Computerized QT and QTc Measurements from Bedside ICU Monitors are Similar to those Derived from a Standard 12-lead ECG

by

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Computerized QT and QTc Measurements from Bedside ICU Monitors are Similar to those Derived from a Standard 12-lead ECG

Arthur Murray

Abstract

Purpose: QT and QTc (heart rate corrected) prolongation on the electrocardiogram (ECG) is associated with an increased risk for torsade de pointes (TdP). In at-risk hospitalized patients, it is common practice to obtain a standard 12-lead ECG to assess QT/QTc prolongation, which is costly and time-consuming. Our hospital recently introduced bedside monitors in the intensive care unit (ICU) that include software that continuously measures the QT/QTc. However, only six ECG leads are available on the bedside monitor, rather than all 12-leads offered on a standard ECG. Therefore, the purpose of this study was to evaluate the agreement between computerized QT/QTc measurements from the bedside monitor (six leads) and a standard 12-lead ECG. Design: Prospective observational study in three adult intensive care units (ICUs). **Methods:** QT/QTc measurements were obtained from a convenience sample. Patients with a standard 12-lead ECG that could be closely matched in time to bedside monitoring data were included. The agreement between the two methods (bedside monitor [six-leads] versus standard 12-lead), was evaluated using Bland-Altman analysis. **Results**: A total of 60 patients were included. The mean bias difference for QT measurements between the bedside monitor (six-leads) versus the standard 12-lead was not statistically different (β=-2.47, 95% CI=5.50 to -11.05; p=0.44; limits of agreement (LOA)=-64.37 to 59.44). Similar non-statistical differences

were observed for QTc (β=-3.20, 95% CI=5.50 to -11.05; p = 0.44; LOA=-67.43 to 61.03). C**onclusion**: There was good agreement for both QT and QTc measurements between six-lead bedside monitor derived values and those obtained with a standard 12-lead ECG. These pilot data are promising and suggest QT/QTc measurements generated from bedside monitors may be an acceptable alternative to obtaining additional standard 12-lead ECGs for assessing QT/QTc prolongation. However, an evaluation of agreement between these two methods in a larger sample is warranted.

Keywords: electrocardiographic monitoring, intensive care unit, measurements, QT/QTc, standard 12-lead electrocardiogram, computerized measurements

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ECG: Electrocardiogram

QT: QT Interval

QTc: QT corrected

CI: Confidence Interval

LOA: Limits of Agreement

Introduction

Torsade de pointes (TdP) is a polymorphic ventricular tachycardia that can lead to syncope and even sudden death. The term “TdP” refers to the characteristic electrocardiographic (ECG) pattern that translated, means “twisting of the points,” which refers to the characteristic QRS complex pattern seen with this arrhythmia (**Figure 1**). TdP was first identified in 1966, [1] and was found to be linked to QT interval prolongation. The entire QT interval represents both the depolarization and repolarization phase of the cardiac cycle and is visualized via an action potential. QT/QTc prolongation causes pre-mature action potentials in the ventricular myocytes during the late phase of depolarization, which increases the risk for TdP. [2] QT/QTc prolongation can appear in a primary, or secondary form. The most common primary type is congenital, so called long-QT syndrome, which can be seen among families, but can also occur in the general population. The secondary type is an “acquired” form, typically associated with medications that can prolong the QT/QTc and can lead to the same untoward outcomes as the primary form (i.e., deterioration to ventricular fibrillation and even sudden death). [2, 3]

In hospitalized patients, the acquired form of QT/QTc prolongation is of particular concern. For example, among intensive care unit (ICU) patients, the acquired type of QT/QTc is increased because of clinical and pharmacological factors that are common among critically ill patients (**Table 1**).One study found a 24% prevalence rate (QT >500 msec >15 minutes), in 1,039 consecutive ICU patients. [4] In this study, patients with QT/QTc prolongation had a longer length of stay (276 hours vs. 132 hours, $p < 0.0005$) and higher risk of mortality (OR 2.99;

95% CI 1.1 - 8.1) as compared to patients without QT prolongation. Others have reported that there is considerable QTc variability in ICU patient during an admission [5] and one study showed a diurnal variation. [6] The later presumably because of the timing of routine medications (e.g., AM and PM medication administration), which can change the QT/QTc following medication administration.

The most recently published Practice Standards for In-hospital ECG Monitoring, identified QT/QTc interval monitoring as a high priority in at-risk patients and recommended that hospitals establish uniform protocols for QT/QTc monitoring. [3] Specific recommendations include: defining a standard procedure for serial measurements; defining criteria for ECG lead(s) selection: consistent use of the same lead(s) for subsequent measurements; educating clinical staff on how to identify the onset of the QRS and the end of the T-wave; documentation every 8-12 hours and more frequently when QT/QTc prolonging drug(s) are administered; and/or when known patient risk factors are present. [3] While there are known demographic and clinical characteristics that place patients “at-risk,” it is routine nursing practice to measure the QT/QTc in all ICU patients with bedside ECG monitoring. This measurement is typically performed by nurses in the one or two ECG leads displayed on the bedside monitor at the start of each shift either by hand, or if available electronic calipers. However, physicians and/or providers may also request that measurements be obtained from a standard 12-lead ECG(s) when there is heightened concerned in select patients. The rational for using a standard 12-lead ECG, is that all 12 ECG leads are used and the QT/QTc is calculated automatically by a software algorithm. However, the steps necessary to obtain a standard 12-lead ECG can disrupt

the flow of patient care, delay findings, increase costs and a standard 12-lead ECG is only a 10-second “snapshot” assessment; thus, there are limitations of this approach.

Given the incidence and dynamic nature of QT/QTc prolongation among ICU patients, continuous measurements would be ideal. Recently, software that continuously and automatically measures the QT/QTc, has been introduced in some bedside ICU monitors. [7, 8] One ICU study showed acceptable accuracy between QTc values from the bedside monitor versus QTc values derived from a standard 12-lead ECG. [5] We are aware of only this one prior ICU based study, therefore validation in a new ICU cohort would be of value. In addition, the bedside monitor software at our hospital calculates the QT/QTc in only four (I, II, III and V1) of the seven available ECG leads (i.e., augmented unipolar limb leads are not used), rather than all 12 leads offered on a standard 12-lead ECG. Therefore, the purpose of this study was to evaluate the agreement between computerized QT/QTc measurements from the bedside monitor (four leads) and a standard 12-lead ECG obtained at the same date and time.

Methods

Study Design

This was a prospective observational study conducted at a 600-bed academic medical center. The following adult ICU units were included: cardiac, medical/surgical, and neurological (medical/surgical). The Institutional Review Board approved the study with a waiver of patient consent due to the purely observational nature of the study and we did not collect private health information from patients, or nurse related variables (IRB# 21-34690).

Sample

The QT/QTc data were obtained in adult (>18 years) ICU patients from one of three ICU types: (1) cardiac (n=28 beds); medical/surgical (n=32 beds); and neurological (n=29 beds). We collected patient age (if >90 years we grouped patients into a ≥90 years of age category), sex, and ICU unit type to characterize the sample. However, the unit of analysis for this study were QT/QTc measurements generated from the bedside monitor (four-lead computerized), and those obtained from a standard 12-lead ECG (computerized) that was obtained by hospital personnel as part of routine patient care.

QT/QTc Measurements

Our research team collected data on five different days. We attempted to collect QT/QTc data from all patients admitted to a unit on the day of data collection; hence no patient was excluded. Computerized QT/QTc measurement comparisons were made between a standard 12-lead ECG obtained from a hospital device as part of routine clinical care and the ICU bedside monitor (details below). If a patient did not have a standard 12-lead ECG available, they were not included in the study. We identified the QT/QTc from a hospital acquired standard 12-lead ECG located in the patient's chart and then used the date and time to compare the QT/QTc measurement derived from the bedside monitor. We set a goal of comparing the two methods within 30 minutes of each other to ensure that medications, and/or clinical factors that could change the QT/QTc did not influence potential differences. Below is a description of how QT/QTc values are calculated by the devices used during our study.

Computerized Bedside QT/QTc Measurements

The bedside ECG monitor in use during the study had QT/QTc software installed (Philips Healthcare, IntelleVue MX800, Cambridge, MA). The QT/QTc software was configured in the bedside monitor as 'on;' thus, values were displayed on the bedside monitor and automatically saved. The software updates the QT/QTc at one-minute time intervals. While the bedside monitor records seven ECG leads (i.e., I, II, III, aVR, aVL, aVF, and a V lead [default V1]), the software calculates QT/QTc only in leads I, II, III, and the V lead, generating a "global" QT/QTc. [7, 8] Every 15-seconds, the algorithm performs a QT analysis to determine the average heart rate in order to calculate the QTc using Bazett formula (QTc = QT interval in seconds /ÖRR interval in seconds). When the QT/QTc cannot be reliably analyzed by the software (i.e., atrial fibrillation, flat T-waves, artifact, small R-waves, or QT out of range [<200 or >800 msec]), an inoperative message alert occurs, and neither the QT, nor QTc is calculated.

Standard 12-lead QT/QTc Measurements

At the start of the study, the standard 12-lead ECG cart used in the hospital was the MAC 5500 Resting ECG Analysis System (GE Medical Systems Technologies; GE Healthcare, Milwaukee, WI). In this study, we will refer to this standard 12-lead ECG device as device #1. In the second half of the study the hospital purchased new standard 12-lead ECG devices (Philips DXL, Philips Healthcare, Andover, MA). In this study, we will refer to this standard 12-lead ECG device as device #2. Of note, device #2 is the same manufacturer as the bedside ICU monitor. **Table 2** shows how the algorithm for each manufacturer's device calculates the QT/QTc

interval. As with the bedside monitor, both devices used the Bazett's formula to calculate the QT/QTc.

Comparisons Between Bedside Monitor and Standard 12-lead ECG

QT/QTc values are reported in milliseconds (msec). The date and time of the QT/QTc from the standard 12-lead ECG QT/QTc was used to identify an ECG at the same date/time from the bedside monitor for comparisons. In a small number of instances, the computerized bedside measurements were not calculated at the exact time of the standard 12-lead ECG because motion artifact was present in the ECG signal. In these cases, a bedside monitor QT/QTc was obtained as close in time as possible just prior to, or after the date/time of the standard 12-lead ECG, which was typically within minutes. An attempt was made to obtain QT/QTc measurements in all the patients admitted to the ICU on the day of data collection. However, in some instances a standard 12-lead ECG had not been obtained in the ICU, so no comparisons could be made. For example, this could occur if a standard 12-lead ECG was obtained in the emergency department or a non-ICU setting (i.e., step-down, medical surgical unit), prior to ICU admission.

Statistical Analysis

All analyses were conducted under the guidance of a statistician. The characteristics of the sample were analyzed using SPSS (version 29.0.0.0 IBM Corporation, Armonk, NY). For the primary analysis that compared QT/QTc values between the standard 12-lead ECG to those measured by the bedside monitor were performed using R version 4.0.0 (Vienna, Austria).

Because there were two different hospital 12-lead ECG devices in use during the study, we report results by device and in the overall sample. Scatter plots were generated to evaluate the relationship between the measurement methods (bedside monitor versus standard 12-lead ECG). In addition, a Bland-Altman analysis was used to evaluate the agreement between the measurement methods (bedside monitor versus standard 12-lead ECG). [9] This approach plots the mean differences for QT/QTc between the two methods against the average of the two measurements. A mean difference of zero or close to zero indicates strong agreement. Unlike scatter plots, the Bland-Altman test can uncover measurement bias if one of the two methods is systematically inaccurate at capturing values at either end of the range of values for QT/QTc measurements. The Bland-Altman analysis identifies the estimated difference between the two measurements with 95% limits of agreement (LOA) around the estimate (mean difference of ±1.96 SD), and was conducted in R v4.0.0 using the BlandAltmanLeh package v0.3.1. [9-11] The mean difference and confidence intervals were determined by a linear mixed model using lme4 v1.1.27.1.[11] P-values <0.05 were considered statistically significant.

Results

A total of 60 QT/QTc measurements from 60 unique ICU patients were examined. As shown in **Table 3**, 33 (55%) of the sample was male, 27 (45%) of the sample was female, and the mean age was 58 (±18 years). The ICU type was: cardiac (38%); medical-surgical (33%); and neurological (28%). The mean time difference between measurements (four lead bedside monitor versus 12-lead) was 7 minutes 51 seconds (± 38 minutes). The overall mean QT in the sample was 377 ± 63 msec and the overall mean QTc was 455 ± 50 msec.

QT and QTc Measurement Comparisons by 12-Lead ECG Device

Because our hospital switched standard 12-lead ECG devices during the study, we examined QT/QTc differences by device. Device #1: As shown in **Table 4 and Figures 2 (QT) and 3 (QTc),** the mean bias difference for measurements between the bedside monitor (four leads) versus the standard 12-lead was not statistically different. Device #2: As shown in **Table 4 and Figures 2 (QT) and 3 (QTc)**, the mean bias difference for measurements between the bedside monitor (four leads) versus the standard 12-lead was not statistically different.

Overall QT/QTc Measurement Comparisons - Bedside Monitor versus Standard 12-lead

Here, we report the overall QT and QTc analysis combining data from both device #1 and device #2. As shown in **Table 5 and Figure 4**, the mean bias difference for QT measurements between the bedside monitor (four leads) versus the standard 12-lead was not statistically different (β=-2.47, 95% CI=5.78 to -10.18; p=0.53; limits of agreement (LOA)=-64.37 to 59.44). As shown in **Table 5 and Figure 5**, similar non-statistical differences were observed for QTc (β=-3.20, 95% CI=5.50 to -11.05; p = 0.44; LOA=-67.43 to 61.03).

Discussion

In this study that included 60 ICU patient, we found good agreement between QT and QTc measurements comparing those generated from the bedside ICU monitor, using only four ECG leads, to those obtained from a standard 12-lead ECG. These data suggest that continuous and automatically generated QT/QTc's from bedside monitors are comparable to those of a standard 12-lead ECG and may be a useful alternative. However, our sample was

small and only included ICU patients, which limits the generalizability of our findings and is not sufficient for instituting a major practice change until a larger sample, including non-ICU patients, are examined.

The mean QT bias of 2 milliseconds reported in our study, was lower than those found by Helfenbein et al., who reported a mean difference of 8.1 + 40 milliseconds. [9] In their study, 95 computerized QT intervals were compared to those measured by a cardiologists using a two lead ECG during a 15 minute recording. In both studies computerized measurements were examined. In a prior study that examined both human and computerized QT/QTc's, expert nurse measurements were consistently longer than both computerized and those measured by bedside nurses. [12] However, bedside nurses measured shorter QT/QTc's than both expert nurses and computerized measurements, suggesting that measurement variability can occur between nurses and computer generated measurements. These findings are similar to a different study showing that there was higher variability between manual physician measurements as compared to computerized measurements. [5] An overall interpretation is that mixing computerized and nurse/physician measured QT/QTc's can vary; thus, in clinical practice a consistent measurement technique is important and is in line with current practice recommendations. [3]

In our study, despite a mean time difference of seven minutes when comparing bedside monitor derived measurements to a standard 12-lead ECG, we did not find statistically different mean bias differences, which suggests that using these two methods interchangeably is likely to yield similar QT/QTc values. It is worth noting, that in our study there were two different

standard 12-lead ECG devices during the data collection period. This occurred because our hospital had purchased new devices from a different vendor. Despite two different standard 12-lead ECG devices, we did not find statistical differences for QT/QTc measurement between standard 12-lead ECG and those from the bedside monitor. Again, suggesting that computerized bedside monitor derived measurements are similar to standard 12-lead ECG device measurements.

Mean bias differences for QTc were also not statistically different. Our results are similar to those of Janssen et al., who compared bedside monitor derived QTc's to a standard 12-lead in 119 ICU patients. In their study the mean bias was 7.8 milliseconds, whereas in our study the mean bias difference was 3.20 milliseconds, which does not appear to be clinically significant. In their study, patients with a QRS of <120 milliseconds were examined, whereas in our study we did not account for QRS duration, which is a limitation of our study. However, their study included mostly cardiothoracic patients, whereas our study had an evenly distributed group of cardiac, medical/surgical and neurological ICU patients.

Limitations

There are several limitations worth noting. First, our study included a small sample of 60 patients and only included ICU patients, which limits the generalizability of our findings. It is worth noting that we could have included as many as 120 patients on the five days we collected data. However, a substantial number of patients did not have a standard 12-lead ECG recorded during their ICU stay; hence, were not included in our study. Rather, the standard 12-lead ECG had been obtained in the emergency department, and/or another hospital unit (step-down, or

medical surgical unit) prior to ICU admission. We were somewhat surprised by this finding since at one time it was common practice to record a daily standard 12-lead ECG, and/or following a change in a patient's condition (i.e., acuity level, electrolyte disturbance, vital sign changes, arrhythmia, QT prolonging medication and/or symptoms), which is common in ICU patients. Whether this practice is similar at other hospitals is an important consideration and is another limitation of our study. Regardless of the rational for this practice, our data suggest that QT/QTc interval measurements are often not assessed using a standard 12-lead ECG in a substantial number of ICU patients, which again may be hospital specific. This does imply that nurse measured (each shift) and those from the bedside monitor, if available, become an important assessment tool when a 12-lead ECG has not been recorded.

One could also argue that a limitation was that we did not compare manual nurse/physician measurements to the bedside and standard 12-lead ECG derived measurements. However, our group examined this in a different study and showed good agreement between nurse measured, both bedside and expert nurses, to computerized bedside ICU monitor derived QT/QTc's. [12] This study builds on those findings by showing that bedside ICU monitor derived QT/QTc's, even in only four leads, is in good agreement to those generated from a standard 12-lead ECG. Finally, we used two different standard 12-lead ECG devices because our hospital introduced a new vendor's device during the study. However, we did not find differences when we compared each device, albeit in a small sample of ICU patients.

Given that as many as 69% of ICU patients have one or more American Heart Association indication for QT/QTc interval monitoring [13], careful and consistent assessment

for QT/QTc prolongation is clinically important. We found that standard 12-lead ECGs were often not recorded in our ICU sample; thus, nurse measured and/or those from the bedside monitor are often relied upon for this assessment.

Conclusions

While this study examined a small number of ICU patients at a single-center during only five days of data collection, our findings suggest that QT/QTc measurements generated from the bedside monitor using only four ECG leads may be an acceptable alternative to obtaining a standard 12-lead ECG. This may reduce disruptions in clinical care, lower costs and provide real-time data that could identify QT/QTc prolongation earlier, which is important given the often subtle and dynamic nature of the QT/QTc interval. However, a future study in a larger sample that includes non-ICU patients is needed prior to an overall practice change.

Table 1. Risk factors for Torsade de Pointes in hospitalized patients.[1]

Clinical factors
- QTc >500 milliseconds
- Use of drugs known to prolong the QT interval
- Heart disease (heart failure, myocardial; infarction)
- Advanced age
Electrolyte disturbance - Hypokalemia - Hypomagnesemia - Hypocalcemia
Treatment with diuretics
Hepatic dysfunction
Bradycardia (sinus, heart block, incomplete heart block with pauses)
Premature ventricular complexes especially short-long-short cycles
Congenital long QT syndrome

Table 2. Comparison of how the algorithm of each electrocardiographic device measures QT/QTc.

Device Manufacturer	QT/QTc Measurement Method
Device #1	Uses all 12-leads ventricular rate is computed by counting the number of beats detected and dividing by the time difference between the first and last beats QT interval is measured from the earliest detection of depolarization in any lead to the latest detection of repolarization in any lead. Bazett's formula
Device #2	Uses all 12 ECG leads median QT value in "reliable leads." A lead is considered reliable if the beat-by-beat onset/offset determinations have a low variance. This helps to eliminate leads with small amplitudes and high respiratory variation, as well as leads with high noise content Algorithm locates the nadir of the intersection of T and U QT is measured individually and then combined into a global measurement Calculates both Bazett and Fridericia; hospital uses Bazett's
Intensive Care Unit Bedside ECG Monitor (same manufacturer as Device #2)	Uses leads I, II, III, and the V lead (V1 at our hospital) All QRS complexes detected by the beat detection algorithm within a discrete 15-second time period are saved for subsequent QT interval analysis. In order to calculate the QTc interval, an averaged heart rate (QT-HR) is generated. QT-HR is computed using all the valid beats in the 15-second window used for the QT interval measurement. QTc is then calculated using the rate correction formula selected. The QTc interval is also measured in milliseconds

Table 3. Sample characteristics among 60 intensive care unit patients.

Characteristic **n=60**	**n (%)**	
Intensive care unit type Cardiac (28 beds) Medical-Surgical (32 beds) Neurological (29 beds)	 23 (38) 20 (33) 17 (28)	
Age in years (mean ± SD)	58 ± 18	
Gender Male Female	 33 (55) 27 (45)	
Overall mean (± Standard Deviation) QT/QTc in the sample in milliseconds (msec)		
	Bedside Monitor (four ECG leads)	Standard 12-lead
QT	380 ± 62 msec	377 ± 63 msec
QTc	459 ± 40 msec	455 ± 50 msec

Table 4. Bland-Altman analysis of QT and QTc measurement comparisons by standard 12-lead ECG device used. The values shown are in milliseconds. The p-value reports the test of the mean bias using a linear mixed model.

Comparison Group	Bias (Mean)	95% CI	95% LOA Lower, Upper	p-value
Device #1 n=39				
QT				
Standard 12-lead vs Bedside Monitor	-2.23	5.23 to 9.05	-48.08 to 43.62	0.53
Standard 12-lead vs Bedside Monitor	-2.90	16.19 to 20.14	-88.41 to 82.60	0.74
Device #2 (same manufacturer as bedside monitor) n=21				
QT				
Standard 12-lead vs Bedside Monitor	-3.51	4.64 to 11.26	54.94 to 47.92	0.28
QTc				
Standard 12-lead vs Bedside Monitor	-2.62	16.62 to 19.48	-87.12 to 81.88	0.74

Abbreviations: CI=confidence interval; LOA=limits of agreement

Table 5. Bland-Altman analysis of QT and QTc measurement comparisons in the overall sample combining device #1 and #2. The values shown are in milliseconds. The p-value reports the test of the mean bias using a linear mixed model.

Comparison Group	Bias (Mean)	95% CI	95% LOA Lower, Upper	p-value
QT				
Standard 12-lead vs Bedside Monitor	-2.47	5.78 to –10.18	-64.37 to 59.44	0.53
QTc				
Standard 12-lead vs Bedside Monitor	-3.20	5.50 to –11.05	-67.43 to 61.03	0.44

Abbreviations: CI=confidence interval; LOA=limits of agreement

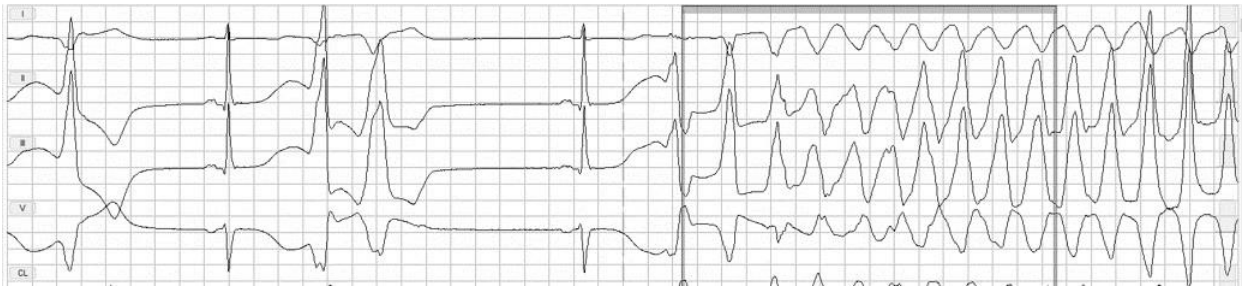
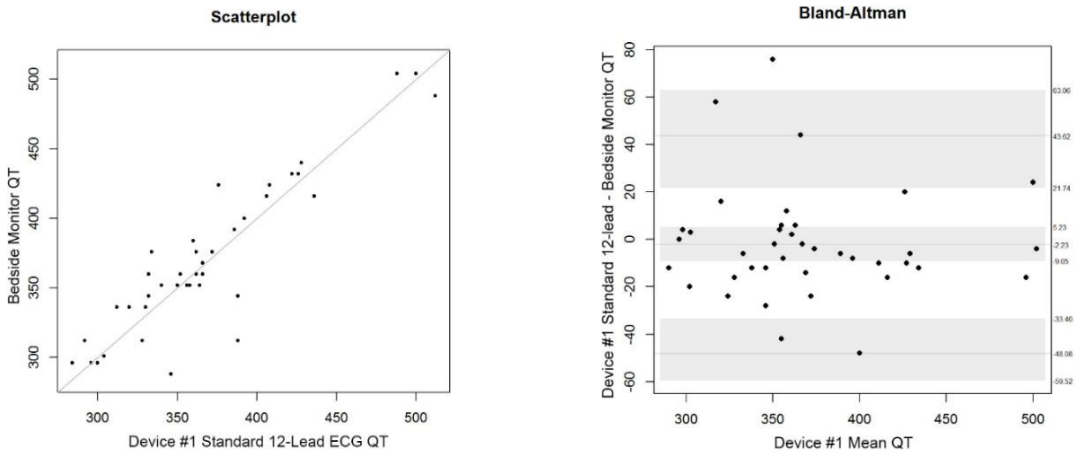


Figure 1. Illustrates Torsades de Pointes (TdP), a multifocal ventricular tachycardia associated with long QT syndrome. Shown are leads I, II, III and V1. Note the lengthened QT interval (5th beat) of >600 milliseconds followed by an R-on-T type premature ventricular complex that initiates TdP.

A. Device #1 n=39 patients.



B. Device #2 n=21 patients.

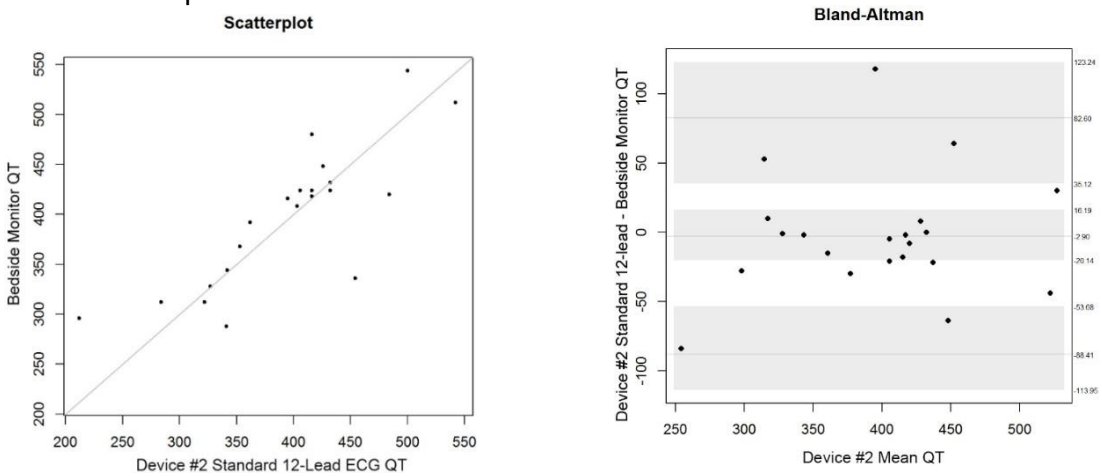
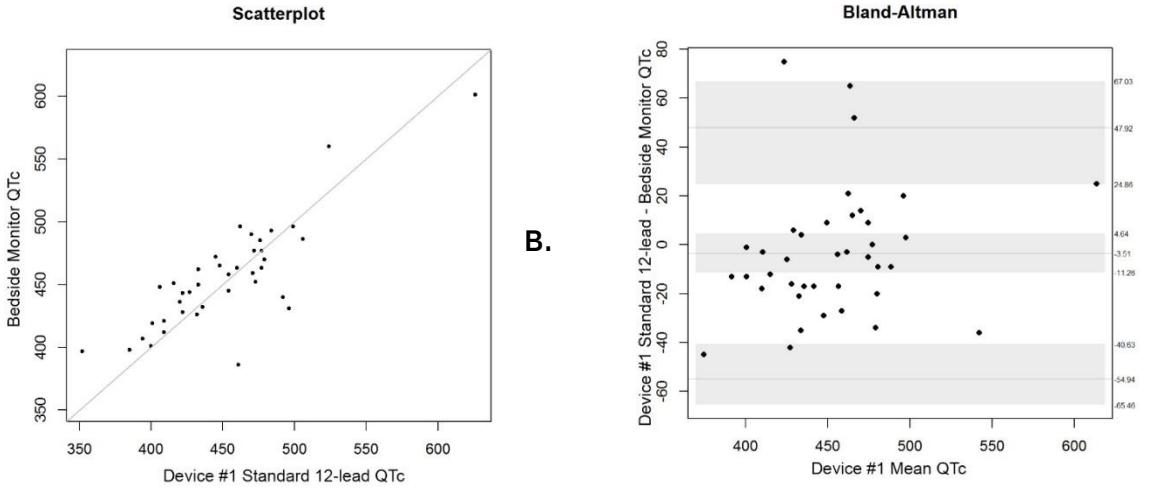


Figure 2. QT measurements using standard 12-lead ECG device #1 (A, n=39 patients) and device #2 (B, n=21 patients). Shown are scatterplots (left) and Bland-Altman plots (right) comparing computerized measurements from the bedside monitor (four lead) to the standard 12-lead ECG for each device. The line in the middle of the Bland-Altman figure represents the mean difference, and the gray shading is the upper and lower limits for the 95% confidence interval (CI) around the mean difference. The lighter dashed lines above and below the mean difference are the upper and lower limits where 95% of the data lie.

A. Device #1 n=39 patients.



B.

Device #2 n=21 patients.

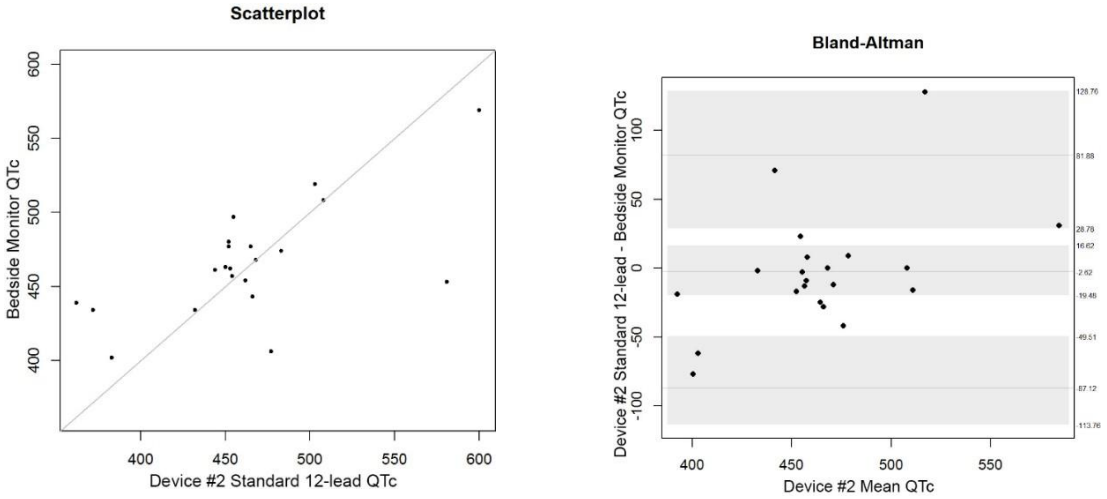


Figure 3. QTc measurements using standard 12-lead ECG device #1 (A, n=39 patients) and device #2 (B, n=21 patients). Shown are scatterplots (left) and Bland-Altman plots (right) comparing computerized measurements from the bedside monitor (four lead) to the standard 12-lead ECG for each device. The line in the middle of the Bland-Altman figure represents the mean difference, and the gray shading is the upper and lower limits for the 95% confidence interval (CI) around the mean difference. The lighter dashed lines above and below the mean difference are the upper and lower limits where 95% of the data lie.

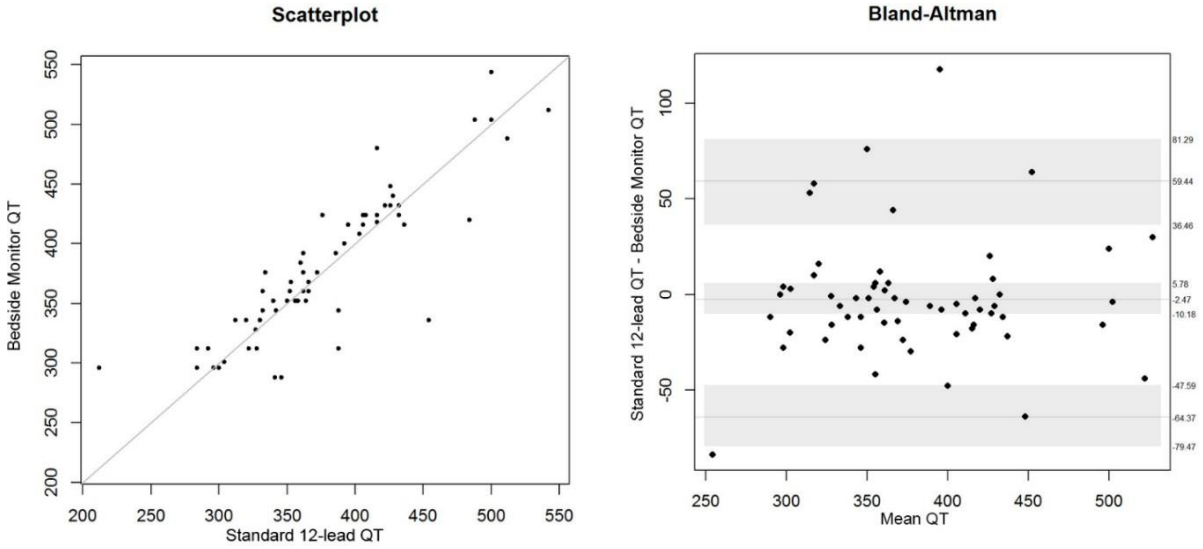


Figure 4. QT measurements in the overall sample (n=60 patients), both device #1 and #2,. Shown is a scatterplot (left) and Bland-Altman plot (right) comparing computerized measurements from the bedside monitor (four leads) to the standard 12-lead ECG. The line in the middle of the Bland-Altman figure represents the mean difference, and the gray shading is the upper and lower limits for the 95% confidence interval (CI) around the mean difference. The lighter dashed lines above and below the mean difference are the upper and lower limits where 95% of the data lie.

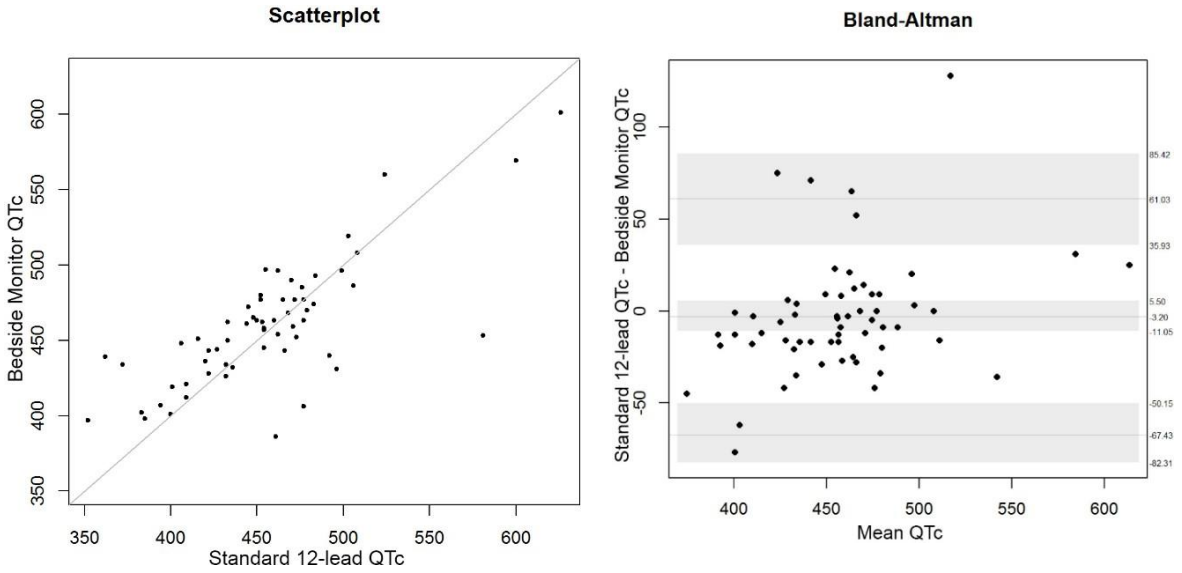


Figure 5. QTc measurements in the overall sample (n=60 patients), both device #1 and #2,. Shown is a scatterplot (left) and Bland-Altman plot (right) comparing computerized measurements from the bedside monitor (four lead) to the standard 12-lead ECG. The line in the middle of the Bland-Altman figure represents the mean difference, and the gray shading is the upper and lower limits for the 95% confidence interval (CI) around the mean difference. The lighter dashed lines above and below the mean difference are the upper and lower limits where 95% of the data lie.

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