Portable single-lead electrocardiogram device is accurate for QTc evaluation in hospitalized patients

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BACKGROUND Many commonly used drugs can prolong the QTc interval (QTc), which can lead to potentially life-threatening arrhythmias. In the current era of the COVID-19 pandemic, it is worth mentioning that the disease itself and several drugs used for its treatment have been associated with QTc prolongation.

OBJECTIVE To evaluate the agreement and clinical precision of a portable single-lead electrocardiogram (ECG) device to measure the QTc interval compared to the standard 12-lead ECG.

METHODS In sequential tests, QTc of ECG recordings obtained with the KardiaMobile (KM-1L) device (AliveCor, San Francisco, CA) were compared to QTc obtained with conventional 12-lead ECG. Agreement was evaluated using Bland-Altman plots and Lin's concordance coefficient. Consistency between the 2 devices in determining QTc prolongation (QTc ≥470 ms in males or ≥480 ms in females) was evaluated with kappa statistics.

RESULTS A total of 128 patients with a presumed or confirmed diagnosis of COVID-19 admitted to a university hospital were included. QTc intervals measured with KM-1L were similar to QTc measured with conventional ECG (442.45 ± 40.5 vs 441.65 ± 40.3 ms, P = .15). Bland–Altman analysis showed no significant difference in QTc values (average difference of -0.797, 95% limits of agreement:-13.179; 11.585). Lin's concordance coefficient showed an excellent agreement (0.988, P < .001). Concordance between the 2 devices for determining QTc prolongation was excellent (kappa >0.90).

CONCLUSION ECG recordings obtained with KM-1L allow an accurate QTc interval assessment. Considering its simplicity of use, this approach has advantages over conventional ECG and can provide an alternative for the evaluation of QTc in hospitalized patients, during the current time of the COVID-19 pandemic and beyond.

KEYWORDS COVID-19; Electrocardiography; KardiaMobile; Mobile applications; QT/QTc interval; Smartphone; Single-lead ECG device; Ventricular arrhythmias

Introduction

Prolongation of QTc interval may cause potentially fatal cardiac arrhythmias, such as torsades de pointes (TdP).[1] Multiple risk factors have been associated with QTc prolongation, including congenital QTc prolongation, female sex, age greater than 65 years, ischemic cardiomyopathy, severe bradycardia, electrolyte imbalance, and liver/kidney insufficiency. Also, more than 170 drugs may prolong QTc interval, including antiarrhythmics, antipsychotics, and antifungal agents.[2] In patients with risk factors, QTc interval monitoring with 12-lead derivation electrocardiogram (ECG) is recommended to prevent fatal arrhythmia due to QTc prolongation.

Rapid expansion of the COVID-19 pandemic has driven a worldwide use of a variety of drugs for first-line therapy and prophylaxis. Pharmacological treatments have included off-label use of anti-inflammatory, antiviral, and antiparasite drugs, among others, some with the potential risk of QTc interval prolongation. Such drugs are potential inductors of TdP and ventricular fibrillation, increasing the risk of sudden cardiac death. SARS-CoV-2 infection also increases cytokine levels, especially IL-6. IL-6 directly blocks the human ether-à-go-go-related gene (hERG) potassium ion channel, with the consequent prolongation of action potential duration and delay in phase 3 of repolarization, causing QTc prolongation and risk of TdP development.[3,4] Performing 12-lead ECG in patients with suspected or confirmed COVID-19 increases the risk of infection for patients without this disease and for healthcare workers.[5,6]

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KEY FINDINGS

■ Electrocardiogram (ECG) recordings obtained with portable single-lead devices are feasible and allow accurate assessment of the QTc interval. In this study, we obtained a very good correlation of the QTc interval measured with the KardiaMobile 1L device (AliveCor, San Francisco, CA) compared to the standard ECG.

■ The advantage of the KardiaMobile 1L device is the simplicity of its use, so it can be used by both healthcare personnel and patients themselves, and could be applied for ambulatory monitoring, which is likely to increase over time even after the pandemic has subsided.

■ An interesting finding is that concordance was lower in patients with SARS-CoV-2 infection compared to patients without the infection. This group of patients also presented the greatest variation in the heart rates obtained by the different evaluation methods, which may be related to autonomic anomalies that have been described in these patients in autonomic tests.

To reduce the risk of SARS-CoV-2 infection, easy-to-use alternatives such as portable single-lead ECG devices (eg, KardiaMobile [KM], iWatch) have been proposed for evaluating QTc. Such devices have proven to be accurate in detecting atrial fibrillation compared to 12-lead ECG (gold standard) and have been used for this purpose in clinical practice.[7–10] However, information on the diagnostic accuracy of portable single-lead ECG devices is limited, not only for COVID-19 patients but also for the general population.

The goal of the present study is to evaluate the numerical and clinical precision of a portable single-lead ECG device to measure QTc interval as compared to the standard 12-lead ECG for its use in hospitalized patients. We include patients with confirmed or suspected SARS-CoV-2 infection.

Methods

This is a prospective study of a diagnostic test carried out at Hospital Universitario San Ignacio, in Bogotá D.C., Colombia, from June to November 2020. The study included hospitalized adult patients with probable or confirmed COVID-19 (polymerase chain reaction test). Patients with atrial fibrillation rhythm, external electrical stimulation (pacemakers, cardiac defibrillators, and cardiac resynchronization therapy), ventricular assist devices, or extracorporeal membrane oxygenation therapy were excluded. The Ethics and Research Committee of the Faculty of Medicine of Pontificia Universidad Javeriana and Hospital Universitario San Ignacio approved the study. According to Colombian legislation, taking an ECG or using the KM device are classified as minimal- or no-risk procedures, and therefore our proposed investigation was also thus classified. Consequently, the aforementioned committee approved the exemption of informed consent (Approval code: 10/2020). This study was done in accordance with the standards specified in the International Council for Harmonization Guidelines for Good Clinical Practice and the principles of the Declaration of Helsinki.

A portable single-lead electrocardiographic KM device was used. The device is small and lightweight, is available for iOS and Android platforms, and can be connected wirelessly to smartphones. The device consists of 2 conductive plates (stainless steel electrodes) to make contact with the patient's fingers and record a bipolar lead and a software application named Kardia® (AliveCor, San Francisco, CA).

To perform a recording, 1 finger of each hand (regardless of which fingers) must rest on the electrodes of the KardiaMobile device (AliveCor, San Francisco, CA) for at least 30 seconds. This technique automatically produces an electrocardiographic recording in D1 in the Kardia app. The recording is saved in PDF format, labeled, and sent by e-mail for analysis.[11,12]

For each patient a KM tracing and a conventional 12-lead ECG were performed consecutively, and then compared. For each tracing, average QTc was calculated using Bazett's formula, with 3 consecutive QTs and the corresponding R-R intervals.

In conventional ECG, D1, D2, and V_5 derivations were used to measure QT intervals. Three expert investigators performed blind measurements and defined QT and QTc values by consensus.

Figure 1 presents an example of tracing with a KM device and with a conventional ECG in 1 patient of the study.

Definitions and statistical analysis

General characteristics of the population were analyzed using descriptive statistics. The difference among QTc values was analyzed using a paired t test to determine the mean difference.

The Bland–Altman analysis was used to test the agreement between QTc measured with conventional 12-lead ECG and portable ECG device.[13] Additionally, the Lin's concordance coefficient was calculated.[14] Numerical precision was defined as the proportion of QT and QTc measurements where KardiaMobile value had less than 10 ms of difference with conventional ECG values. Clinical precision was calculated through concordance estimation by conformity between QT and QTc values measured by KM or conventional ECG, assuming the conventional ECG as reference standard. For each measurement method, 2 categories were created based on the existence or absence of QTc interval prolongation (QTc $\geq$470 ms in postpubertal males or $\geq$480 ms in postpubertal females). Concordance between diagnostic methods was analyzed using kappa statistics, with a level of alpha significance of 0.05. For patients available for analysis, a power higher than 80% was calculated. All the statistical calculations were performed using
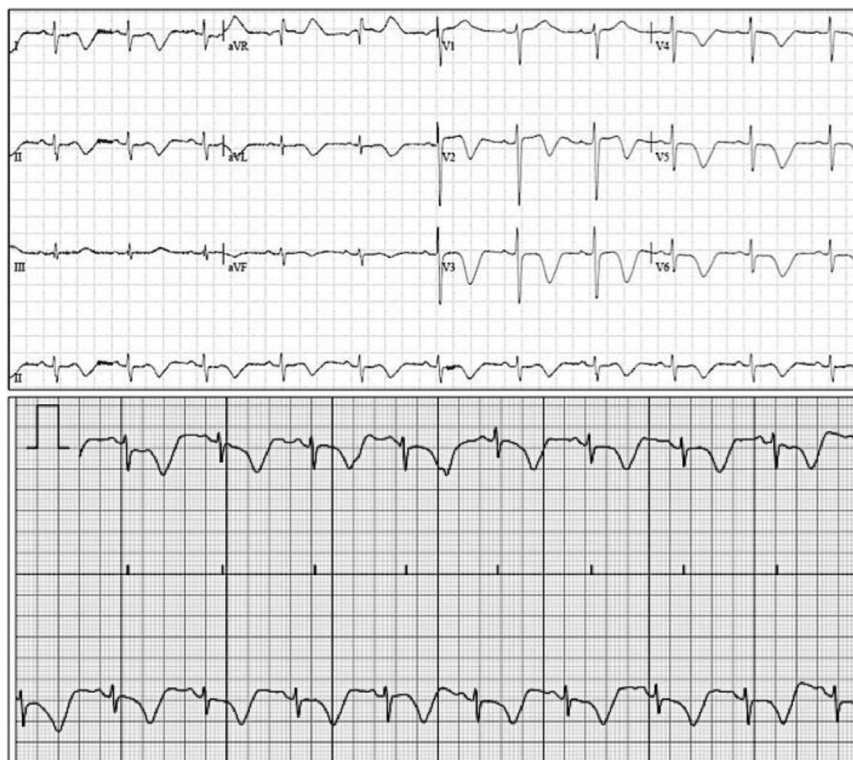
Figure 1 Conventional electrocardiogram (ECG) and electrocardiographic tracing, obtained with KardiaMobile (KM-1L) device (AliveCor, San Francisco, CA), of a patient admitted in Hospital Universitario San Ignacio. **Top:** 12-lead ECG showing a heart rate of 69 beats/min and a QTc of 583 ms. **Bottom:** Record taken with KM-1L showing a heart rate of 69 beats/min and a QTc of 583ms. In both records, QT interval prolongation is visible.

StataCorp 2020 statistical package (StataCorp. 2020. Stata Statistical Software: Release 16. StataCorp LP, College Station, TX).

Table 1 Characteristics of the patients at baseline

Characteristics	Results (N = 128)
Sex, n (%)	
Male	61 (47.7%)
Female	67 (52.3%)
Age, years (mean ± SD)	60.3 ± 17.4
Indication of hospitalization, n (%)	
Cardiopathy	40 (31.3%)
Infectious disease	37 (28.9%)
Hematologic disease	15 (11.7%)
Oncologic condition	8 (6.3%)
Gastrointestinal disease	4 (3.1%)
Vascular disease	4 (3.1%)
Neuropathy	3 (2.3%)
Rheumatological disease	1 (0.8%)
Others	16 (12.5%)
SARS-CoV-2 infection, n (%)	
Confirmed	33 (25.8%)
Ruled out	95 (74.2%)
History of heart failure, n (%)	53 (41.4%)
History of blood hypertension, n (%)	78 (60.9%)
Drugs used for COVID-19, n (%)	
Lopinavir/ritonavir	1 (0.8%)
Hydroxychloroquine	2 (1.6%)
Azithromycin	22 (17.2%)
None	103 (80.5%)
Potentially QT-prolonging drugs, n (%)	65 (50.8%)

COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Results

Records of 128 patients were evaluated, 47.7% men and 52.3% women. The average age was 60.3 years. Cardiopathy was the most frequent cause of hospitalization (31.3%). History of heart failure, use of potentially QT interval–prolonging drugs, and history of high blood pressure were present in 41.4%, 50.8%, and 60.9% of patients, respectively. SARS-CoV-2 was confirmed in 25.8 % of patients. Table 1 presents the characteristics of these patients.

The uncorrected QT interval averages were statistically different, but not clinically, between KM and conventional ECG (409.0 ± 51.1 vs 413.3 ± 52.5 ms, $P = .006$). Values of the QTc interval were practically the same for both devices (442.45 ± 40.5 vs 441.65 ± 40.3 ms, $P = .15$).

Agreement between conventional 12-lead ECG and portable ECG device

The Bland–Altman analysis showed no significant difference in QTc values between conventional 12-lead ECG and portable ECG device, with an average difference of -0.797 (95% limits of agreement: -13.179; 11.585), indicating suitable agreement between the 2 measurements (Figure 2). Lin's concordance coefficient showed an excellent agreement (0.988, 95% CI 0.983;0.992, $P < .001$).

Numerical precision of KardiaMobile device

Numerical precision, defined as the proportion of measurements in which QT interval measurement from KardiaMobile
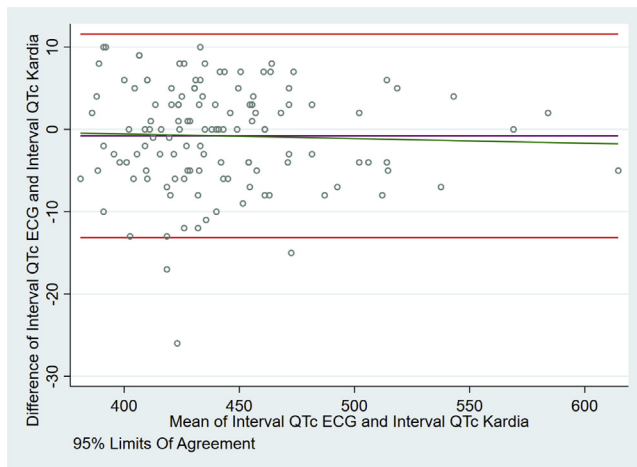
Figure 2 Bland–Altman analysis. No significant difference in QTc values between conventional 12-lead electrocardiogram (ECG) and portable ECG device are observed.

had less than 10 ms of difference with the measurement in conventional ECG, was 71.9% for uncorrected QT interval and 93% for QTc. The patient with the greatest variation in heart rate had a difference of 10 beats between the 2 assessment methods.

Numerical precision compared by subgroups only found a difference in the SARS-CoV-2 infection category. Numerical precision was 85% in this group of patients vs 96.6% in cases in which infection was ruled out ($P = .017$). The greatest variation in the heart rates obtained in the different evaluation methods was observed in the group of patients with probable or confirmed COVID-19. No differences were found in categories of sex, history of heart failure, blood hypertension, and use of QT-prolonging medications (Table 2).

Concordance by conformity among tests

Table 3 presents analysis of concordance between the KM device and the conventional ECG to determine presence of QTc prolongation. Prolongation corresponded to a QTc value ≥ 480 ms in female patients and ≥ 470 ms in male patients. Concordance was excellent in both groups of patients, being slightly superior in male compared to female (kappa = 0.946 and 0.901, respectively) (Table 3).

Discussion

Our study evaluated the agreement between a portable ECG device and the conventional ECG for QTc interval evaluation and the numerical and clinical precision of the device. The study found an excellent agreement and no statistically significant differences in the QTc interval measurement using these different methods.

Previous studies evaluating portable ECG device precision for QTc were limited by the small number of evaluated patients or by the inclusion of healthy subjects and hospitalized ill patients.[15,16] Even so, the results were similar to those in this study.

Table 2 Subgroup analysis in function of KardiaMobile numerical precision compared to conventional electrocardiogram

Characteristics	N	Numerical precision[†]		P
		Cases	Percentage	
Number	128	119	93.0%	
Sex				
Male	61	56	91.8%	
Female	67	63	94.0%	.623
SARS-CoV-2 infection				
Probable and confirmed	40	34	85.0%	
Ruled out	88	85	96.6%	.017[‡]
Heart failure history				
Yes	53	49	92.5%	
No	75	70	93.3%	.848
Blood hypertension history				
Yes	78	74	94.9%	
No	50	45	90.0%	.293
Potentially QT-prolonging drugs				
Yes	65	60	92.3%	
No	63	59	93.7%	.766

Data are presented as number and percentage.
P value obtained through χ^2 test.
[†]Numerical precision was defined as the proportion of KardiaMobile (AliveCor, San Francisco, CA) QT interval measurements with less than 10 ms difference from conventional electrocardiogram measurements.
[‡]$P < .05$.

A recent study in the COVID-19 pandemic evaluated 100 consecutive patients recruited in the ambulatory setting or in the emergency room. An ECG tracing obtained with a smart watch yielded corrected QT interval measurements that were adequate for reading in 85% of patients when the device was worn on the left wrist. That value rose to 94% when the position of the smart watch was modified to improve the quality of electrocardiographic tracing and amplitude of the T wave. Once the optimal position was found, concordance between devices was excellent, similar to the results in our study.[17]

Table 3 Estimates of concordance by conformity of QTc interval measurement between KardiaMobile and conventional electrocardiogram

KardiaMobile	Conventional ECG		
	Prolonged QTc	Nonprolonged QTc	Total
Male (QTc ≥ 470 ms)			
Prolonged QTc	11 (18.0%)	0 (0%)	11 (18%)
Nonprolonged QTc	1 (1.7%)	49 (80.3%)	50 (82%)
Total	12 (19.7%)	49 (80.3%)	61 (100%)
Kappa: 0.946 ± 0.127			
Female (QTc ≥ 480 ms)			
Prolonged QTc	5 (7.5%)	0 (0%)	5 (7.5%)
Nonprolonged QTc	1 (1.5%)	61 (91%)	62 (92.5%)
Total	6 (9.0%)	61 (91%)	67 (100%)
Kappa: 0.901 ± 0.122			

Data are shown by number (percentage of total patients in the group).
Kappa value ± standard error is also shown.
ECG = electrocardiogram.

Frisch and colleagues[18] reported the evaluation of a KardiaMobile-6L ECG device with the accompanying KardiaStation tablet application to evaluate the QTc in an inpatient setting including 6 patients (3 of them with COVID-19), to evaluate if they were able to record their own ECG tracings at least once without any assistance. They found that the device had the ability to provide reliable QT/QTc interval measurements. Hospitalized patients were able to perform recordings when requested after receiving simple instructions at the time of first use. Unlike this 6-lead device, we used a single-lead device and found excellent agreement compared to the conventional 12-lead ECG when evaluating QTc using the Bazett formula, suggesting that a simpler device could be equally reliable. Future studies are needed to assess whether patients themselves, as reported by Frisch, could perform the measurement with a single-lead device.

A portable ECG device with 6 leads has been evaluated in settings different from COVID-19. An artificial intelligence–enabled 12-lead ECG algorithm to determine the QTc was evaluated in 686 patients with genetic heart disease (50% with long QT syndrome). A strong agreement was observed between deep neural network–predicted QTc values derived from manual ECG (mECG) tracings and those annotated from 12-lead ECGs by a QT expert (-0.45 ± 24.73 ms), with values very similar to our findings.[19] These results suggest that QTc measured with wearable devices could be applied for ambulatory surveillance, which is likely to increase over time, even after the pandemic has subsided.

Numerical precision of KM was similar for categories of sex, history of heart failure, blood hypertension, and use of QT-prolonging drugs. An interesting finding is that concordance was lower in patients with confirmed SARS-CoV-2 infection compared to patients without the infection. This is the first time this situation has been described. One possible explanation is that the greatest variation in the heart rates obtained by the different evaluation methods was observed in this group of patients. Autonomic abnormalities on autonomic tests have been described in these patients, and could be related to the changes in the heart rates observed in our study.[20] This may be owing to abnormalities related to the viral infection or the clinical status of patients. It is necessary to evaluate these hypotheses in the future in other studies. Differences were also identified between the QT and QTc intervals, which can also be explained by the variations between the heart rate values described. It is important to mention that it was necessary to modify the position in which the electrocardiographic record was taken with the KM device, from supine to sitting in some patients in our study, to improve the quality of the tracing obtained. Variation of heart rate has been associated with postural changes. Resting heart rate is faster in upright postures such as standing and sitting, compared with the lying position. In a recent study, it was described that postural change from supine to sitting increases heart rate by 10 beats per minute in both sexes, and postural change from supine to standing increases heart rate by 30 beats per minute in females and males. The mechanisms proposed for such differences have been related to

baroreceptor stimulation as well as the regulation of cardiovascular hormones.[21–31] Postural changes from supine to sitting or standing are also known to affect QT/QTc intervals or QT dispersion. Stretching of the QT interval may partly explain these findings. This is the phenomenon that occurs when the QT interval is not shortened in proportion to the shortening of the R-R interval (when heart rate increases). Taking into account that the measurement of the QT interval is directly related to the R-R interval, several mathematical formulas have been designed to "correct" the QT interval and adapt it to the heart rate or, what is the same, to the R-R interval. Therefore, the clinically useful QT interval is the corrected QT interval.[32–34]

When the graph obtained by applying the Bland–Altman analysis was analyzed, 3 outliers were identified close to the limits of agreement, suggesting significant differences between the QTc measured by the device and the conventional 12-lead ECG. The patients with these findings are part of the group of patients with SARS-CoV-2 infection and they are the ones with the greatest differences in the heart rate values obtained by the different evaluation methods.

This study is, to our knowledge, the largest reported to date to assess the accuracy and concordance of the KM device compared to the conventional 12-lead ECG. Our study is also among the first to evaluate the validity of the single-lead KM device specifically for the measurement of the QTc interval.

Regarding the limitations of our study, we must emphasize that it was carried out in a single center and with a single device. Furthermore, the number of patients with QTc interval prolongation was relatively small. Further studies are required to evaluate the characteristics of KM in other clinical settings and to strengthen the conclusions in patients with prolonged QTc. Noisy recordings have been reported with the use of the KM device, which can also be a limitation. In our protocol, it was considered necessary to repeat the recordings when noise was identified to obtain clear and interpretable traces. For an anterior precordial lead, the device can be placed on the lower left side of the chest, just below the pectoral muscle.[35] This way of obtaining the record was not included in our protocol, but it can be a strategy to solve the difficulty of dealing with noisy traces.

The results of this study demonstrate that the single-lead KM has adequate precision and agreement in compare with 12-lead ECG, justifying its clinical use to assess the QTc interval. Because it is quick and convenient to use, KM is ideal for reducing the exposure time of healthcare workers in the COVID-19 pandemic. Further studies should evaluate whether these characteristics are observed in outpatients or in low-complexity institutions.

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