Original Article

The Clinical Utility of Continuous QT Interval Monitoring in Patients Admitted With COVID-19 Compared With Standard of Care: A Prospective Cohort Study

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ABSTRACT

Background: QT interval monitoring has gained much interest during the COVID-19 pandemic because of the use of QT-prolonging medications and the concern about viral transmission with serial electrocardiograms (ECGs). We hypothesized that continuous telemetry-based QT monitoring is associated with better detection of prolonged QT episodes.

Methods: We introduced continuous cardiac telemetry (CCT) with an algorithm for automated QT interval monitoring to our designated COVID-19 units. The daily maximum automated heart rate-corrected QT (Auto-QTc) measurements were recorded. We compared the proportion of marked QTc prolongation (Long-QTc) episodes, defined as QTc ≥ 500 ms, in patients with suspected or confirmed COVID-19 who were admitted before and after CCT was implemented (control group vs CCT group, respectively). Manual QTc measurement by electrocardiogram (ECG) was compared with Auto-QTc.

Results: A total of 598 patients admitted with COVID-19 between April 7 and May 9, 2020, were included. Compared with the control group, the proportion of Long-QTc episodes was significantly higher in the CCT group (1.1% vs 0.2%, P < 0.001). The proportion of Auto-QTcLong-QTc episodes was significantly higher than that of Manual-QTcLong-QTc (1.1% vs 0.2%, P < 0.001). The proportion of marked QTc prolongation with good agreement (kappa = 0.87, P < 0.001).

Conclusion: Continuous cardiac telemetry is associated with better detection of QT prolongation compared with standard of care. The COVID-19 pandemic has brought multiple challenges to the health care system. One of which is the use of QT-prolonging medications with no clear evidence to guide monitoring. Although clinicians are familiar with managing patients taking QT-prolonging medications, the current situation is different in 3 respects. First, combination therapy of 2 or more proarrhythmic anti-COVID-19 therapies is not uncommon and carry a greater risk of ventricular arrhythmias. Second, direct myocardial injury seen with COVID-19 has been shown in basic and clinical studies to increase the susceptibility to QT prolongation. Third, the usual practice of performing serial electrocardiograms (ECGs) to monitor QT interval is being discouraged because of the risk of viral transmission, which limits the use of previously recommended protocols. As such, it is critical to find an alternative practical and safe method of monitoring the QT interval in these patients. Automated QT interval monitoring using continuous cardiac telemetry (CCT) systems is an appealing alternative because of the minimal contact with patients and its potential ability to detect episodes of transient QT prolongation that could be missed with intermittent QT measurements. We hypothesized that continuous QT monitoring with CCT for patients admitted to critical care units with COVID-19 would detect more episodes of prolonged QT than standard of care.

Methods

This was a single-centre prospective cohort study that included consecutive patients admitted to critical care units affiliated with The Ottawa Hospital (5 units) with confirmed or suspected COVID-19 between April 7 and May 9, 2020.

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The clinical response to Long-QTc episodes is suboptimal. of care in detecting episodes of Long-QTc with minimal need for ECGs. Conclusions: Continuous QT monitoring and COVID-19 Alqarawi et al. 593

The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. See Supplemental Table S1 for the STROBE checklist.

On April 28, 2020, CCT was implemented in all critical care units receiving COVID-19 patients at The Ottawa Hospital. Patients receiving CCT were considered the active group (CCT group) and those admitted before CCT were considered controls (control group). Patients were followed until discharge or death. This quality improvement initiative was granted an exemption by the Ottawa Health Science Network Research Ethics Board.

CCT group

Patients admitted after the implementation of CCT were attached to a cardiac monitor connected electronically to servers at the Arrhythmia Monitoring Centre at the University of Ottawa Heart Institute. The QT interval monitoring algorithm previously validated by Philips was used. Briefly, this system measures heart rate-corrected QT intervals (QTc) every 30 minutes and displays the results in a table attached to the daily report, which was then posted on the electronic medical record. Bazett’s formula is used for heart rate correction. No correction for wide QRS is used. The end of the T wave is determined by a novel algorithm that measures vertical distances from a line connecting the peak of the T wave to a heart rate-adjusted point forward in time. The point with the maximum vertical distance is considered the end of the T wave. A 15-second ECG strip at the time of the maximum QTc measured in 24 hours was attached to the report. Supplemental Figure S1 shows an example of such a report. Intermittent ECGs were performed in this group at the discretion of the treating team. For the purpose of this study, the daily maximum QTc provided by the system is called automated QTc (Auto-QTc).

The prespecified primary outcome of the study was the proportion of new Long-QTc episodes (≥ 500 ms) in each group. Secondary outcomes were episodes of (TdP), the proportion of ECGs performed during the monitoring period, and the proportion of Long-QTc episodes that were treated with recommended therapies. There was 1 episode of torsade de points in the control group and none in the CCT group.

Conclusions: Continuous QT interval monitoring is superior to standard of care in detecting episodes of Long-QTc with minimal need for ECGs. The clinical response to Long-QTc episodes is suboptimal.

Control group

Patients admitted before the implementation of CCT received the standard of care, which consisted of standard bedside telemetry without automated QT measurements and intermittent ECG monitoring at the discretion of the treating team. All ECGs were reviewed and the recorded QTc intervals were collected (ECG-QTc).

Data collection

Data on baseline characteristics including age, sex, comorbidities, QT-prolonging medications, QTc recorded on ECG at admission, and baseline serum K, Ca, Mg, and creatinine levels were collected. Patients with at least 1 positive nasopharyngeal swab were labelled as “confirmed COVID-19” and the rest were labelled as “suspected COVID-19.” QT-prolonging antimicrobial therapy for confirmed COVID-19 patients were recorded. Electronic medical records were reviewed for all patients daily to record the QTc, the number of ECGs performed, and whether there was death or torsade de points (TdP). Auto-QTc for the CCT group and ECG-QTc for the control group (when available) were used to report daily maximum QTc.

In days with marked QTc prolongation (Long-QTc), defined as Auto-QTc ≥ 500 ms in the CCT group and ECG-QTc ≥ 500 ms in the control group, additional data were collected and included K, Ca, and Mg levels, medication adjustment (defined as stopping QT-prolonging medications), and electrolytes supplementation.

Outcomes

The prespecified primary outcome of the study was the proportion of new Long-QTc episodes (≥ 500 ms) in each group. Secondary outcomes were episodes of (TdP), the proportion of ECGs performed during the monitoring period, and the proportion of Long-QTc episodes that were
associated with guideline-recommended clinical response including medication adjustment or electrolyte supplementation. Progress notes were reviewed to record whether Long-QTc episodes were documented in notes by any physician.

**Automated QTc validation**

Two cardiac electrophysiologists (Eps) (W.A. and C.R.) blinded to the Auto-QTc over-read a total of 66 consecutive measurements (32% of all Auto-QTc) using a predefined protocol. Supplemental Figure S2 shows an example of manual QT measurement:

- Tangent method to determine the end of T-wave.
- Bazett’s formula for heart rate correction.
- Averaged QTc for 5 consecutive beats in atrial fibrillation.
- Adjusted QTc for wide QRS: adjusted QTc = QTc – (QRS – 120).

**Statistical analysis**

A formal, *a priori* calculation of sample size was carried out before collecting data. We estimated the proportion of Long-QTc to be 30% and 10% in the CCT group and control group, respectively. A sample size of 62 monitoring days in each group was calculated, which provides an 80% power to detect a statistically significant difference. Because of the uncertainty about the agreement between Auto-QTc and EP-QTc in detecting Long-QTc, we continued collecting data until we had > 62 monitoring days with EP-QTc measurements.

Continuous data were reported as median (interquartile range) and categorical data as numbers (percentages). Wilcoxon rank sum test, $\chi^2$ test, and Fisher exact test were used when appropriate to analyze outcome data. We used mixed effect multivariate logistic regression modelling to adjust for important confounders. Age was categorized into 2 groups on the basis of previous literature (≥ 68 and < 68 years). Correlation and agreement between Auto-QTc and EP-QTc were assessed with Pearson correlation coefficient ($\rho$) and $k$ statistics, respectively. Analyses were performed using SAS (version 9.4, SAS Institute, Inc, Cary, NC) and $P$ values of < 0.05 were considered statistically significant.

**Results**

We included 33 patients with 451 monitoring days: 14 patients (206 monitoring days) in the CCT group and 19 patients (245 monitoring days) in the control group.

**Patient characteristics**

Table 1 includes a summary of patient characteristics. Patients in the control group were older and had more confirmed COVID-19 cases whereas the CCT group had more female patients. Both groups had comparable comorbidities, baseline electrolyte levels, baseline QTc on ECG, and similar proportions of patients receiving QT-prolonging medications. Only 1 patient had QTc > 500 ms at baseline and was in the CCT group.

QT-prolonging antimicrobial therapy for confirmed COVID-19 included hydroxychloroquine/azithromycin combination in 3 patients, hydroxychloroquine alone in 1 patient, and azithromycin alone in 5 patients including the patient in the CCT group. In-hospital mortality was similar between the groups.

| Table 1. Patient characteristics |
|----------------------------------|
|                                | Control group (n = 19) | CCT group (n = 14) | $P$ |
|------|-------------------|-------------------|-----|
| Age, years | 67 (57-74) | 56 (41-63) | 0.036* |
| Female sex | 4 (21) | 7 (50) | 0.136 |
| Confirmed COVID-19 status | 8 (42) | 1 (7) | 0.046* |
| PMH | | |
| CAD | 2 (11) | 1 (7) | 1.0 |
| AF | 3 (16) | 1 (7) | 0.62 |
| HTN | 11 (58) | 4 (29) | 0.158 |
| CHF | 3 (16) | 3 (21) | 1.0 |
| DM | 8 (42) | 2 (14) | 0.131 |
| Stroke | 1 (5) | 1 (7) | 1.0 |
| Depression | 3 (16) | 0 (0) | 0.244 |
| CKD | 1 (5) | 1 (7) | 1.0 |
| Cirrhosis | 1 (5) | 2 (14) | 0.561 |
| COPD | 2 (11) | 3 (21) | 0.629 |
| Creatinine, $\mu$mol/L | 80 (62-95) | 99 (71-247) | 0.075 |
| K, mmol/L | 4.2 (3.7-4.6) | 4.2 (3.9-5) | 0.289 |
| Mg, mmol/L | 0.8 (0.8-0.9) | 0.9 (0.7-1.1) | 0.156 |
| Ca, mmol/L | 2.1 (2.2-2.2) | 2.1 (1.7-2.2) | 0.333 |
| Receiving QT-prolonging medications | 5 (26) | 4 (29) | 0.886 |
| QTc on admission ECG, ms | 445 (428-478) | 445 (431-490) | 0.614 |
| Average length of stay, days | 10 (9-12) | 10 (6-19) | 0.828 |
| In-hospital death | 6 (32) | 4 (29) | 1.0 |

Data are presented as median (interquartile range) or number (percentage).

AF, atrial fibrillation; CAD, coronary artery disease; CCT, continuous cardiac telemetry; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HTN, hypertension; PMH, medical history.

* Significant $P$ value.
Proportions of new marked Long-QTc

Long-QTc was more frequently detected in the CCT group compared with the control group (69/206 [34%] vs 26/245 [11%]; \( P < 0.0001 \)). Because important factors were not balanced between the 2 groups, we performed a sensitivity analysis adjusting for these factors (age, sex, COVID status, and the number QT-prolonging anti-COVID 19 therapies). Being in the CCT group remained significantly associated with Long-QTc (adjusted odds ratio, 4.10; 95% confidence interval, 2.47-6.83; \( P < 0.0001 \)). Two patients in each group had a single episode of Long-QTc and the rest had repeated episodes.

Also, because auto-QTc did not correct for wide QRS, we performed a second sensitivity analysis excluding patients with wide QRS. The CCT group remained significantly associated with more episodes of Long-QTc (63/199 [31%] vs 10/216 [14%]; \( P < 0.0001 \)).

Proportion of ECGs performed

ECGs were performed less frequently in the CCT group compared with the control group (32/206 [16%] vs 78/245 [32%]; \( P < 0.0001 \)).

Clinical response to new marked Long-QTc

Overall, 27/95 (28%) Long-QTc episodes were associated with electrolyte supplementation and none were associated with medication adjustment. Extended electrolytes were checked in 71/95 (75%) of Long-QTc episodes. There was no difference between the 2 groups in checking or supplementing extended electrolytes. In 37 episodes of Long-QTc where the Mg level was < 1 mmol/L, only 17 (46%) had Mg supplementation.\(^3\,6\,13\,14\) Table 2 depicts outcomes associated with each group and Figure 1 shows clinical response to Long-QTc episodes.

One episode of TdP was observed in the control group and none in the CCT group. ECG-QTc was 577 ms after the TdP episode and 565 ms 1 day earlier. Extended electrolytes were checked and supplemented on both days, but no medication adjustment was made (the patient was receiving propofol, which was not stopped).

Auto-QTc validation

There was strong correlation between Auto-QTc and EP-QTc (\( r = 0.8; P < 0.0001 \)) and excellent agreement in detecting Long-QTc (\( \kappa = 0.8; P < 0.008 \)). The sensitivity of Auto-QTc in detecting any episode of EP-QTc \( \geq 500 \) ms was 100% and the specificity was 84%. The difference between Auto-QTc and EP-QTc was assessed in 66 pairs and showed that Auto-QTc overestimated QTc by a median of 3 ms (interquartile range, 0-40 ms). Figure 2A shows the distribution of this difference and Figure 2B is a dot plot diagram of all 66 paired measurements. Because Auto-QTc overestimated QTc compared with EP-QTc, we performed a sensitivity analysis excluding Auto-QTc that was not validated by EP (ie, comparing EP-QTc vs ECG-QTc). The difference in the proportion of Long-QTc between the 2 groups remained significant (23/66 [35%] vs 26/245 [11%]; \( P < 0.0001 \)).

Discussion

Our study showed that continuous QT interval monitoring detects more episodes of prolonged QTc than standard of care. Also, the institution of CCT was associated with a reduction in the number of ECGs being performed, which is likely because of the availability of continuous QT monitoring for serial ECGs, notwithstanding potential residual confounding. Our findings have important clinical implications for COVID-19 and, potentially, non-COVID-19 patients who are treated with medications that are either known to be proarrhythmic or with an uncharacterized risk profile.

QT interval monitoring is the first step in the effort to mitigate the risk of ventricular arrhythmias in hospitalized patients.\(^3\) Although there are no clear recommendations to guide choosing the best strategy of QT monitoring, performing serial ECGs is the most common practice.\(^3\,6\,15\) This strategy, however, has several limitations. First, it neglects the dynamic nature of the QT interval.\(^15\) Sympathetic tone, hormones, medications, and electrolytes influence the QT interval and are highly variable during the course of the day of any hospitalized patient.\(^6\,17\) This explains why intermittent QT monitoring could miss periods of prolonged QT interval even if done daily. Second, the best time to assess QT interval after administration of any QT-prolonging medications is often unknown because the degree and timing of QT prolongation varies depending on the pharmacokinetics of the medication used, route of administration, and renal and hepatic function of the patient.\(^6\) This is particularly challenging when higher doses or new combinations of known proarrhythmic medications are used such as the use of high-dose

Table 2. Outcome data per group

|                          | Control (n = 245 days) | CCT (n = 206 days) | \( P \)   |
|--------------------------|-----------------------|--------------------|----------|
| Episodes of Long-QTc     | 26/245 (11)           | 69/206 (34)        | < 0.0001*|
| Daily ECGs performed during monitoring period | 78/245 (32)          | 32/206 (16)        | < 0.0001*|
| Episodes of Long-QTc during which extended electrolytes were checked | 20/26 (77)           | 51/69 (74)         | 0.763    |
| Any clinical response to Long-QTc\(^1\) | 5/26 (19)            | 22/69 (32)         | 0.223    |
| Physician notes documenting Long-QTc | 2/26 (8)             | 0 (0)              | 0.073    |
| Episodes of TdP          | 1 (0.4)               | 0 (0)              | 1.0      |

Data are presented as n (%) except where otherwise noted.

CCT, continuous cardiac telemetry; ECG, electrocardiogram; Long-QTc, marked QTc prolongation of \( \geq 500 \) ms; TdP, torsade de pointes.

* Significant \( P \) value.

\(^1\) These were only assessed in episodes of Long-QTc.
hydroxychloroquine and the combination of azithromycin/hydroxychloroquine during the current COVID-19 pandemic.3,18 Last, performing serial ECGs mandates additional contact with infected patients, which is particularly disadvantageous in patients with a highly infectious disease like COVID-19.

Although continuous QT monitoring is appealing, one needs to be cautious not to rely on the automated QTc readings provided by the monitoring system without validation. Indeed, our study showed that the automated QTc systematically overestimates manual QTc measurement by EPs. This is likely the result of using different methods to identify the end of the T wave and the failure of automated QTc measurements to adjust for wide QRS. However, this should not preclude using automated QTc measurements in daily practice because it could be used as a “screening” tool to identify QTc measurements that need to be verified by physicians. This is supported by the high sensitivity of automated QTc in detecting any episode of QTc ≥ 500 ms. Moreover, many experts recommend initiating electrolyte supplementation and stopping QT-prolonging medication at a threshold lower than 500 ms.1,12 As such, most episodes detected using the automated QTc measurement in our study likely fall in the category of episodes that deserve intervention.

Regardless of the strategy and method of QT interval monitoring used, one can only expect improvement in clinical outcomes if episodes of prolonged QTc are treated properly. Despite numerous recent publications recommending preventative measures in patients with prolonged QTc, most episodes with marked QTc prolongation in our study were not treated with these measures.1,12,19,20 This suggests that simply reporting the prolonged QTc is not enough to alert the primary team. Akin to the automated infectious disease consultation for Staphylococcus bacteremia and the automated notification of critical lab values used in many institutions, efforts to establish clinical pathways to better manage episodes of prolonged QTc are necessary.21,22 Jain et al.23 developed a protocol in which ECGs from COVID-19 patients were tagged for expedited review. An automated phone consult by the electrophysiology service was then initiated for any patient with prolonged QTc. This led to identifying significant numbers of prolonged QTc episodes and instituting relevant interventions. Future studies will need to examine whether...
these interventions lead to more adherence to recommended therapies and, more importantly, improvement in clinical outcomes.

Most patients in our study had more than 1 episode of marked QTc prolongation during their admission. This is likely because these patients have factors such as age, sex, ethnicity, and/or genetic variants that predispose them to prolonged QTc every time they are re-exposed to a risk factor. Only 1 of these episodes was associated with TdP, which is in line with previous reports. It is critical that this is not used to lighten our concerns about QTc prolongation. Although there are multiple risk factors for TdP, prolonged QTc is the single most important modifiable risk factor than can be treated effectively with low-risk interventions. As such, we should continue every effort to find the best strategy of preventing, detecting, and treating episodes of QTc prolongation.

Our study has several limitations. First, this was not a randomized clinical trial. However, differences in the baseline characteristics of and disease severity are unlikely to explain our results and that was supported by our adjusted analysis. Second, our results are specific to the QT interval monitoring algorithm by Philips, which might not be generalizable to other systems. The lack of QTc correction for wide QRS is an important limitation of this system. However, the difference between the 2 groups remained significant after excluding patients with wide QRS. As discussed previously, a strategy of using the automated system as a screening tool for marked QTc prolongation is practical and safe. Similarly, our study only included patients admitted to critical care units. These patients, however, typically receive more monitoring than patients admitted to non-critical care units and, as such, this is unlikely to bias the result away from the null. Last, the small number of ECGs performed in the CCT group prevent any meaningful analysis to correlate Auto-QTc with ECG-QTc. However, this is not necessary because manual QTc measurement from telemetry strips is a well accepted method that is endorsed by all relevant organizations and is been used in studies on hospital-acquired QTc prolongation.

In conclusion, we report herein an improvement in detecting episodes of marked QTc prolongation with the use of continuous QT monitoring in a cohort of patients with suspected or confirmed COVID-19. Screening QTc intervals with an automated QTc algorithm is feasible. Efforts to improve adherence to recommended therapies of prolonged QTc episodes is needed.

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Disclosures
The authors have no conflicts of interest to disclose.

References

1. Sapp JL, Alqarawi W, MacIntyre CJ, et al. Guidance on minimizing risk of drug-induced ventricular arrhythmia during treatment of COVID-19: a statement from the Canadian Heart Rhythm Society. Can J Cardiol 2020;36:948-51.
2. Mercuro NJ, Yen CF, Shim DJ, et al. Risk of QT interval prolongation associated with use of hydroxychloroquine with or without concomitant azithromycin among hospitalized patients testing positive for coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5:1036-41.
3. Chorin E, Wadhwa L, Magnani S, et al. QT interval prolongation and torsade de points in patients with COVID-19 treated with hydroxychloroquine/azithromycin. Heart Rhythm 2020;17:1425-33.
4. Lazzerini PE, Boujadir M, Capecci PL. COVID-19, arrhythmic risk, and inflammation: mind the gap! Circulation 2020;142:7-9.
5. Lazzerini PE, Capecci PL, Laghi-Pasini F. Systemic inflammation and arrhythmic risk: lessons from rheumatoid arthritis. Eur Heart J 2017;38:1717-27.
6. Drew BJ, Ackerman MJ, Funk M, et al. Prevention of torsade de points in hospital settings: a scientific statement from the American Heart Association and the American College of Cardiology Foundation. Circulation 2010;121:1047-60.
7. von Elm E, Altman DG, Egger M, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ 2007;335:806-8.
8. Zhou SH, Helfenbein ED, Lindauer JM, Gregg RE, Feld DQ. Philips QT interval measurement algorithms for diagnostic, ambulatory, and patient monitoring ECG applications. Ann Noninvasive Electrocardiol 2009;14(suppl 1):S3-8.
9. Bazett H. Analysis of the time-relationships of electrocardiograms. Heart 1920;7:35-70.
10. Lepeschkin E, Surawicz B. The measurement of the Q-T interval of the electrocardiogram. Circulation 1952;6:378-88.
11. Tooley L, Ouyang D, Hadley D, et al. Comparison of QT interval measurement methods and correction formulas in atrial fibrillation. Am J Cardiol 2019;123:1822-7.
12. Giudicessi JR, Noseworthy PA, Friedman PA, Ackerman MJ. Urgent guidance for navigating and circumventing the QTc-prolonging and torsadogenic potential of possible pharmacotherapies for coronavirus disease 19 (COVID-19). Mayo Clin Proc 2020;95:1213-21.
13. Tisdale JE, Jaynes HA, Kingery JR, et al. Development and validation of a risk score to predict QT interval prolongation in hospitalized patients. Circ Cardiovasc Qual Outcomes 2013;6:479-87.
14. Lazzerini PE, Bertolozzi I, Finizola F, et al. Proton pump inhibitors and serum magnesium levels in patients with torsades de pointes. Front Pharmacol 2018;9:363.
15. Page A, Aktaş MK, Soyata T, Zareba W, Couderc JP, “QT clock” to improve detection of QT prolongation in long QT syndrome patients. Heart Rhythm 2016;13:190-8.
16. Pham TV, Rosen MR. Sex, hormones, and repolarization. Cardiovasc Res 2002;53:740-51.
17. Magnano AR, Holleran S, Ramakrishnan R, Reifel JA, Bloomb_field DM. Autonomic nervous system influences on QT interval in normal subjects. J Am Coll Cardiol 2002;39:1820-6.
18. Gautret P, Lagier JC, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label
non-randomized clinical trial. Int J Antimicrob Agents 2020;56:105949.

19. Wu CI, Postema PG, Arbelo E, et al. SARS-CoV-2, COVID-19, and inherited arrhythmia syndromes. Heart Rhythm 2020;17:1456-62.

20. Roden DM, Harrington RA, Poppas A, Russo AM. Considerations for drug interactions on QTc interval in exploratory COVID-19 Treatment. J Am Coll Cardiol 2020;75:2623-4.

21. Martin L, Harris MT, Brooks A, Main C, Mertz D. Management and outcomes in patients with Staphylococcus aureus bacteremia after implementation of mandatory infectious diseases consult: a before/after study. BMC Infect Dis 2015;15:568.

22. Kuperman GJ, Teich JM, Tanasijevic MJ, et al. Improving response to critical laboratory results with automation: results of a randomized controlled trial. J Am Med Inform Assoc 1999;6:512-22.

23. Jain S, Workman V, Ganeshan R, et al. Enhanced electrocardiographic monitoring of patients with coronavirus disease 2019. Heart Rhythm 2020;17:1417-22.

24. Paulussen AD, Gilissen RA, Armstrong M, et al. Genetic variations of KCNQ1, KCNH2, SCN5A, KCNE1, and KCNE2 in drug-induced long QT syndrome patients. J Mol Med (Berl) 2004;82:182-8.

25. Splawski I, Timothy KW, Tateyama M, et al. Variant of SCN5A sodium channel implicated in risk of cardiac arrhythmia. Science 2002;297:1333-6.

26. Mitcheson JS, Chen J, Lin M, Calberson C, Sanguinetti MC. A structural basis for drug-induced long QT syndrome. Proc Natl Acad Sci U S A 2000;97:12329-33.

27. Locati EH, Zareba W, Moss AJ, et al. Age- and sex-related differences in clinical manifestations in patients with congenital long-QT syndrome: findings from the International LQTS Registry. Circulation 1998;97:2237-44.

28. Saleh M, Gabriels J, Chang D, et al. The effect of chloroquine, hydroxychloroquine and azithromycin on the corrected QT interval in patients with SARS-CoV-2 infection. Circ Arrhythm Electrophysiol 2020;13:e008662.

29. Jankelson L, Karam G, Becker ML, Chinitz LA, Tsai MC. QT prolongation, torsades de pointes and sudden death with short courses of chloroquine or hydroxychloroquine as used in COVID-19: a systematic review. Heart Rhythm 2020;17:1472-9.

30. Sandau KE, Funk M, Auerbach A, et al. Update to practice standards for electrocardiographic monitoring in hospital settings: a scientific statement from the American Heart Association. Circulation 2017;136:e273-344.

Supplementary Material
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