QTc interval prolongation, inflammation, and mortality in patients with COVID-19

Simone Gulletta1 · Paolo Della Bella1 · Luigi Pannone2 · Giulio Falasconi2 · Lorenzo Cianfanelli2 · Savino Altizio2 · Elena Cinel2 · Valentina Da Prat3 · Antonio Napolano2 · Giuseppe D’Angelo1 · Luigia Brugliera4 · Eustachio Agricola2,5 · Giovanni Landoni2,6 · Moreno Tresoldi3 · Patrizia Querini Rovere2,3 · Fabio Ciceri2,7 · Alberto Zangrillo2,6 · Pasquale Vergara1

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Abstract

Purpose Systemic inflammation has been associated with corrected QT (QTc) interval prolongation. The role of inflammation on QTc prolongation in COVID-19 patients was investigated.

Methods Patients with a laboratory-confirmed SARS-CoV-2 infection admitted to IRCCS San Raffaele Scientific Institute (Milan, Italy) between March 14, 2020, and March 30, 2020 were included. QTc-I was defined as the QTc interval by Bazett formula in the first ECG performed during the hospitalization, before any new drug treatment; QTc-II was the QTc in the ECG performed after the initiation of hydroxychloroquine drug treatment.

Results QTc-I was long in 45 patients (45%) and normal in 55 patients (55%). Patients with long QTc-I were older and more frequently males. C-Reactive protein (CRP) and white blood cell (WBC) count at hospitalization were higher in patients with long QTc-I and long QTc-II. QTc-I was significantly correlated with CRP levels at hospitalization. After a median follow-up of 83 days, 14 patients (14%) died. There were no deaths attributed to ventricular arrhythmias. Patients with long QTc-I and long QTc-II had a shorter survival, compared with normal QTc-I and QTc-II patients, respectively. In Cox multivariate analysis, independent predictors of mortality were age (HR = 1.1, CI 95% 1.04–1.18, p = 0.002) and CRP at ECG II (HR 1.1, CI 95% 1.0–1.1, p = 0.02).

Conclusions QTc at hospitalization is a simple risk marker of mortality risk in COVID-19 patients and reflects the myocardial inflammatory status.

Keywords COVID-19 · Inflammation · QTc · QT interval · SARS-CoV-2

Abbreviations

COVID-19 Coronavirus disease 2019
CRP C-Reactive protein
SARS-CoV-2 Severe acute respiratory syndrome coronavirus 2
WBS White blood cells

Simone Gulletta and Paolo Della Bella equally contributed to the study and are shared first authors.

Pasquale Vergara
pasqualevergara@hotmail.com

1 Arrhythmia Unit and Electrophysiology Laboratories, IRCCS San Raffaele Scientific Institute, Milan, Italy
2 IRCCS San Raffaele Scientific Institute, Vita-Salute University, Milan, Italy
3 Division of Immunology, Transplantation and Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy
4 Department of Rehabilitation and Functional Recovery, IRCCS San Raffaele Scientific Institute, Milan, Italy
5 Cardiac Imaging Unit, Cardio-Thoracic Department, IRCCS San Raffaele Scientific Institute, Milan, Italy
6 Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute, Milan, Italy
7 Department of Hematology and Stem Cell Transplantation, IRCCS San Raffaele Scientific Institute, Milan, Italy
1 Introduction

Since December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was associated with coronavirus disease 2019 (COVID-19) [1–4]. The clinical spectrum of COVID-19 is wide, encompassing asymptomatic infection, mild upper respiratory tract illness, and acute respiratory distress syndrome, with a high mortality rate [5–7]. Despite multiple advanced critical care interventions, acute respiratory distress syndrome in COVID-19 patients is still associated with prolonged ventilation and high short-term mortality [8]. Small case series reported cardiac arrhythmias, cardiomyopathy, and cardiac arrest as terminal events in patients with COVID-19 [9–13].

Arrhythmias in COVID-19 patients are related to multiple factors including myocardial injury, systemic and local inflammation, QTc-prolonging drugs, and electrolytic imbalances [14]. QTc prolongation plays a major role in ventricular arrhythmias (VAs) in the setting of acute infection. According to the “multi-hit theory,” systemic inflammation itself significantly prolongs QTc interval, thus contributing to increase the risk of cardiac arrest [15]. The risk of QTc prolongation in COVID-19 has been reported to be higher in patients treated with the anti-malarian agent hydroxychloroquine, even if the correlation of this event with arrhythmias and in general cardiovascular adverse events is unclear [16]. The purpose of the present study was to evaluate the effects of inflammation and hydroxychloroquine on QTc interval in COVID-19 patients and to correlate these findings with the clinical outcome.

2 Methods

This is a single-center, retrospective study including 100 consecutive patients with a laboratory-confirmed COVID-19, admitted to the Emergency Rooms (ER) of the San Raffaele University Hospital (Milan, Italy) between March 14 and March 30, 2020.

2.1 Data collection

Upon presentation, a nasopharyngeal swab (COPAN Diagnostic, Inc., Murrieta, CA) was obtained in each patient to test for SARS-CoV-2 and processed in a local laboratory with RT-PCR assay. Hs-Troponin T (cTn-T) was obtained with Elecsys® Troponin T-high sensitive assay, at admission (cTn-T-adm) and peak (cTn-T-peak) in all patients, and a cutoff of 15 ng/mL was used based on the upper 99th percentile. Clinical and laboratory data were retrospectively collected on a shared electronic medical record. Deaths were collected on a daily basis, and causes of death were recorded. Clinical data were extracted from the electronic medical records and merged with the ECG data; data were carefully reviewed and confirmed by two independent researchers to guarantee the accuracy of the data extraction (EC and VDP). The primary endpoint of the study was death for any cause. Atrial and ventricular arrhythmia data were collected. The study complied with the Declaration of Helsinki; the Ethic Committee approved the study [17].

2.2 12-Lead ECG

Standard resting 12-lead ECG was obtained in all patients using a MAC 5500 digital ECG recorder (GE Medical Systems, Milwaukee, Wisconsin). Two ECGs were obtained: ECG I performed at admission, before any new drug treatment; ECG II performed after initiation of hydroxychloroquine (HCQ) drug treatment during the hospitalization. All patients were treated with HCQ.

The following ECG parameters were calculated: RR interval (ms), QT interval, QTc interval with the Bazett formula in DII, and in V2 leads in ECG I and ECG II. All ECGs were analyzed using digital calipers by two groups of two independent physicians (LP and GF, SA, and LC), each group analyzing one-half of ECGs. The mean of the two independent measured values was used for analysis. If the difference between the two measured values was more than 20 ms, a third experienced electrophysiologist (PV) measured QTc. QTc-I was defined as the QTc interval in the ECG I; QTc-II was defined as the QTc in the ECG II. QTc intervals were classified as long when at least one among QTc in lead DII or in lead V2 was longer than 440 ms for men and 460 ms for women; when these criteria were not met, QTc intervals were considered normal. AQTc was defined as the difference between QTc-II and QTc-I in lead DII.

2.3 Statistical methods

Descriptive statistics were expressed in terms of median and interquartile range (IQR) for continuous variables, while frequency distribution and percentage were reported for categorical variables. All variables were tested for normality with Shapiro–Wilk test. Since normality distribution assumption in the whole population sample was not met, Mann–Whitney test or Fisher’s exact test was applied to compare patient groups, respectively in presence of continuous or categorical variables. QTc-I and QTc-II were compared with Wilcoxon signed-rank test. Correlation analysis was performed with Pearson correlation test and coefficient. Kaplan–Meier’s curves were drawn to describe the patients’ freedom from death during the follow-up period. The covariates entered in the multivariable Cox’s proportional hazard model were chosen according to their clinical significance.
and to whether the variable showed as statistically significant at univariate analysis. The following covariates were entered in the model: age, C-reactive protein (CRP) at ECG II, and dichotomized QTc-I. Significant variables were then selected through a stepwise backward approach. The alpha level was set at the conventional 0.05 level. Analyses were performed using the R statistical software version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria).

3 Results

3.1 Patients’ characteristics

One hundred consecutive patients with confirmed SARS-CoV-2 infection, admitted to the ER of San Raffaele Hospital, were included in the study. Median age at presentation was 65.0 years (IQR: 58.8–76.0); 74 (74.0%) were males. All patients were taking HCQ and 47 patients (47%) also azithromycin.

QTc-I was long in 45 patients (45%) and normal in 55 patients (55%). Patients with long QTc-I were older and more frequently males. C-Reactive protein (CRP) and white blood cell (WBC) count at hospitalization were higher in patients with long QTc-I (102.6 mg/L (66.9–172.1 mg/dL) and 7.9 × 10⁹/L (5.3–11.5)), than in patients presenting with normal QTc-I (57.2 mg/L (33.4–139.2 mg/dL), p = 0.029; and 6.0 × 10⁹/L (4.5–8.5), p = 0.05). QTc-II was recorded after a median of 5 days (IQR 3–7 days) of treatment. During hospitalization, QTc interval in lead DII increased from 435 ms (IQR 413–453) to 446 ms (IQR 417–469) (p = 0.007 for comparison QTc-I vs QTc-II); median ΔQTc was 17.5 ms (IQR 10–36). QTc also increased in lead V2 (QTc-I in lead V2: 435.5 ms (IQR 424–470), p = 0.002). Complete patients’ characteristics based on dichotomized QTc-I are summarized in Table 1; patients’ characteristics based on dichotomized QTc-II are summarized in Table 2.

3.2 Inflammation and QTc in COVID-19

QTc-I in V2 lead showed a significant correlation with CRP determined at the first ECG (r = 0.19, Pearson p = 0.05; Fig. 1, panel A). ΔQTc showed a significant correlation with CRP determined at the second ECG (r = 0.22, Pearson p = 0.02; Fig. 1, panel B). There was no significant correlation between QTc-I and WBC, and between ΔQTc and WBC. The cTn-T-peak showed a significant correlation with CRP determined at the first ECG (r = 0.26, Pearson p = 0.03) and CRP determined at the second ECG (r = 0.24, Pearson p = 0.05); cTn-T-adm showed no correlation with CRP. QTc-I in V2 lead was long in 25 patients (50.0%) with elevated cTn-T-adm and in 21 patients (42.9%) with non-elevated cTn-T-adm (p = 0.79). Twenty-seven patients (52.9%) with elevated cTn-T-peak and 15 patients (32.3%) with non-elevated cTn-T-peak had long QTc-I in V2 lead (p = 0.13).

3.3 Primary endpoint

During a median follow-up of 83.0 days (20.5–117.5), 14 patients (14%) died. Causes of death were end-stage respiratory failure in 11 patients (78%), septic shock in 2 patients (14%), and hemorrhagic shock in 1 patient (7%); all events occurred during hospitalization. There were no deaths due to ventricular arrhythmias. Twelve patients (12%) experienced de novo atrial fibrillation. Intensive care unit admission was necessary in 14 patients (14%), in 7 patients (15.6%) with long QTc-I, and in 7 patients (12.7%) with normal QTc-I.

Patients with long QTc-I had a shorter survival, compared with normal QTc-I patients (75.6% vs 94.5%, log-rank p = 0.01; Fig. 2, panel A). Long QTc-II patients had a shorter survival, compared with normal QTc-II patients (79.6% vs 93.5%, log-rank p = 0.047; Fig. 2, panel B).

In Cox univariate analysis, significant predictors of mortality were age (HR 1.10, CI 95% 1.04–1.17, p = 0.001), long QTc-I (HR 4.59, CI 95% 1.28–16.44, p = 0.019), CRP at ECG II (HR 1.01, CI 95% 1.00–1.01, p = 0.007), and cTn-T-peak (HR 1.02, CI 95% 1.01–1.03, p = 0.005). In Cox multivariate analysis, the independent predictors of mortality were age (HR = 1.1, CI 95% 1.04–1.18, p = 0.002) and CRP at ECG II (HR = 1.1, CI 95% 1.0–1.1, p = 0.02).

4 Discussion

4.1 Main findings

Our study is the first to demonstrate a correlation between inflammation and QTc in COVID-19 patients. Inflammation, as expressed by CRP levels, appeared to be an independent risk factor for mortality; QTc can be used as a simple cardiac risk marker in patients with COVID-19.

4.2 Arrhythmogenesis in COVID-19 infection

SARS-CoV-2 replication causes direct cellular damage in target tissues, including lung epithelial cells, enterocytes of the small intestine, endothelial cells, and arterial smooth muscle cells; dying cells release inflammatory alarmins. Alveolar endothelial damage can progress into a microvascular lung vessels obstructive thrombo-inflammatory syndrome and hesitate in atypical ARDS [18].

Arrhythmias in COVID-19 patients are the result of the interplay between myocardial injury and prolonged QTc secondary to inflammation or drugs [19]. Cardiac injury,
as demonstrated by troponin elevation, is associated with a higher incidence of ventricular arrhythmias [20]. The mechanisms of myocardial injury in patients with COVID-19 are not clearly understood, yet. Direct damage to the cardiomyocytes, systemic inflammation, myocardial interstitial fibrosis, interferon-mediated immune response, and exaggerated cytokine response, in addition to coronary plaque destabilization, myocarditis, and hypoxia might all be involved [21]. In a study by Chen et al. [22], levels of NT-proBNP, troponin-I, and CRP, i.e., markers of myocardial injury and inflammation, were significantly correlated with disease severity and critical illness. However, despite a high frequency of arrhythmias, mostly atrial fibrillation [23], only half of patients in intensive care units had acute cardiac injury; this evidence stimulated the search for other risk factors in COVID-19 patients’ arrhythmogenesis [20].

QTc prolongation secondary to inflammation and drug treatments is an attractive additional candidate.

Our study is the first to demonstrate a correlation between inflammation and QTC in COVID-19 population. Inflammation, as reflected by CRP levels, is a predictor of mortality in COVID-19 patients: in a machine learning model, hs-CRP with a cutoff of 41.2 mg/L was a key node in the classification tree [24]. A significant relationship between systemic inflammation, QTc prolongation, and TdP occurrence during the active phase of infections was demonstrated in non-COVID-19 patients [15]. They showed that inflammation causes QTc prolongation secondary to increased expression of K+ channel gene KCNJ2. In their study, the mean QTc interval was 461 ms, that is higher than our findings of 435 ms; the longer QTc interval was probably related to the older age [25] of their study population. The frequency

Table 1 Patients characteristics by ECG at hospital admission

|                         | Normal QTc-I (N=55) | Long QTc-I (N=45) | Overall (N=100) | p value |
|-------------------------|---------------------|-------------------|-----------------|---------|
| Age (years)             | 62.0 (57.5, 71.0)   | 74.0 (61.0, 79.0) | 65.0 (58.8, 76.0) | 0.002   |
| Gender (M)              | 36 (65.5%)          | 38 (84.4%)        | 74 (74.0%)      | 0.04    |
| BMI (kg/m2)             | 25.0 (23.4, 27.6)   | 26.1 (23.6, 28.9) | 25.1 (23.5, 28.7) | 0.68    |
| Hypertension            | 25 (45.5%)          | 28 (62.2%)        | 53 (53.0%)      | 0.11    |
| CAD                     | 6 (10.9%)           | 18 (40.0%)        | 24 (24.0%)      | <0.001  |
| DM2                     | 8 (14.5%)           | 3 (6.7%)          | 11 (11.0%)      | 0.33    |
| CKD                     | 2 (3.6%)            | 4 (8.9%)          | 6 (6.0%)        | 0.40    |
| Neoplasia               | 7 (12.7%)           | 10 (22.2%)        | 17 (17.0%)      | 0.29    |
| Death                   | 3 (5.5%)            | 11 (24.4%)        | 14 (14.0%)      | 0.009   |
| QTc-I in lead DII       | 416.0 (401.5, 428.5)| 458.0 (441.0, 475.0)| 435.0 (413.0, 453.0) | <0.001  |
| QTc-I in lead V2        | 415.0 (400.5, 429.5)| 463.0 (453.0, 480.0)| 435.0 (413.0, 462.0) | <0.001  |
| HR baseline (bpm)       | 91.0 (80.0, 100.0)  | 84.0 (80.0, 98.5) | 88.0 (80.0, 100.0) | 0.35    |
| SBP (mmHg)              | 130.0 (118.5, 140.0)| 140.0 (120.0, 140.0)| 133.0 (120.0, 140.0) | 0.30    |
| DBP (mmHg)              | 74.5 (65.0, 80.0)   | 75.5 (69.0, 82.0) | 75.0 (65.2, 80.0) | 0.39    |
| EF (%)                  | 56.9 (56.2, 57.2)   | 56.4 (55.5, 57.3) | 56.7 (55.9, 57.1) | 0.32    |
| pO2 (mmHg)              | 81.9 (65.9, 97.9)   | 67.8 (58.8, 76.5) | 71.2 (62.7, 88.5) | 0.007   |
| fiO2                    | 32.0 (21.0, 75.0)   | 40.0 (21.0, 70.0) | 36.0 (21.0, 70.0) | 0.94    |
| WBC (×10^9/L)           | 6.0 (4.5, 8.5)      | 7.9 (5.3, 11.5)   | 7.3 (4.8, 10.4)  | 0.05    |
| IL6 (pg/mL)             | 35.1 (33.1, 83.4)   | 47.3 (12.8, 120.2)| 38.9 (12.6, 101.2)| 0.35    |
| CRP ECG I (mg/L)        | 57.2 (32.4, 139.2)  | 102.6 (66.9, 172.1)| 85.0 (40.4, 165.4)| 0.03    |
| CRP ECG II (mg/L)       | 36.7 (10.2, 95.1)   | 29.0 (7.2, 103.0) | 36.4 (7.3, 99.6) | 0.79    |
| cTn-T-adm (ng/L)        | 14.1 (6.6, 26.7)    | 19.8 (8.2, 45.0)  | 16.1 (6.9, 29.1) | 0.21    |
| cTn-T-peak (ng/L)       | 13.6 (6.8, 23.5)    | 19.6 (10.6, 44.2) | 17.5 (8.0, 30.3) | 0.09    |
| KAL ECG I (mEq/L)       | 4.2 (3.9, 4.5)      | 4.1 (3.9, 4.4)    | 4.2 (3.9, 4.5)   | 0.37    |
| CA ECG I (mEq/L)        | 2.1 (2.0, 2.2)      | 2.1 (2.0, 2.2)    | 2.1 (2.0, 2.2)   | 0.09    |
| AF                      | 5 (9.1%)            | 7 (15.5%)         | 12 (12.0%)       | 0.46    |
| Diuretics               | 29 (52.7%)          | 37 (82.2%)        | 66 (66.0%)       | 0.003   |
| Beta-blockers           | 8 (14.5%)           | 16 (35.5%)        | 24 (24.0%)       | 0.016   |
| Amiodarone              | 3 (5.5%)            | 4 (8.9%)          | 7 (7.0%)         | 0.69    |

AF, atrial fibrillation; BMI, body mass index; CA, calcium blood level; CAD, coronary artery disease; CKD, chronic kidney disease; CRP, C-reactive protein; cTn-T-adm, hs-troponin T admission; cTn-T-peak, hs-troponin T peak; DBP, diastolic blood pressure; DM2, diabetes mellitus type 2; EF, ejection fraction (echocardiography); HR, heart rate; KAL, potassium blood level; SBP, systolic blood pressure; WBC count, white blood cell count.

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Table 2 Patients characteristics by ECG after hydroxychloroquine

|                  | Normal QTc-II (N=46) | Long QTc-II (N=54) | Overall (N=100) | p value |
|------------------|-----------------------|--------------------|------------------|---------|
| Age              | 65.5 (58.2, 75.8)     | 65.0 (59.0, 76.0)  | 65.0 (58.4, 76.0) | 0.92    |
| Gender (M)       | 30 (65.2%)            | 44 (81.5%)         | 74 (74.0%)       | 0.07    |
| BMI (kg/sqm)     | 25.1 (23.1, 27.0)     | 25.1 (23.9, 29.4)  | 25.1 (23.5, 28.7) | 0.19    |
| Hypertension     | 21 (45.7%)            | 32 (59.3%)         | 53 (53.0%)       | 0.23    |
| CAD              | 9 (19.6%)             | 15 (27.8%)         | 24 (24.0%)       | 0.36    |
| DM2              | 8 (17.4%)             | 3 (5.6%)           | 11 (11.0%)       | 0.11    |
| CKD              | 3 (6.5%)              | 3 (5.6%)           | 6 (6.0%)         | 1.00    |
| Neoplasia        | 9 (19.6%)             | 8 (14.8%)          | 17 (17.0%)       | 0.59    |
| Death            | 3 (6.5%)              | 11 (20.4%)         | 14 (14.0%)       | 0.08    |
| QTc-II in lead DII | 416.0 (400.0, 430.0) | 468.0 (460.0, 488.8) | 446.0 (417.5, 469.0) | <0.001 |
| QTc-II in lead V2 | 422.5 (410.8, 434.5) | 469.0 (459.0, 490.0) | 443.0 (422.8, 470.5) | <0.001 |
| HR baseline (bpm) | 86.0 (80.0, 96.0)    | 92.0 (80.0, 102.0) | 88.0 (80.0, 100.0) | 0.28    |
| SBP (mmHg)       | 131.5 (115.0, 140.0)  | 134.5 (120.0, 140.0) | 133.5 (120.0, 140.0) | 0.20    |
| DBP (mmHg)       | 70.0 (64.8, 80.0)     | 80.0 (70.0, 82.8)  | 75.0 (65.2, 80.0) | 0.011   |
| pO2 (mmHg)       | 70.9 (64.5, 89.0)     | 72.5 (60.6, 86.6)  | 71.2 (62.7, 88.5) | 0.54    |
| fiO2             | 31.0 (21.0, 80.0)     | 38.0 (21.0, 62.5)  | 36.0 (21.0, 70.0) | 0.70    |
| WBC (×10^9/L)    | 6.3 (5.0, 7.7)        | 7.3 (5.8, 10.0)    | 7.0 (5.6, 8.5)   | 0.01    |
| CRP ECG I (mg/L) | 65.0 (21.4, 145.5)    | 91.7 (53.9, 162.4) | 81.2 (37.3, 150.6) | 0.06    |
| CRP ECG II (mg/L)| 20.1 (5.4, 67.6)      | 47.7 (11.1, 109.8) | 36.4 (7.3, 99.6) | 0.04    |
| KAL ECG I (mEq/L)| 4.3 (3.9, 4.7)        | 4.1 (3.8, 4.6)     | 4.2 (3.8, 4.7)   | 0.52    |
| CA ECG I (mEq/L)| 2.1 (2.1, 2.2)        | 2.1 (2.1, 2.2)     | 2.1 (2.1, 2.2)   | 0.47    |
| AF               | 2 (100.0%)            | 10 (90.9%)         | 12 (92.3%)       | 1.00    |
| Diuretics        | 26 (56.5%)            | 40 (74.1%)         | 66 (66.0%)       | 0.09    |
| Azithromycin     | 22 (47.8%)            | 25 (46.3%)         | 47 (47.0%)       | 1.00    |
| Amiodarone       | 3 (6.5%)              | 4 (7.4%)           | 7 (7.0%)         | 1.00    |
| HCQ              | 46 (100%)             | 54 (100%)          | 100 (100%)       | 1.00    |

AF, atrial fibrillation; BMI, body mass index; CA, calcium blood level; CAD, coronary artery disease; CKD, chronic kidney disease; CRP, C-reactive protein; DBP, diastolic blood pressure; DM2, diabetes mellitus type 2; HCQ, hydroxychloroquine; HR, heart rate; KAL, potassium blood level; SBP, systolic blood pressure; WBC count, white blood cell count

Fig. 1 Panel A Correlation between QTc V2 in ECG I and CRP at ECG I. Panel B Correlation between ∆QTc and CRP at ECG II
of prolonged QTc interval was more than 3 times higher than the control group, and the QTc duration correlated with CRP levels and inflammatory marker levels. In our cohort, there was a significant correlation between CRP and QTc-I at ECG I, but not with QTc-II; CRP was reduced at ECG II, while QTc-II was prolonged. Therefore, QTc-II prolongation was related not only to the extent of systemic inflammation, but also to the drug treatment.

Some drugs used in COVID-19 infection are known to cause QTc prolongation; this is the case of HCQ and azithromycin [19]. In our cohort, in which all patients were taking HCQ and 47 patients (47%) azithromycin, no arrhythmic deaths were observed, suggesting a relatively safe arrhythmic profile of HCQ in COVID-19 patients. This is consistent with the results from a randomized controlled clinical trial that did not observe ventricular tachycardias in 438 HCQ recipients [26]. In a recent systematic review including 1515 patients with COVID-19, ventricular arrhythmias occurred in only 2 patients within a subgroup of 28 patients treated with high-dose chloroquine [27]. This could be explained by the fact that QTc prolongation is modest, as also reported in the prospective observational study by Priori et al. [16]; in their experience, median QTc prolongation was 18 ms, similar to our finding of 17.5 ms, and no life-threatening arrhythmic events were reported. Furthermore, malignant ventricular arrhythmias in these patients represent a minority of cardiovascular deaths, and they are frequently associated with severe metabolic derangement [28].

4.3 Clinical role of QTc in COVID-19 infection

In our study, patients with long QTc-I or QTc-II had a higher mortality than patients with normal QTc. At univariate analysis, long QTc-I was a significant predictor of death. At multivariate analysis, age and CRP at ECG II were significant predictors of death. Age and inflammation status thus appeared as the main determinants of mortality, while QTc is a marker of cardiac involvement in high-risk patients. Age has been already identified as a major risk factor for mortality in COVID-19 patients in several studies, with age ≥ 65 years associated with a twofold increased risk of death [29], and a 20-fold-increased risk of mortality in patients aged ≥ 80 years, compared with those aged 50–59 [30].

cTn-T is another known risk factor for mortality in COVID-19 patients [11, 12]. We did not find any significant correlation between cTn-T-adm, cTn-T-peak, and QTc-I in V2; also, 32.3% patients with non-elevated cTn-T-peak had long QTc-I; these observations might hint QT prolongation as the expression of a cardiac involvement that goes beyond overt necrosis. Only cTn-T-peak, but not cTn-T-adm, was a significant predictor of mortality, thus suggesting that QTc-I at clinical presentation might provide prognostic information earlier than cTn-T. Our results are in agreement with Farrè et al. who demonstrated that a prolonged QTc was independently associated with a higher mortality in COVID-19 patients [31].

Our data point towards QTc at clinical presentation as a simple and easily available marker of initial myocardial disease that identifies patients at higher risk of death.

4.4 Strengths and limitations

This study was a retrospective single-center study from a university hospital in Lombardy region, one of Italian areas hit harder by the COVID-19 outbreak. The main limitation of this study is the limited number of patients included. However, statistically significant differences from these
preliminary data add robustness to our hypothesis-generating observations.

5 Conclusions

QTC at clinical presentation (QTC-I) is a simple cardiac risk marker in COVID-19 patients. Its use in clinical practice needs a more extensive validation for triaging patients at higher risk of death.

Data availability Data is available on request to the corresponding author.

Declarations

Ethics approval The study complied with the Declaration of Helsinki; the Ethic Committee approved the study.

Competing interests The authors declare no competing interests.

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