOMES.113.000651

Bos JM, Attia ZI, Albert DE, Noseworthy PA, Friedman PA, Ackerman MJ. Use of Artificial Intelligence and Deep Neural Networks in Evaluation of Patients With Electrocardiographically Concealed Long QT Syndrome From the Surface 12-Lead Electrocardiogram. JAMA Cardiol 2021; Published online February 10, 2021
https://jamanetwork.com/journals/jamacardiology/fullarticle/2776241

http://www.patientsafetysolutions.com/

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