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Editorial

QTc Dispersion Predicts Prognosis in COVID-19 Disease

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▸ See the article "Electrocardiographic Manifestations in Patients with COVID-19: Daegu in South Korea" in volume 51 on page 851.

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Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global public health threat. It has been associated with more than 200,000 cases resulting in more than 2,000 deaths in South Korea as of August 2021.

Various arrhythmias and electrocardiographic (ECG) abnormalities can occur in COVID-19 disease, especially in critically ill patients.[1-3] Medications including hydroxychloroquine and azithromycin, previously used for COVID-19, may prolong QT interval. However, it has been reported that QT prolongation can develop independently in recent research. Rubin et al.[4] found that COVID-19 infection had a prolonged corrected QT interval (QTc) in hospitalized patients than those without COVID-19 infection. It is intriguing that 25.0% of patients with COVID-19 who had not received hydroxychloroquine nor azithromycin still had a QTc interval of 500 ms or greater, compared with 10.8% of their COVID-negative peers. In multivariable analysis, factors significantly associated with prolonged QTc in COVID-19 patients were age 80 years and older, severe chronic kidney disease, elevated high-sensitivity troponin, and elevated lactate dehydrogenase.

In drug-related acquired long QT syndrome, the blockade of delayed rectifying potassium channel (I_{Kr}) is responsible for action potential prolongation and proarrhythmia. Blockade of I_{Kr} current results in a reduction in the net outward current, a prolongation of the action potential, and the possible development of T/U wave abnormalities. Many viruses result in myocarditis. It is not determined whether the arrhythmogenicity in viral infection results from myocarditis or comes directly from channelopathies. Recent data suggest that viruses can encode their ion channels and also regulate the ion channels expressed by host cells.[5] Emerging data shows that SARS-CoV-2 genes encode K^+ channels and may dysregulate the action potential and Ca^{2+} handling in cardiomyocytes, resulting in decreased cardiac contractility and increased susceptibility to arrhythmias.[6]

In this issue of the *Korean Circulation Journal*, Bae et al.[7] reported ECG parameters and their relationship with disease severity in Korean patients with COVID-19. They screened 822 patients admitted to hospitals in Daegu for COVID-19 treatment and enrolled 267 subjects who underwent an ECG on admission day. The heart rate, PR interval, QRS interval, T

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inversion, QT interval, and interval between peak to end in a T wave (Tpe) were analyzed. Patients were divided into three groups according to clinical severity score. Patients with severe symptom scores showed increased dispersion of QTc and Tpe-c, and the QTc dispersion of more than 56.1ms could predict the mortality in multivariable analysis (odd ratio, 11.6). This study shows a unique findings of the association between QT dispersion and disease severity in COVID-19.

There is no convincing evidence for the independent association between QT prolongation and disease severity of COVID-19. It has been reported that QTc of >455 ms in males and >465 ms in females are predictors of mortality,[8] and the absence of QT prolongation was associated with a good prognosis.[9] In contrast, Changal et al.[10] reported that QTc prolongation was not associated with increased ventricular arrhythmias or mortality in multivariate analysis. Because QT prolongation is in part a result of myocardial damage, it cannot be discriminated independently. Whether the association is independent or not, these observations suggest that changes in QT may be an early predictor of myocyte viral damage, a viral channelopathy, and may herald the development of arrhythmias.[6]

This study has several limitations. First, only 32% of the admitted patients underwent ECG. These patients are more likely to have cardiac problems than those who do not have ECG examinations. In addition, ECG was not followed up during the admission period. QT interval tends to change over time according to patients' status. The study period represents the first outbreak in Korea. It was not easy to repeat ECG in these highly contagious patients amid running out of medical resources and limited knowledge of these new viruses. Second, 58 patients (21.7%) were deceased in this study. Some patients might have ventricular arrhythmia and Torsades de Pointes. The cause of death was not clarified. Finally, the use of medications that prolongs QT interval was not analyzed.

It is frustrating that we do not have appropriate armaments against COVID-19 disease. QT prolongation is likely associated with virus-induced myocardial damage and channelopathies. Efforts should be made to correct all possible contributing factors, including fever, electrolyte imbalances, and avoiding medications known to prolong QT intervals.

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