Available online at www.sciencedirect.com

ScienceDirect

Journal of Electrocardiology xx (2017) xxx – xxx

JOURNAL OF Electrocardiology

www.jecgonline.com

Hypokalemia in women and methadone therapy are the strongest non-cardiologic factors associated with QT prolongation in an emergency department setting

Keith A. Marill, MD, MS,* Emily S. Miller, MD

Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Abstract

Background: Our primary objective was to determine the adjusted quantitative associations of clinical predictors with QT prolongation, a defining cause of Torsades de Pointes (TdP).

Methods: A retrospective cohort study was performed on consecutive emergency department patients identified by ECG acquisition date, and heart rate corrected QT (QTc) and QRS durations. QTc was modeled as a function of clinical predictors with multiple linear regression.

Results: 1010 patients were included. The strongest predictors of QTc and their coefficients were: antidysrhythmic (26.1 ms, 95% CI 15.6–36.6) and methadone (43.6 ms, 95% CI 28.1–59.2) therapies, and genetic long QT syndrome diagnosis (32.6 ms, 95% CI -4.7-70.0). The association of QTc with serum potassium was approximated by a two piecewise linear function that differed by sex. For potassium below 3.9 mmol/L, QTc increased by 43.0 ms (95% CI 26.2–59.7) and 29.5 ms (95% CI 19.1–40.0) for every 1 mmol/L decrease in potassium in women and men, respectively. TdP occurred in only 4/686 (0.6%) of patients with QTc $\geq$ 500 and QRS < 120, but mortality during the visit including hospitalization was 8.0%.

Conclusions: QTc duration is highly sensitive to hypokalemia, particularly in women. Methadone prolongs QTc remarkably compared to other non-cardiologic medicines. QTc > 500 with normal QRS often signifies profound illness and substantial mortality risk, though not necessarily imminent TdP.

Keywords: Long QT syndrome; Hypokalemia; Methadone; Torsades de pointes; Cohort studies

Introduction

A host of factors may modulate and prolong the electrocardiographic QT interval increasing the risk of Torsades de Pointes (TdP), a life-threatening ventricular tachydysrhythmia [1–3]. These include: genetics [4], electrolytes [5,6], pharmacologic and toxicologic agents [7], myocardial infarction (MI) [8] and cardiomyopathy, intracranial hemorrhage (ICH) [9] or cerebrovascular accident (CVA) [10], and diurnal variation [11,12].

Though imperfect, Bazett's correction formula is commonly used to adjust for QT interval heart rate dependence [13,14]. The individual unadjusted quantitative contributions of some other factors to QT prolongation including serum potassium [5,15], calcium [6], and treatment with sotalol [16] or psychotropics [17], have been described in specific subpopulations. These estimates may poorly approximate the true associations in a general patient population.

The primary goal of this study was to determine the quantitative relationships between the measured QTc interval and the major known and suspected factors associated with QT duration in all emergency department (ED) patients using a multivariate model. This information can be used to anticipate when dangerous QT prolongation may occur and to suggest the most important factors to treat it and prevent life-threatening TdP. Secondary goals were to determine the prevalence of TdP and mortality during the hospital visit.

Methods

Study design

A single center retrospective cohort study of ED patients who had an ECG was performed after Partners Healthcare institutional review board approval with waiver of informed consent.

* Corresponding author at: MGH, Dept. Emergency Medicine, Zero Emerson Place, Suite 3B, Boston, MA 02114.

E-mail address: kmarill@partners.org

http://dx.doi.org/10.1016/j.jelectrocard.2017.02.001

0022-0736/

Study setting and population

The setting was a 900 bed urban hospital with annual ED census of 100,000. We studied ED patients because the ED visit is a clinical care event where concentrated and contemporaneous evaluation and testing are performed, often before initiation of confounding therapies.

The study was designed with an intention to include two groups of patients: those with QTc greater or less than 500 ms. Upon collecting cases with QTc > 500 ms, it became clear that many had QTc > 500 ms due to QRS > 120 ms. The cases of greatest interest were those with QTc prolongation not due to delayed depolarization. Therefore, a third group was added after initiation of the study to make three (Fig. 1): 1) ECG with QTc < 500 ms 2) ECG with QTc ≥ 500 ms, 3) ECG with QTc ≥ 500 ms and QRS < 120 ms. For comparison in Table 1, patients in the second group with QRS < 120 ms were moved to the third group to provide three mutually exclusive groups. A 500 ms threshold was chosen to yield a sample enriched with QTc substantially above normal with increased TdP risk.

Study protocol

We used a written study protocol, and data collection manual and instrument to guide data abstraction. One investigator who was not blinded to the study objectives inspected all ECG's and collected data from all included cases. One hundred of the first 720 cases were randomly selected for data abstraction reliability analysis. A second investigator blinded to the study goals abstracted data for these cases. Both investigators are practicing board-certified emergency physicians.

We identified ECG's using the hospital MUSE ECG system (GE Healthcare, Milwaukee) based on ED location, date, and QTc and QRS intervals. The first satisfactory ECG obtained for each ED visit was included. If the ECG was noisy obscuring the relevant onset or offsets, incomplete with some leads missing, or rapid with overlap of the terminal T wave and the next cycle P or QRS waves, then the next ECG obtained during the same ED visit was assessed. If there was no satisfactory ECG, then the case was excluded (Fig. 1). Only the first visit with a satisfactory ECG was included for patients with multiple ED visits.

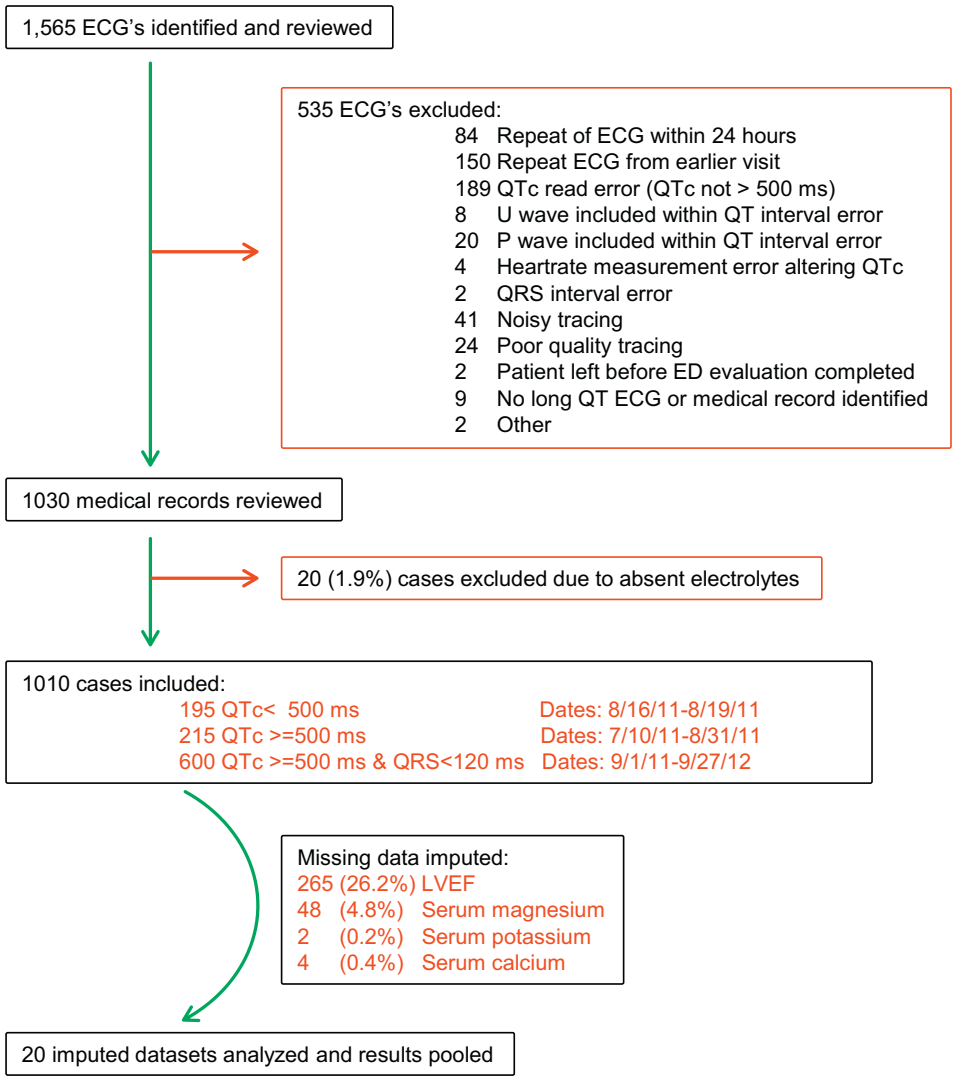

Fig. 1. Flowchart of recruitment, exclusions, inclusions, and missing data.