Prolonged QT predicts prognosis in COVID-19

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Abstract

Background

COVID-19 causes severe illness and multi-organ dysfunction. An abnormal electrocardiogram is associated with poor outcome, and QT prolongation during the illness has been linked to pharmacological effects. This study sought to investigate the effects of the COVID-19 illness on the corrected QT interval (QTc).

Method

For 293 consecutive patients admitted to our hospital via the emergency department for COVID-19 between 01/03/20 - 18/05/20, demographic data, laboratory findings, admission electrocardiograph and clinical observations were compared in those who survived and those who died within 6 weeks. Hospital records were reviewed for prior electrocardiograms for comparison with those recorded on presentation with COVID-19.

Results

Patients who died were older than survivors (82 vs 69.8 years, p<0.001), more likely to have cancer (22.3% vs 13.1%, p=0.034), dementia (25.6% vs 10.7%, p=0.034) and ischaemic heart disease (27.8% vs 10.7%, p<0.001). Deceased patients exhibited higher levels of C-reactive protein (244.6mg/L vs

146.5mg/L, p<0.01), troponin (1982.4ng/L vs 413.4 ng/L, p=0.017), with a significantly longer QTc interval (461.1ms vs 449.3ms, p=0.007). Pre-COVID electrocardiograms were located for 172 patients; the QTc recorded on presentation with COVID-19 was longer than the prior measurement in both groups, but was more prolonged in the deceased group (448.4ms vs 472.9ms, pre-COVID vs COVID, p<0.01). Multivariate Cox-regression analysis revealed age, C-reactive protein and prolonged QTc of >455ms (males) and >465ms (females) (p=0.028, HR 1.49 [1.04-2.13]), as predictors of mortality. QTc prolongation beyond these dichotomy limits was associated with increased mortality risk (p=0.0027, HR 1.78 [1.2-2.6]).

Conclusion

QTc prolongation occurs in COVID-19 illness and is associated with poor outcome.

Keywords: COVID-19, prolonged QTc, Electrocardiogram, Sars-Cov-2, mortality

Abbreviations

ARDS = Acute respiratory distress syndrome

ACE2 = Angiotensin-converting enzyme 2

COVID-19 = Coronavirus disease - 2019

ECG = Electrocardiogram/Electrocardiograph

g/L = grams per litre

µmol/L = micromole per litre

mmol/L = millimole per litre

mg/L = milligrams per litre

mm/mV = millimetres per millivolt

mm/s = millimetres per second

ms = milliseconds

ng/L = nanograms per litre

NEWS = National Early Warning Score

QTc = Corrected QT

Introduction

COVID-19 causes viral pneumonia and severe illness resulting in organ dysfunction including acute respiratory distress syndrome (ARDS) and acute cardiac injury and renal injury (1). There is also an increased incidence of arrhythmias, especially in the those requiring intensive care (2). As yet, few data are available regarding the effects of the infection on the electrophysiology of the heart. Electrocardiography (ECG) can be used to detect cardiac involvement in multisystem disorders, and often provides prognostic information. In COVID-19, left bundle branch block and ST segment deviation may be associated with increased risk of mortality (3). The effects on repolarisation remain unclear. A risk of QT prolongation was highlighted in cases of COVID-19 treated with hydroxychloroquine and Azithromycin, but the QT abnormality observed may have been more than just a pharmacological effect (4).

Method

We screened patients who were admitted to our institute via the emergency department with the Sars-Cov-2 virus infection at the height of the COVID-19 outbreak locally. In total, 406 patients presenting to the department tested positive for the infection between 1st March – 18th May 2020. Of these, 293 patients were recruited in to the study; 106 were excluded as they did not require hospital admission and were discharged from the emergency department and 7 were excluded due

to the presence of a paced cardiac rhythm. Data were collected and analysed for patient demographics, admission ECG, chest x-ray and blood biochemical and haematological profiles. The left ventricle ejection fraction was calculated by a certified echocardiographer using the Simpson's biplane method; when this was not possible, the visual estimation was accepted. A comparison was performed of patients who succumbed to the infection ('deceased' group) and those who remained alive to the time of last accessing the hospital record at >6 weeks after presentation ('survived' group). The study proposal was approved by the research ethics committee and complies with the principles of the Declaration of Helsinki.

Where appropriate continuous variables were conveyed as a mean ± standard deviation and categorical variables as a number and percentage. Statistical analysis was performed using the independent t-test and where applicable, the paired t-test to compare continuous variables. The Chi-squared test was applied to compare categorical variables. A p-value of <0.05 was regarded as statistically significant. A multivariate regression analysis (Prism 9.0.0, Graphpad software, CA, USA) and a Cox-regression analysis (SPSS v26, IBM Corp., Chicago, IL, USA) was performed for variables associated with mortality; Kaplan-Meier curve was used for survival analysis.

ECG analysis

All patients underwent a standard 12-lead ECG at 25 mm/s paper speed and amplitude of 10 mm/mV (MAC 5500 HD ECG system, GE healthcare, Chicago, IL, USA) on admission. This was stored in the patient electronic medical records on the hospital server. For all patients included in this study, this baseline ECG was retrieved from the electronic records and analysed. During the study time-frame, testing for COVID-19 in the UK was performed only in a hospital setting, and the delay

from the performance of a test to the availability of a diagnosis was 24-72 hours. At the time of recording of the baseline ECG, the diagnosis of COVID-19 had therefore not been confirmed in any of our patients, so no specific therapy had been commenced.

Basic information including rhythm, rate, QRS duration and morphology, corrected QT interval (QTc), ST segment deviation and T-wave changes were derived from the baseline ECG. The QTc was calculated manually by a cardiologist. The QT intervals from all leads of the individual patient ECG were screened and the lead with the longest QT duration was accepted (5). Measurement was from the onset of the Q-wave to the T-wave offset, which was the point of intersection of the downward slope tangent-line with the baseline (**figure 1**) (5). Correction was performed using Bazett's formula (6). Corrected QT clinical limits of >450 milliseconds (ms) for males and >460 ms for females were accepted as prolonged (7). ECGs showing an abnormal prolonged QTc were re-checked by an experienced cardiac electrophysiologist. For all patients included in the study, the pre-existing medical record was searched for a prior ECG. These pre-COVID ECGs, when available, were analysed in the same manner as the baseline ECG.

Results

In this study the deceased patients (n=133) were older (82±10.5 vs 69.8±17.6 years, p<0.001) with a significantly higher proportion having a prior diagnosis of cancer (22.3% vs 13.1%, p=0.034),

ischaemic heart disease (27.8% vs 10.7%, p<0.001) and dementia (25.6% vs 10.7%, p<0.001). They were sicker on arrival to the emergency department (4.02 vs 3.24 NEWS score, p=0.015), were more likely to require an ITU admission (15.8% vs 6.9%, p=0.015) and they experienced a significantly longer hospital stay (10.7 ± 8.2 vs 8.8 ± 7.9 days, p=0.047). There was a similar proportion of male patients in both groups (55.6% vs 59.4%, deceased vs survived, respectively, p=0.52) with similar clinical observations on admission including heart rate (91.9 vs 90.7 beats per minute, deceased vs survived, p=0.64) and temperature (37.2°C vs 37.3°C, deceased vs survived, p=0.728); the baseline respiratory rate was significantly faster in the deceased cohort (23.9 vs 22 breaths per minute, deceased vs survived, p=0.007) **(table 1)**.

Blood biochemistry on admission revealed a similar level of potassium (p=0.5), adjusted calcium (p=0.3) and magnesium (p=0.3) in the deceased and those who survived. There was however a significantly higher level of C-reactive protein (CRP) (p<0.001), high-sensitivity cardiac troponin I (p=0.017) and creatinine (p=0.003) noted in the deceased group. Troponin was found to be elevated above the reference range (>46 ng/l) in a significantly higher proportion of deceased patients (44.4% vs 12.4%, p<0.001) (**table 1**).

ECG analysis of both cohorts revealed a significantly longer corrected QT interval on the baseline ECG for the patients who subsequently died (461.1ms vs 449.3ms, deceased vs survived, p=0.007) in the context of a similar QRS duration (95.5ms vs 92.1ms, deceased vs survived, p=0.181) and similar left ventricular function (52.3% vs 55.5%, deceased vs survived, p=0.053) **(table 1)**. For the deceased patients in whom a pre-COVID ECG was available (n=63), the QT interval was found to have increased significantly from the pre-COVID ECG to the baseline ECG on presentation with COVID

(448.4 vs 472.9 ms, respectively, p<0.001); this increase was also observed in those who survived (n=109; 435.1 vs 451 ms, pre-COVID vs COVID, p<0.001) but the degree of prolongation was greater in the patients who subsequently died **(figure 2)**. Of the cases found to have a prolonged QTc, troponin was higher in the deceased patients compared to those who survived, although this difference did not reach statistical significance (2002.5 vs 1115.7 ng/L, respectively, p=0.52).

Predictors of mortality

Multivariate regression analysis was performed for predictors of mortality. This revealed that age (OR 1.11 [1.07-1.16], p<0.001), CRP (OR 1.013 [1.008-1.02], p<0.001) and QTc (OR 1.02 [1.0096-1.04], p=0.001) were significantly associated with an increased risk of mortality. A Cox-regression analysis was also performed which identified Age and CRP as independent variables associated with mortality. Prolonged QTc was also highlighted as an independent predictor in this analysis (**table 2**). All patients with a prolonged QTc in the fourth quartile (>469 ms) were associated with an increased risk of mortality comparatively to patients in the lower quartiles (p=0.006, HR 1.98 [1.2-3.2]) (**figure 3**). Gender discrimination revealed that patients exhibiting a corrected QT-prolongation exceeding dichotomy limits of >455 ms (male) and >465 ms (female) were less likely to survive compared to patients with a normal QTc (p<0.01, HR 1.78 [1.2-2.6]) (**figure 4**).

Discussion

We have shown that the QTc interval lengthens during COVID-19 infection, and that the degree of lengthening is greater in those who subsequently die during the illness. This finding was based on the admitting ECG before exposure to any pharmaceutical known to prolong the QT-interval, and is suggestive of mechanisms beyond cardiotoxicity that may alter ventricular repolarisation (4)(8). Complementing previous reports of ECG abnormalities in COVID-19 (3)(4), this ECG anomaly may also be associated with poor outcome and therefore the findings of this study could have meaningful clinical implications.

The mechanism by which the COVID-19 infection prolongs ventricular repolarisation remains speculative: The Sars-Cov-2 virus has a high affinity for the ACE2 receptor and through its occupancy of this receptor can lead to over-expression of angiotensin-II (9). An inhibitory effect exerted by angiotensin-II on the rapidly activating components of myocyte delayed rectifier potassium current (I_{Kr}) has been described previously and may result in prolonged action potential duration, thus QT prolongation (10). Cardiac injury may also be a contributing factor as it is an established feature of COVID-19 infection (8) and is associated with an increased incidence of ventricular arrhythmia (11). In our study cardiac injury was more prevalent in the deceased cohort, as evidenced by a higher degree of troponin leak in this group (1982.4 vs 413.4 ng/L, p=0.017) and greater proportion of cases with a troponin level raised above the reference range than the patients who survived.

COVID-19 associated QT-prolongation may also be a secondary feature, reflecting the severity of a multi-system illness. In our study, the deceased patients were significantly more unwell on-admission as indicated by their higher National Early Warning Score (NEWS), a United Kingdom adopted scoring system implemented to detect patients requiring critical care (12). The intense inflammatory response characteristic of COVID-19 could produce QT prolongation both by direct and indirect mechanisms (11). The up-regulation of angiotensin-II by Sars-Cov-2 via binding to the ACE2 receptor can result in excessive inflammation and injury (9); the QTc could be an expression of the degree of inflammation. This is consistent with reports which have indicated that ITU stay was associated with QT prolongation (13) and patients admitted to ITU were disposed to arrhythmias (1)(2).

The multivariate analysis revealed that prolonged QTc on presentation was independently associated with an increased risk of mortality in COVID-19 (p=0.001). This finding has rarely been reported and could easily have been overlooked (3)(14). Romero et al demonstrated that new T-wave inversion in COVID-19 was associated with mortality (14). The ECGs reproduced in their manuscript to illustrate this T-wave inversion also demonstrate marked prolongation of the QTc, although this finding was not remarked upon and the interval was apparently not measured. Lanza et al did find a prolonged QT in a small proportion (5.8%) of COVID-19 patients (3). By treating QT prolongation as a binary variable, we believe that previous authors may have missed instances in which the interval was prolonged beyond the level that was normal for that patient, but did not exceed the range defined as normal for the population. By contrast, we measured the QTc in all patients and compared the results both to the reference range and when available, to the pre-COVID value in the same patient. This difference in methodology may have given us a greater capacity to detect the effects of COVID-19 on ventricular repolarisation.

QT-prolongation is not a binary event and the accepted definitions of a prolonged QTc (>450 ms in male; >460 ms in female) (7) are designed for application in a healthy population for predicting risk of ventricular arrhythmia. In our cohort, patients expressing a QTc in the fourth quartile (>469 ms) were likely to succumb to the illness. This is in keeping with prior evidence. Previous large observational studies showed a significantly increased all-cause mortality risk at >460 ms (15)(16), with accentuated risk as the QT lengthens further (17)(18). Using the Cox-regression analysis, we also identified QTc limits of >455 ms in males and >465 ms in females as the gender discriminated optimum dichotomy points for the association with mortality. This gender difference of 10 ms is also consistent with the literature (7) and studies with gender QTc specificities have indicated an augmented mortality risk in males with a QTc of >450 ms (18) and in females with a QTc ranging over 460 ms (19) and 470 ms (18).

The QT-interval responds to changes in heart rate (20) and body temperature (21) and is sensitive to electrolyte disturbance, owing to its dynamic nature. All methods of QT interval correction for heart rate are vulnerable to inter-individual variation and all have proved inaccurate at extremes of the heart rate spectrum. Within our series the groups are well matched for the baseline heart rate and metabolic state, and therefore it is unlikely these factors can explain the differences in the QT interval. The association between QTc prolongation and mortality is also unlikely to be affected by the heart-rate correction formula used (16).

Clinical implication

Prolongation of the QTc in COVID-19 infection is a harbinger of death and may represent the severity of the illness. The findings of our study can be used to triage COVID-19 patients and tailor treatment according to their mortality risk. Our observation should also prompt more caution in the use of QTc prolongation medications for COVID-19 patients during the peak phase of the illness. The long-term effect of Sars-Cov-2 virus on the QT interval is yet to be determined although presumably it should normalise. Future risk of acquired long-QT syndrome in these patients however remains a theoretical concern. Non-cardiac causes of QT prolongation are common and include circadian rhythm, age and drug-induced abnormal repolarisation (5). Long term QTc surveillance may be beneficial to monitor for risk of sudden cardiac death.

Limitations

The ECGs analysed in this series were recorded at the arbitrary time-point of first arrival at our hospital. Therefore, the time interval between the onset of COVID-19 and ECG measurement cannot be accurately determined which may have an implication to the QTc prolongation as it is possible that the QTc prolongation is a dynamic process, it may worsen as the condition worsens or improves when one recovers. This potential wide spectrum of disease severity is difficult to quantify and correct for statistically. Also, the Bazett's corrected QT-interval at high heart rates may be over-

estimated but it is a consistent approach and the use of this formula should not affect the mortality risk associated with prolonged-QT.

Conclusion

Prolongation of the QTc interval is associated with mortality in COVID-19 infection and appears to be independent of drug-toxicity. Frequent QTc monitoring on ECG is advocated in the risk stratification of COVID-19 patients.

Contributorship statement

All the authors have contributed significantly to this work. Data collection was completed by Zaki Akhtar, Victoria Ewasiuk and Louise Gregory. The corrected QT measurements were verified by Dr Mark M. Gallagher and the methodology by Dr Yee Guan Yap and Dr Zhong Chen. Data analysis was performed by Zaki Akhtar, Ahmed I. Elbatran and Sumeet Sharma. The manuscript drafting was undertaken by Zaki Akhtar, Mark M. Gallagher, Yee Guan Yap, Lisa WM Leung and Sumeet Sharma. Critical review was performed by all the authors, in particular Brendan Madden, Aodhan Breathnach, Zhong Chen and David S. Fluck. Final approval received significant contribution from all the authors.

References

1. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA. 2020 Mar 17;323(11):1061.

2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020 Feb;395(10223):497–506.

3. Lanza GA, De Vita A, Ravenna SE, D'Aiello A, Covino M, Franceschi F, et al. Electrocardiographic findings at presentation and clinical outcome in patients with SARS-CoV-2 infection. EP Eur. 2020 Oct 23;euaa245.

4. Anupama BK, Adhikari S, Chaudhuri D. Prolonged QT Interval in a Patient With Coronavirus Disease-2019: Beyond Hydroxychloroquine and Azithromycin. J Investig Med High Impact Case Rep. 2020 Jan;8:232470962094840.

5. Camm AJ, Yap YG, Malik M, editors. Measurement of the QT Interval and Repolarization Assessment. In: Acquired Long QT Syndrome [Internet]. Malden, Massachusetts, USA: Blackwell Publishing; 2004 [cited 2020 Dec 1]. p. 24–59. Available from: http://doi.wiley.com/10.1002/9780470994771.ch3

6. Asensio E, Acunzo R, Uribe W, Saad EB, Sáenz LC. Recommendations for the measurement of the QT interval during the use of drugs for COVID-19 infection treatment. Updatable in accordance with the availability of new evidence. J Interv Card Electrophysiol. 2020 Nov;59(2):315–20.

7. Rautaharju PM, Surawicz B, Gettes LS. AHA/ACCF/HRS Recommendations for the Standardization and Interpretation of the Electrocardiogram. J Am Coll Cardiol. 2009 Mar;53(11):982–91.

8. Merino JL, Martínez-Cossiani M, Iniesta A, Escobar C, Rey JR, Castrejón-Castrejón S. COVID-19 and QT interval prolongation: more than just drug toxicity? EP Eur. 2020 Oct 1;22(10):1479–1479.

9. Ni W, Yang X, Yang D, Bao J, Li R, Xiao Y, et al. Role of angiotensin-converting enzyme 2 (ACE2) in COVID-19. Crit Care. 2020 Dec;24(1):422.

10. Wang YH, Shi CX, Dong F, Sheng JW, Xu YF. Inhibition of the rapid component of the delayed rectifier potassium current in ventricular myocytes by angiotensin II via the AT1 receptor. Br J Pharmacol. 2008 May;154(2):429–39.

11. Lazzerini PE, Boutjdir M, Capecchi PL. COVID-19, Arrhythmic Risk, and Inflammation: Mind the Gap! Circulation. 2020 Jul 7;142(1):7–9.

12. Zaidi H, Bader-El-Den M, McNicholas J. Using the National Early Warning Score (NEWS/NEWS 2) in different Intensive Care Units (ICUs) to predict the discharge location of patients. BMC Public Health. 2019 Dec;19(1):1231.

13. Jain S, Workman V, Ganeshan R, Obasare ER, Burr A, DeBiasi RM, et al. Enhanced electrocardiographic monitoring of patients with Coronavirus Disease 2019. Heart Rhythm. 2020 Sep;17(9):1417–22.

14. Romero J, Alviz I, Parides M, Diaz JC, Briceno D, Gabr M, et al. T-wave inversion as a manifestation of COVID-19 infection: a case series. J Interv Card Electrophysiol Int J Arrhythm Pacing. 2020 Oct 31;

15. Okin PM, Devereux RB, Howard BV, Fabsitz RR, Lee ET, Welty TK. Assessment of QT Interval and QT Dispersion for Prediction of All-Cause and Cardiovascular Mortality in American Indians: The Strong Heart Study. Circulation. 2000 Jan 4;101(1):61–6.

16. de Bruyne MC, Hoes AW, Kors JA, Hofman A, van Bemmel JH, Grobbee DE. Prolonged QT interval predicts cardiac and all-cause mortality in the elderly. The Rotterdam Study. Eur Heart J. 1999 Feb;20(4):278–84.

17. Mercuro NJ, Yen CF, Shim DJ, Maher TR, McCoy CM, Zimetbaum PJ, 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 Sep 1;5(9):1036–41.

18. Straus SMJM, Kors JA, De Bruin ML, van der Hooft CS, Hofman A, Heeringa J, et al. Prolonged QTc Interval and Risk of Sudden Cardiac Death in a Population of Older Adults. J Am Coll Cardiol. 2006 Jan;47(2):362–7.

19. Ishikawa J, Ishikawa S, Kario K. Relationships between the QTc interval and cardiovascular, stroke, or sudden cardiac mortality in the general Japanese population. J Cardiol. 2015 Mar;65(3):237–42.

20. Aytemir K, Maarouf N, Gallagher MM, Yap YG, Waktare JEP, Malik M. Comparison of Formulae for Heart Rate Correction of QT Interval in Exercise Electrocardiograms. Pacing Clin Electrophysiol. 1999 Sep;22(9):1397–401.

21. Van Der Linde HJ, Van Deuren B, Teisman A, Towart R, Gallacher DJ. The effect of changes in core body temperature on the QT interval in beagle dogs: a previously ignored phenomenon, with a method for correction: Temperature and QT interval. Br J Pharmacol. 2008 Aug;154(7):1474–81.
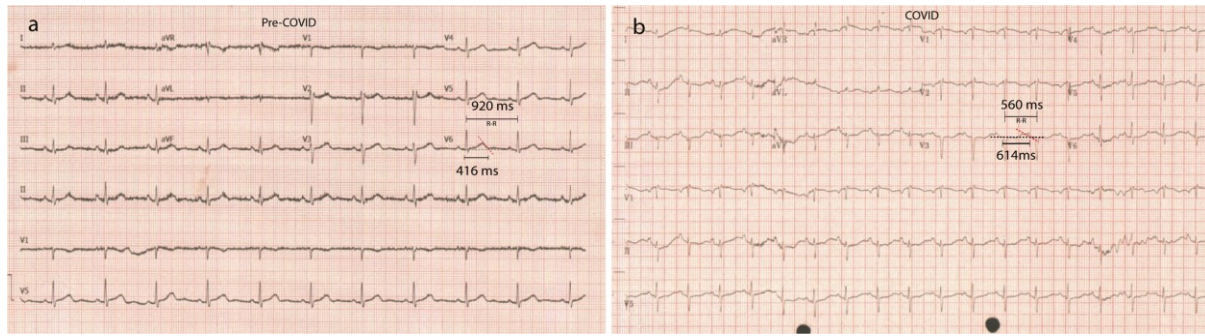
Figure 1: ECG example from the deceased group with QT measurements

a) Pre-COVID and **b)** COVID admission ECG from a deceased patient. There is prolongation of the

QTc with the COVID-19 illness. The annotations demonstrate the QT interval and the R-R interval
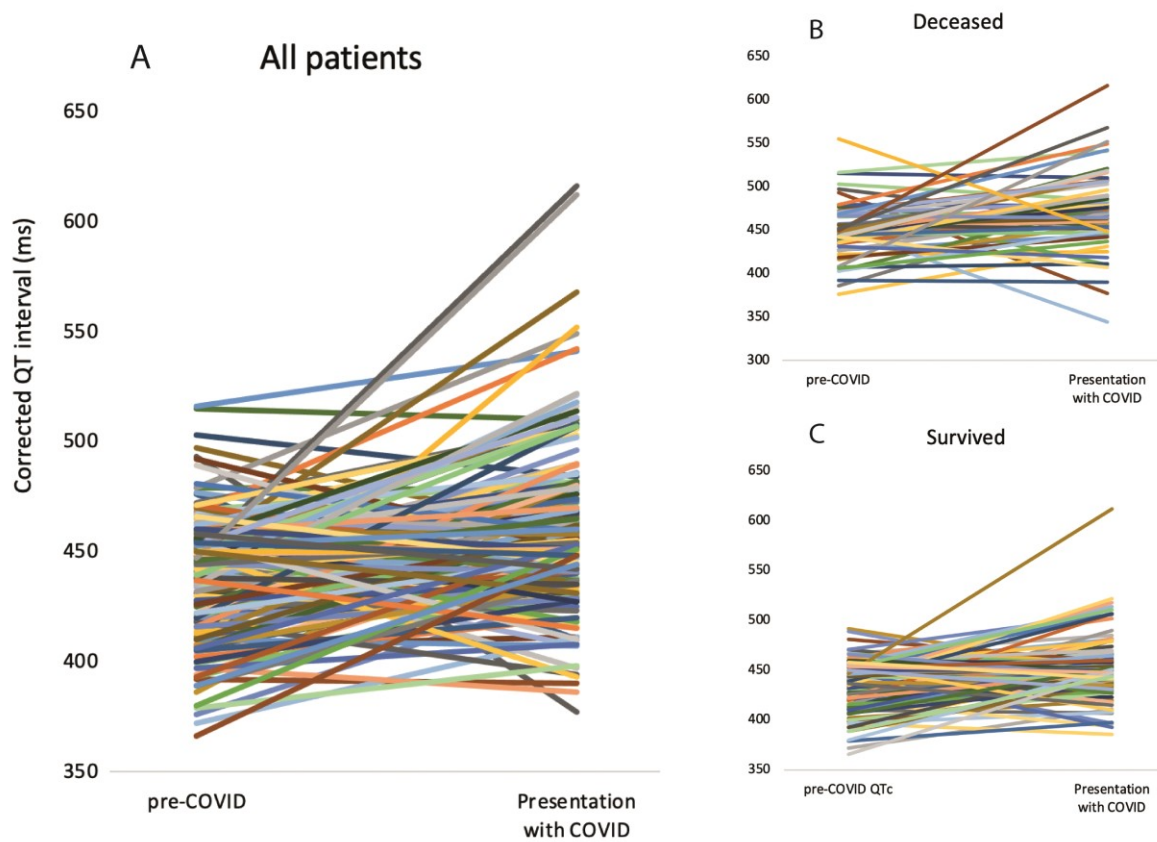
used for correction.

Figure 2: Individual changes of the QTc

(A) There is an overall trend of prolonging QTc with the Covid-19 infection. There was significant prolongation of the QTc from pre-COVID measurement in the **(B)** deceased (p<0.001) and the **(C)** survived patients (p<0.001). The degree of prolongation was notably greater in the deceased patients.
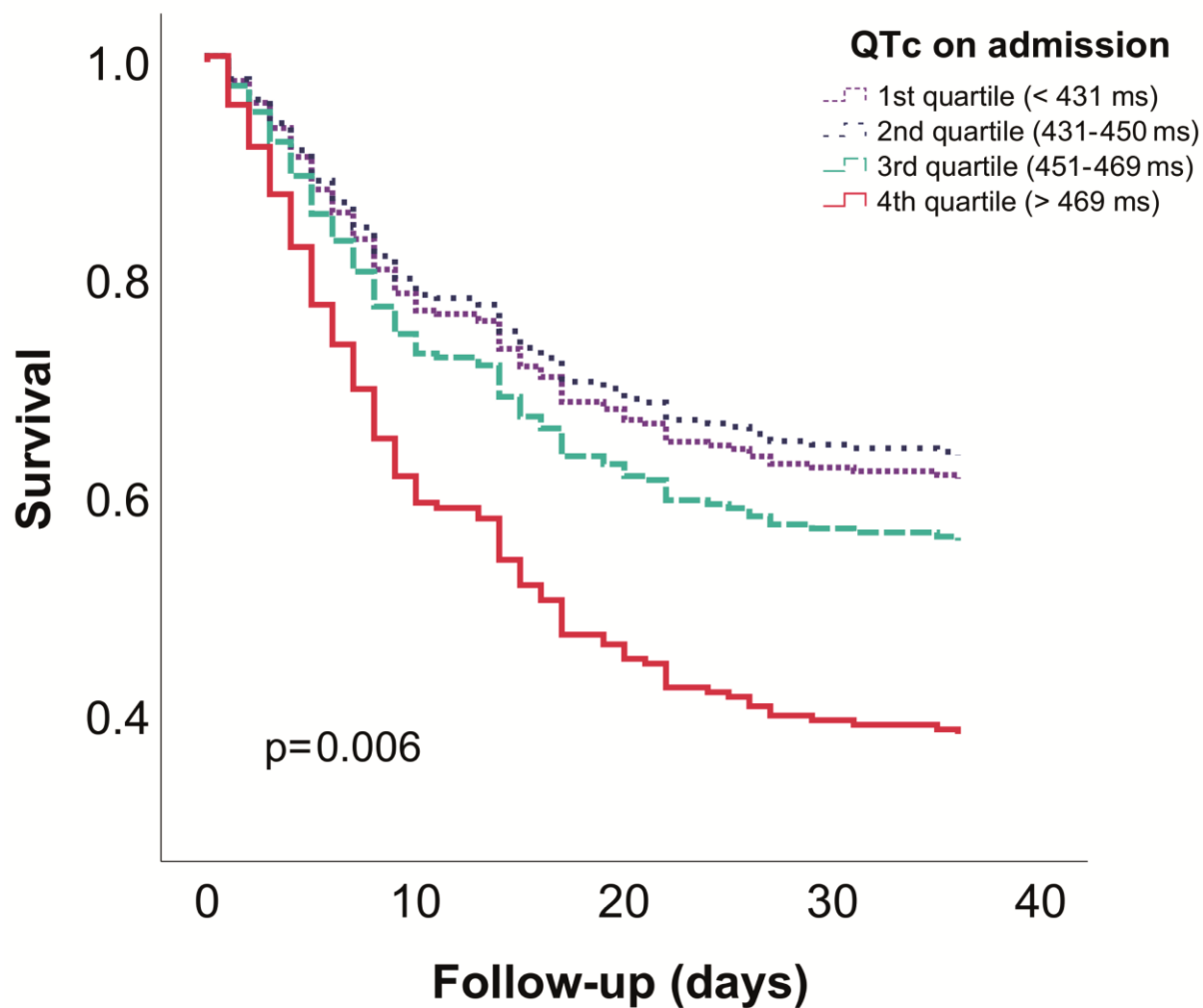
Figure 3: Cox-survival plot comparing mortality risk in QTc quartiles

In our cohort, a prolonged corrected QT-interval in the fourth quartile (>469 ms) was associated with

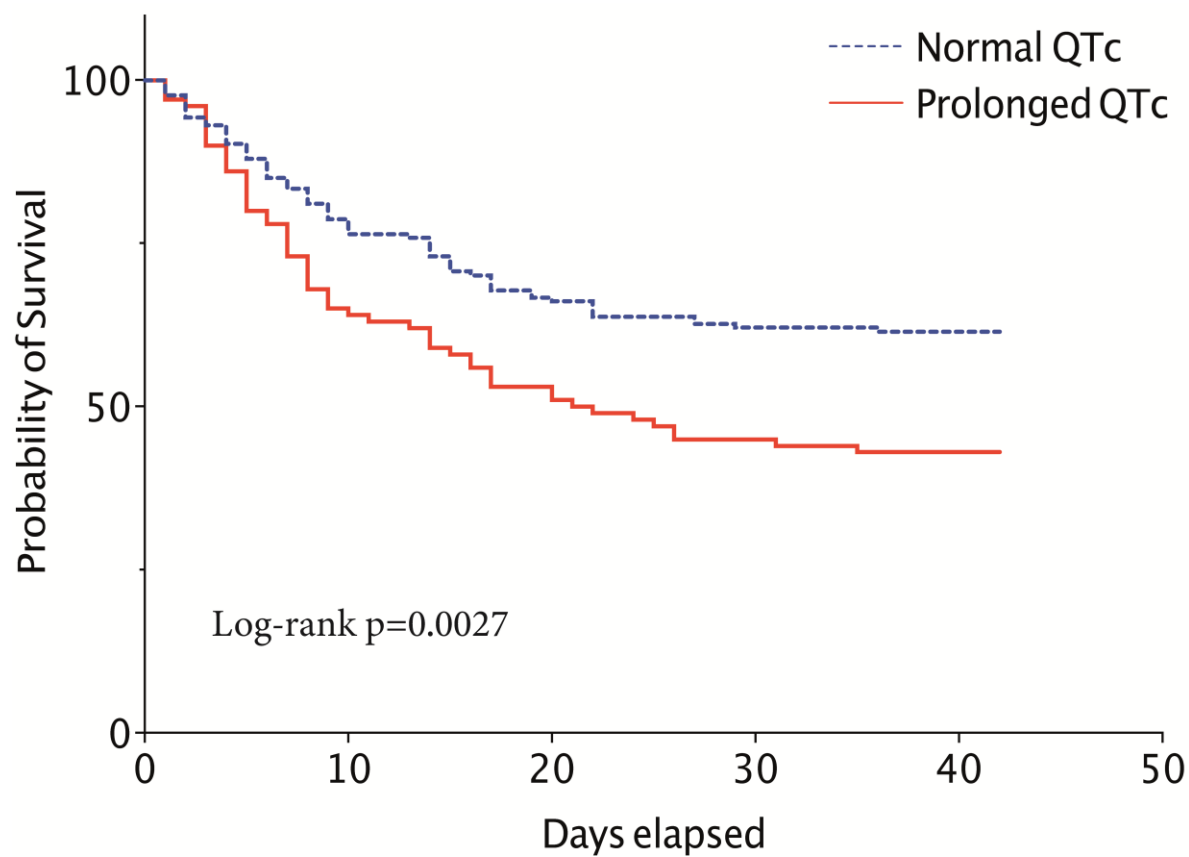an increased risk of mortality when compared to the lower quartiles (p=0.006, HR 1.98 [1.2-3.2]).

Figure 4: Kaplan-Meier survival curve of patients with a prolonged QTc and normal QTc

At 6 weeks from the date of admission, the probability of survival in patients with a prolonged QTc (>455ms male; >465ms female) was significantly lower than those patients who had a normal QTc (p=0.0027, HR 1.78 [1.2-2.6]).

Table 1: Patient demographics of both cohorts

	Deceased	Survived	p-value
N=	133	160	
Age (years)	82.0 ± 10.5	69.8 ± 17.6	<0.001
Male	74 (55.6%)	95 (59.4%)	0.52
Hospital stay (days)	10.7 ± 8.2	8.8 ± 7.9	0.047
ITU/HDU admission	21 (15.8%)	11 (6.9%)	0.015
Diabetes	34 (25.6%)	44 (27.5%)	0.71
Hypertension	84 (63.2%)	94 (58.8%)	0.061
Pre-existing lung condition	28 (21.1%)	35 (21.9%)	0.86
Cancer	30 (22.3%)	21 (13.1%)	0.034
Atrial Fibrillation	74 (55.6%)	82 (51.3%)	0.45
IHD	37 (27.8%)	17 (10.7%)	<0.001
Dementia	34 (25.6%)	17 (10.7%)	<0.001
Stroke	21 (15.8%)	15 (9.4%)	0.096
CKD	21 (15.8%)	23 (14.4%)	0.74
LVEF (%)	52.3 ± 11.3	55.5 ± 6.4	0.053

Lowest Hb (g/L)	105.9 ± 25.1	117.7 ± 20.7	<0.001
Troponin raised	59 (44.4%)	20 (12.5%)	<0.001
Cardiac Troponin (ng/L)	1982.4 ± 5780	413.4 ± 2815	0.017
CRP (mg/L)	244.6 ± 116.4	146.5 ± 101.1	<0.001
Creatinine (µmol/L)	162.4 ± 106.4	122.9 ± 113.4	0.003
D-Dimer (ng/mL)	5523.3 ± 5138	3872 ± 8917	0.347
On admission:			
Potassium (mmol/L)	4.1 ± 0.6	4.08 ± 0.5	0.537
Magnesium (mmol/L)	0.83 ± 0.18	0.8 ± 0.12	0.314
Calcium (mmol/L)	2.32 ± 0.14	2.3 ± 0.14	0.313
Atrial fibrillation	43 (32.3%)	39 (24.4%)	0.13
Bundle branch block (>120 ms)	15 (11.3%)	14 (8.8%)	0.47
QRS duration (ms)	95.5 ± 22.9	92.1 ± 18.6	0.181
QTc (ms)	461.1 ± 37.6	449.3 ± 32.5	0.007
Prolonged QTc (>450ms male/>460ms female)	61 (45.9%)	48 (30%)	0.005
Male QTc	462.1 ± 38.5	448.1 ± 33.4	0.018
Female QTc	456.5 ± 41.3	451.1 ± 31.7	0.44
Heart Rate (beats per minute)	91.9 ± 20.6	90.7 ± 21.3	0.636

Temperature (°C)			
	37.2 ± 0.91	37.3 ± 1.1	0.728
Respiratory rate (breaths per minute)	23.9 ± 6	22 ± 5.6	0.007
National Early Warning Score	4.02 ± 2.8	3.24 ± 2.5	0.015

The patient demographics of both cohorts in addition to the biochemistry and haematological profile during the admission. The electrolytes, ECG intervals and clinical observations were recorded at the onset of admission, on arrival to the emergency department ("**On admission"**).

Table 2: Multivariate regression analyses for mortality

Multivariate regression analysis				
Variable	**Odds Ratio**	**UCL**	**LCL**	**p-value**
Age on admission	1.113	1.16	1.073	<0.0001
C-reactive protein	1.013	1.019	1.008	<0.0001
ECG: prolonged QTc	1.022	1.04	1.0096	0.001
Multivariate Cox-regression analysis				
Variable	**Hazard ratio**	**UCL**	**LCL**	**p-value**
Age on admission	1.04	1.062	1.027	<0.001
C-reactive protein	1.003	1.001	1.004	0.002
***ECG: prolonged QTc**	1.49	2.127	1.04	0.028

*prolonged QTc: >455ms in male, >465ms in female patients

Prolonged QTc was a significantly independent variate associated with mortality, reducing the odds

of survival. In the Cox-regression analysis, prolonged QTc (>455ms [male] and >465ms [female]), age

and C-reactive protein were also independently associated with mortality.