

Prevalence of Prolonged QTc Interval in Patients Discharged Home Directly from the Emergency Department

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ABSTRACT

Background: Long QT syndrome (LQTS) is the prolongation of the QT interval, a surrogate measure of the ventricular action potential on the electrocardiogram (ECG). LQTS may lead to tachydysrhythmias resulting in death. Studies have shown mortality may be as high as 20% within the first year among untreated symptomatic patients. Symptoms include syncope, seizures or palpitations; however, LQTS may be asymptomatic. It is most often associated with the administration of QT-prolonging medications, especially in intensive care unit patients. Few studies have examined the prevalence among those discharged from the emergency department (ED).

Aim: The aim of this study was to observe the prevalence of LQTS among ED patients discharged from a community hospital.

Methods: A retrospective review of sequential ECGs from an electronic health record during the study period was completed. Variables examined were sex, age, heart rate, average QRS interval, and QTc interval according to the Bazett's formula. Patients were excluded if they had a wide QRS complex such as a bundle branch block or paced rhythm, atrial flutter or fibrillation, or supraventricular tachycardia.

Results: Of the 1693 patients examined, 939 patients qualified and 151 (16%) had a prolonged QTc interval.

Conclusion: With nearly two in ten patients discharged with LQTS, judicious use of QT-prolonged medications is advised. More long-term follow-up studies of these patients may also yield interesting insights into the prevalence of cardiac morbidities associated with LQTS.

Keywords

Prolonged QT, Long QT syndrome, Sudden cardiac death.

Introduction

Long QT syndrome (LQTS) describes the prolongation of the QT interval, which spans from the start of ventricular depolarization at the beginning of the QRS complex to ventricular repolarization at the end of the T wave. This interval therefore serves as a surrogate measure of the ventricular action potential on the electrocardiogram (ECG). Lengthening of the ventricular action potential is associated with ventricular tachydysrhythmias such as Torsades de pointes (TdP) which can progress to ventricular

fibrillation, and eventually sudden cardiac death (SCD).

Studies have shown mortality can be as high as 20% within the first year among untreated symptomatic patients [1]. The primary symptoms among patients with LQTS include syncope, seizures or palpitations typically elicited during a period of physical exertion or emotional stress [2].

However, the development of SCD may not necessarily be heralded by any symptoms. It is therefore imperative to obtain a thorough history of syncopal episodes as well as family history of similar presentations including congenital deafness, which is associated

with Jervell and Lange-Nielson Syndrome, an inherited variant of LQTS associated with mortality as high as 50% [3]. These considerations have been emphasized by Schwartz and colleagues in their long QT syndrome diagnostic criteria [4].

The etiology of a prolonged QTc interval can be congenital, acquired, or both. While at least 17 genes of have been implicated, the pathophysiology among patients with congenital LQTS is that of cardiac ion channel derangement mediated by gene mutations. The most common involve loss-of-function mutations of potassium channels and gain-of-function mutations of sodium channels resulting in prolongation of action potential duration [5]. Delayed repolarization leads to the development of early afterdepolarizations which serves as a trigger for ventricular tachyarrhythmias. Acquired LQTS, on the other hand, is commonly caused by medications which interact with the potassium channel, most notably the hERG channel, such as antiarrhythmics, antimicrobials, antihistamines, antiemetics, antidepressants, and psychotropics. These medications interact with the delayed rectifier potassium channel causing a blockade of the outward IKr current which slows repolarization leading to delayed repolarizations [6]. Other precipitating factors for acquired LQTS include electrolyte abnormalities such as hypokalemia, hypomagnesemia or hypocalcemia, bradycardia, drug overdose and structural heart disease such as heart failure or myocardial infarction [7].

Various studies have demonstrated a high prevalence of acquired LQTS among critically ill patients in the intensive care unit due to a combination of metabolic abnormalities as well as administration of QT-prolonging medications; of note, it is difficult to determine whether these patients may also have underlying silent congenital LQTS which may be unmasked by acute illness [8,9]. However, few studies have been performed on the prevalence of LQTS among patients seen in the emergency department (ED); even fewer studies have evaluated the prevalence of LQTS among those discharged from the ED [2,10,11].

Emergency department patients represent a particularly vulnerable population given their acute illness and co-morbidities that hamper homeostatic mechanisms. In addition, this population is commonly administered QT-prolonging medications for symptom control (e.g., ondansetron, loperamide, and furosemide). Early recognition and diagnosis do not only prompt closer monitoring or treatment, but also prevent the inadvertent use of QT-prolonging medications that may lead to SCD.

While preliminary studies appear to suggest no statistical significance in 30-day mortality when comparing non-LQTS and LQTS patients, they appropriately acknowledged that with only 40 deaths the study was underpowered to extrapolate any mortality difference [2]. Due to the severe and real clinical implications of undiagnosed LQTS which can result in SCD and lost-to-follow up patient scenarios following discharge, the aim of this study was to observe the prevalence of LQTS among patients discharged from the ED in a busy community hospital.

Methods

Study Design

This is a single-center, observational, cross-sectional study with retrospectively collected data from adult patients consecutively seen in the ED. The study included patients who received an ECG and were subsequently discharged home from the ED. Every ECG was reviewed through the hospital Electronic Health Record. ECGs were excluded from the analysis if there was a wide QRS complex such as in bundle branch block or paced rhythm, atrial flutter or fibrillation, or supraventricular tachycardia.

All ECG intervals were automatically generated by Mortara Instruments (Milwaukee, WI) Model ELI-380 ECG machines. Variables of interest that were recorded include: sex, age, heart rate, QRS interval, and QTc as measured by the Bazett's formula ($QTc = QT / \sqrt{RR}$). Prolonged QTc was defined as greater than 450 ms in men and 460 ms in women [10,12,13]. This project was approved as an exempt study by the hospital research committee.

Data Analysis

Frequencies and averages were computed using SPSS Version 22 (International Business Machines corp. [IBM]) including the means (maximum, minimum, and average). Frequency (percentages) was calculated to report prevalence.

Results

This retrospective observational study included 1693 consecutive patients who were seen in the emergency department and received an ECG during the study period. Of the 1693 patients, 1017 were discharged.

Within this discharge subgroup, 78 were excluded due to wide QRS complex, paced ventricular rhythm, or atrial fibrillation. Of the remaining 939 patients, 151 (16%), as outlined in Table 1 had prolonged QTc with a female to male ratio of 69 to 82, respectively. The mean age of the study cohort was 53 +/- 18 with a minimum age of 11 and maximum age of 96 years.

Factor	ED Cohort (n = 151)
Age, years, median +/- SD	53 +/- 18
Female, n (%)	69 (45)
Heart rate, bpm, mean +/- SD	91 +/-17
QRS duration, ms, mean +/- SD	95 +/-10
QTc, ms, mean +/- SD	475 +/- 27

Table 1: Emergency department discharged cohort with prolonged QTc demographics.

SD= Standard Deviation; BPM= Beats Per Minute.

As indicated in Figure 1, the most common chief complaint was chest pain in 29 patients (20%); other complaints included shortness of breath in 24 patients (16%); and generalized weakness with dizziness in 21 patients (14%). Nine patients, six men and three women, had severe prolonged QTc intervals defined as QTc > 500 ms with five complaining of palpitations.

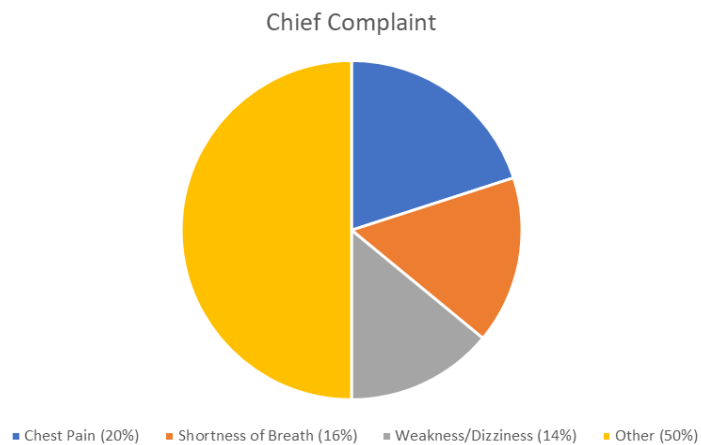


Figure 1: Frequency of presenting chief complaint among discharged cohort with prolonged QTc interval.

The other category includes complaints with less than 10% prevalence in aggregate.

Discussion

This was a single-center retrospective observational study reviewing electrocardiograms conducted on 1693 patients seen in the emergency department over the study period. Our study found the prevalence of LQTS among the 939 patients was 16%. This prevalence includes individuals with a QT interval greater than 450 ms if male and 460 ms if female. Furthermore, nine patients with severe LQTS, or a QTc interval greater than 500 ms regardless of sex, were identified. This finding is particularly notable as QTc > 500 ms is associated with increased risk of TdP [14].

Our findings were similar to Seftchick and colleagues who reported among 1,558 ED patients seen during their study, the prevalence of QTc interval prolongation was 35% (544 patients) with nearly half of these patients discharged (18%); 27 of these patients had QTc greater than 500 ms at the time of discharge and these patients had no follow-up [10]. Other studies since then have supported the high prevalence of QTc prolongation seen in the ED such as from Birda et al whose group reported a prevalence of 34.1% [11]. While they did not follow patients after discharge, they did report that a significant number of their sample with LQTS had chronic kidney disease with concomitant electrolyte abnormalities in addition to heart failure, and ventricular tachycardia. Interestingly, they did not report any difference in duration of hospital stay except in those with markedly prolonged QTc of > 500 ms. In contrast, Anderson and colleagues, whose study identified patients with a prolonged QT interval through an automated QT alert system, revealed a prevalence of a mere 1.2%. However, they reported a higher all-cause mortality of 39% among patients identified by the QT alert system compared to patients without an alert [15]. This may suggest that their QT alert system may be specific but not sensitive. Nonetheless, the higher mortality of their study is consistent with Birda et al. In a more recent study by Scheuermeyer and colleagues, 4,170 of 14,011 (29.8%) ED patients were identified with acquired prolonged QT

[2]. They then randomly selected 834 patients with a prolonged QTc and matched 417 normal QTc patients; approximately 58% from each group had been discharged home. What they found was no statistically significant difference in mortality between the two groups. Interestingly, when comparing LQTS patients with < 500 ms and > 500 ms, deaths in either group did not appear to have been due to ventricular dysrhythmia. Collectively, these conflicting findings between past and recent studies stresses the importance of reaching a consensus on the prognostic value of monitoring prolonged QT intervals as it relates to the morbidity and mortality among ED patients.

This study was not without limitations. This was a single-center study and thus may not be a representation of the population of the typical prevalence of LQTS at other facilities; however, the data we obtained have been concordant with the limited studies that have been published. Additionally, the threshold for abnormal QTc has been revised in several subsequent studies indicating a lack of consensus on what value constitute abnormal [14]. As such, we are using the QTc threshold as outlined by the American Heart Association (AHA) and the American College of Cardiology (ACC) [13]. We are aware that the commonly used Bazett's formula overcorrects the QT interval at extreme heart rates among adults; less than 60 or greater than 100 beats per minute resulting in under-estimation and over-estimation, respectively [15]. Other formulas we considered included the other logarithmic-based correction such as Fredericia which is similar to Bazett's but takes the cube root of heart rate instead, and linear correction formulas referred to as Framingham and Hodges both of which has gained favor with the AHA and ACC; however, Bazett's is still used most often clinically and by this community medical center.

Conclusion

This was the first known study to specifically evaluate consecutive undifferentiated patients who presented to the ED and subsequently was discharged without hospital admission and received an ECG. The prevalence of prolonged QTc intervals among patients discharged from the ED was 16%. This value is within the range of LQTS prevalence found in recent studies. Despite preliminary and recent evidence to indicate no difference in mortality among patients with LQTS and matched controls, until more studies are consistent with this conclusion, it is imperative additional studies be conducted to examine the prognostic value of closer QT interval monitoring in the evaluation of patients in the ED. This is especially important given the common use of QT interval prolonging drugs within the ED among acutely ill patients.

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