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Journal of Electrocardiology xx (2017) xxx – xxx

JOURNAL OF Electrocardiology

www.jecgonline.com

Clinical research

The impact of fever on corrected QT interval

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Abstract

Aims: We were interested in the impact of fever on the QT interval as information on this subject is limited.
Methods: We performed a retrospective, single centre study over a two year period, ending December 31st, 2013. Participants were identified using an electronic chart review of emergency department records linked to an ECG data base. Study subjects were drawn from patients presenting with fever to an academic emergency department in Canada. Our study identified febrile (T > 38.0 °C) patients aged >18 years presenting to our centre. Included participants must have had an ED based ECG at the time of presentation with fever and a comparison ECG performed within 30 days and without fever. Actively paced patients were excluded. QT values were corrected using Bazett's, Fridericia's and The Framingham Formula. QT values for febrile and afebrile cohorts were compared using Related-Samples Wilcoxon Signed Rank Test.
Results: 181 patients satisfied our inclusion/exclusion criteria, 54.1% were female and mean age was 68.9 years old. Mean duration between febrile and afebrile ECGs was 6.1 days. The median corrected QT interval (QTc) was significantly shorter in patients during their febrile presentation, as compared to their afebrile presentation when correcting for QT using both Framingham [QTc = 466.1 ms (445.8–499.5) vs. 507.6 (476.0–539.0); $p < 0.001$] and Fridericia's formula [QTc = 388.7 ms, (371.5–407.5) vs. 406.7 ms, (386.1–434.4); $p < 0.001$]. This difference was independent of gender.
Conclusion: We found fever to shorten the QTc independently of sex in a general emergency department population.

Keywords: Fever; QT interval; Electrophysiology; Electrocardiography

Introduction

The QT interval is clinically of great importance as both prolonged and expedited repolarizations have been associated with development of cardiac arrhythmias and sudden cardiac death [1–3]. Interestingly, a number of small studies suggest that fever may function as a QT modulator [4–7]. Given the commonality of fever as a presentation to emergency departments (ED) worldwide, we feel that this relationship warrants further exploration [8]. While the present literature suggests that fever shortens the QT interval in healthy patients, it conversely shows that those with congenital QT abnormalities are susceptible to potentially life threatening fever-induced QT abnormalities and dysrhythmia [1–3,5–7,9–11]. Should a relationship exist between fever and the QT interval, how it influences patients without congenital defects is of chief interest. We thus sought to determine the impact of fever on the QT interval in the general population. Should a relationship exist, better understanding may refine our ability to understand QT interval physiology and its associated derangements.

Methods

We performed a retrospective, single center study spanning a two year period, ending December 31st, 2013. Recruitment was based out of an academic ED setting in Kingston, Canada affiliated with Queen's University. Patient information was retrieved from an ED electronic medical record. Study inclusion criteria were: age ≥ 18 years old, temperature ≥ 38.0 °C, ECG done within 30 min of febrile ED presentation, and a comparator ECG without fever available within 30 days. Study exclusion criteria were: active pacing, prior enrollment in our study, ambiguous temperature measurements, deceased with inadequate records, and afebrile at time of initial ECG based on an additional temperature measurement identified on further chart review.

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http://dx.doi.org/10.1016/j.jelectrocard.2017.04.006
0022-0736/

This study made use of an opportunity to link our institution's MUSE ECG database with an electronic ED medical record. Our sample size was predicated by both time constraints and availability of participants meeting inclusion/exclusion criteria. Following retrieval of patient information, data were immediately de-identified and henceforth referred to only by study number.

QT interval measurement was based on automated ECG interpretation. This value was screened to ensure accuracy using digital calipers (ICONICO, USA), measuring the distance from the beginning of the Q wave to the end of the T wave in milliseconds in leads II, V5 or V6. This method of QTc measurement is in accordance with 2009 AHA/ACCF/HRS guidelines [12]. If caliper measurements were different from those reported on the ECG print-out (>20 ms difference), caliper measurements were used. The longest recorded QT interval was used. QT interval assessment was verified with electrophysiology staff (AB). For patients with more than one comparator ECG collected within 30 days of their febrile presentation, the most recent ECG was used.

QT intervals were corrected to account for the confounding influence heart rate has on the QT interval. We corrected the QT interval using Bazett's ($QTc = QT/\sqrt{RR}$), Fridericia's ($QTc = QT/\sqrt[3]{RR}$), and The Framingham Formula ($QTc = QT + 0.154(1\text{-}RR)$), where RR is the interval in seconds from one QRS complex to the next [13–15]. Following correction, data were imported into SPSS for statistical analysis. Shapiro–Wilk test was used to assess for normality of data; given non-normal distributions, related-samples Wilcoxon Signed Rank test was used for comparisons between febrile and afebrile groups.

This study received approval from the Queen's University Health Sciences Ethics Review Board.

Results

Between January 1st, 2012 and December 31st, 2013, 2018 patients presented to our center's emergency departments with a temperature ≥ 38.0 °C. After checking inclusion and exclusion criteria, 181 patients were included in the study (Fig. 1).

Patient demographics can be found in Table 1. Heart rates recorded at the time of patients' comparator ECGs were significantly lower than those documented during febrile ECGs (90.1 vs. 108.7; $p < 0.001$). Mean time between temperature measurement and 'febrile' ECG was 24.4 min; and mean duration between 'febrile' and 'alternate' ECGs was 6.1 days. ECGs recorded both before and after the febrile ECG were used as comparators so long as they had occurred during an afebrile state within 30 days. The majority of these ECGS occurred after the febrile incident (147/181, 81.2%). There was no significant difference in the amount of QTc change observed for QT, QTc Bazett's, QTc Fridericia's or QTc Framingham based on whether the comparator ECG was collected prior to or after the febrile episode ($p = 0.98, 0.94, 0.99, 0.93$). Of the 147 patients with comparator ECGs collected after the febrile incident, 26 were repeat presentations to the emergency department and 121 were collected during the patients' course in hospital.

The etiology of patients' presenting fever was predominately infectious (69.6%), with community acquired pneumonia being the most frequent cause (24.3%). A total of 5 and 0 patients were identified to be in atrial fibrillation at the time of their febrile and comparator ECGs (2.8 and 0% respectively).

There were a total of 22 patients with near equivalent heart rates during their febrile and comparator ECGs (within 5 bpm). The mean differences in QT, QTc (Bazett's), QTc (Fridericia's) and QTc (Framingham) in this sub-group were −5.7, −5.4, −5.5 and −4.8 ms, respectively.

Shapiro–Wilk tests of normality found QTc data to be non-normally distributed under febrile and afebrile conditions, after correction with Bazett's, Fridericia's or The Framingham Formula ($p < 0.001$). Related-samples Wilcoxon Signed Rank Test was thus used for comparisons between QTc under febrile and afebrile conditions, regardless of correction formula. Table 2 describes the differences in median QTc between febrile and afebrile conditions in either gender for Bazett's, Fridericia's and Framingham correction formulas.

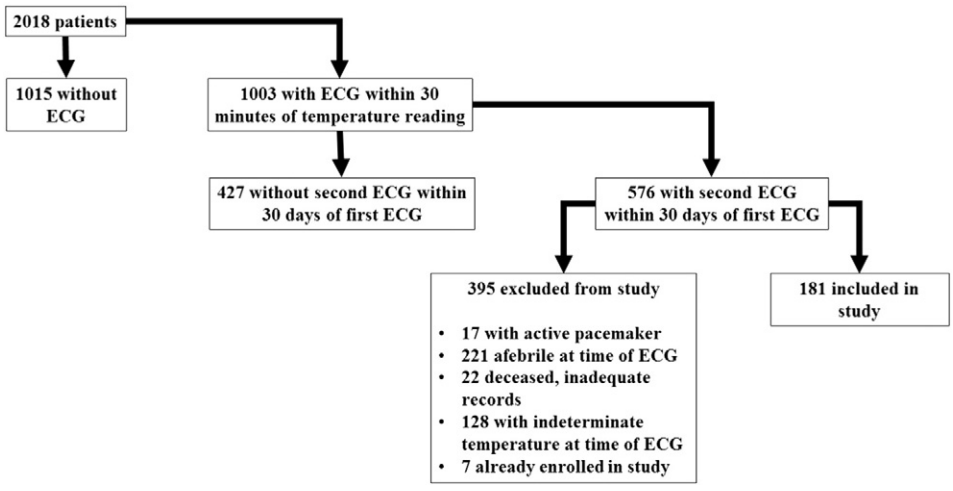

Fig. 1. Flowchart of study recruitment.