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Wide QRS Complex and Left Ventricular Lateral Repolarization Abnormality: The Importance of ECG Markers on Outcome Prediction in Patients with COVID-19

There is a clear reported increased morbidity and mortality with coronavirus disease 2019 (COVID-19) with the presence of cardiac injury.[1-4] Non-ischemic events and ischemic myocardial involvement are the two main pathophysiological mechanisms described for acute cardiac injury in COVID-19 patients.[5] This pandemic is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Up to November 5, 2020, this disease resulted in considerable morbidity and mortality worldwide with 47,596,852 laboratory-confirmed cases and 1,216,357 deaths.

Most of the studies that reported myocardial involvement were based on elevated serum cardiac biomarkers, while others on cardiac magnetic resonance imaging.[1-3] It was reported recently that there is also evidence of direct viral damage of the myocardium causing acute myocarditis detected by histological studies. This was manifested as myocardial edema and acute myocardial injury with the presence of SARS-CoV-2 on electron microscopy.[6] Electrocardiogram (ECG) abnormalities commonly seen in cardiac injury are ST elevation and PR depression. Other ECG abnormalities that can be observed in acute cardiac injury include new-onset bundle branch block, QT prolongation, pseudoinfarct pattern, premature ventricular complexes, bradyarrhythmias and ventricular tachycardia (VT).[1]

In the May issue of the American Journal of The Medical Sciences, Sonsoz MR, et al.[7] demonstrated that two simple ECG parameters can be associated with markers of myocardial injury and clinical outcomes in hospitalized patients with COVID-19. The authors succeded in finding that the presence of QRS duration longer than 120 ms and left ventricular (LV) lateral ST-T segment abnormalities were associated with worse clinical outcome and higher levels of myocardial injury biomarkers. The authors should be commended for their original work which has contributed to shed light on possible ECG markers of outcome prediction in patients with COVID-19. They analyzed in their retrospective, single center, non-randomized observational study a total of 223 hospitalised patients with laboratory-confirmed COVID-19. Primary composite endpoint of mortality, need for invasive mechanical ventilation or intensive care unit were assessed. Forty patients (17.9%) reached the primary composite endpoint. Patients with primary composite endpoint were more likely to have wide QRS complex (>120 ms) and lateral ST-T segment abnormality. Multivariable Cox regression showed increasing odds of primary composite endpoint associated with acute cardiac injury (odds ratio 3.14, 95% CI 1.26 − 7.99; P = 0.016), and QRS duration longer than >120 ms (odds ratio 3.62, 95% CI 1.39 − 9.380; P = 0.008). Patients with wide QRS complex (>120 ms), and abnormalities of lateral ST-T segment had significantly higher median level of troponin T and pro-BNP than patients without. Therefore, the authors concluded that the presence of wide QRS duration and lateral ST-T segment abnormalities were associated with worse clinical outcome and higher levels of myocardial injury biomarkers in hospitalized patients with COVID-19.[7]

The development of ECG abnormalities in the LV lateral wall in the study patients of Sonsoz MR, et al.[7] may have several explanations. The presence of multiple cardiovascular risk factors and the serum elevation of myocardial biomarkers makes myocardial ischemia of notable consideration. Another plausible explanation is type 2 myocardial infarction secondary to severe hypoxia and hypotension in severely ill patients. Moreover, these ECG abnormalities may result from acute myocarditis induced by SARS-CoV-2 direct impact on the cells leading to myocarditis and apoptosis-induced cellular damage via 3C proteinase-mediated apoptosis, disruption of host protein translational mechanisms, loss of cellular homeostasis, and dysregulated host-immune response.[1] Additional prospective studies, including biopsy of endomyocardial tissue and autopsy investigations, are required to define the pattern and proportion of SARS-CoV-2-related cardiac damage due to acute myocarditis versus myocardial injury caused by systemic cytokine storm.

Acute cardiac injury manifested by increased blood levels of cardiac troponin value greater than the 99th percentile reference limit, several electrocardiographic abnormalities, or myocardial dysfunction, seems to be prevalent in hospitalized patients with COVID-19. Shi S, et al.[5] recently reported abnormal ECG findings compatible with myocardial ischemia, namely, T wave depression and inversion, ST-segment depression, and Q-waves in patients with COVID-19 during the period of elevated cardiac biomarkers. In-hospital mortality was found to be more than 6-fold higher in patients with elevated cardiac Troponin T levels which persisted after adjustment for baseline characteristics and medical comorbidities.[5] Therefore, it is reasonable to assume that initial measurement of cardiac biomarkers immediately after hospitalization for SARS-CoV-2 infection may help identifying a subset of patients with possible cardiac injury and, thereby, predict the progression of COVID-19 towards a worse outcome. It remains to be proven whether the SARS-CoV-2-mediated myocardial damage

will have long-term detrimental effects on cardiac function and survival. Hence, follow up data on survivors is required to improve evaluation of the long-term clinical outcomes.

It is not surprising to read the important findings of Sonsoz MR, et al.[7] since wide QRS complex was already previously associated with increased mortality risk in patients without COVID-19 (8-10). Ukena C, et al.[8] reported in patients with suspected miocarditis unrelated to COVID-19 that a QRS width greater than 120 ms in duration was associated with greater risk of cardiac death or need for heart transplantation [8]. Kalra PR, et al.[9] investigated the optimal QRS duration that separates patients with HF into those with a relatively benign versus a poor prognosis. Patients with a QRS $\geq$ 0.12 s had a three-fold increased risk for the combined end point of death or transplantation. Moreover, it has been shown that a wide QRS complex predisposes HF patients to VT, and it was found to be an independent risk factor for VT inducibility in the multivariate analysis. In fact, the risk of inducible VT increased by 2.4% for each 1 ms increase in QRS duration.[10]

As Sonsoz MR, et al.[7] pointed out, due to the retrospective nature of their study, some parameters were not available in all patients. Studies with retrospective design and uncontrolled confounders might bias the real incidence and the influence of wide QRS complex and LV lateral abnormality, and their prognostic value on clinical outcomes. Therefore, there is a neccessity of large-scale, prospective studies to shed more light on this interesting matter. Further clinical investigations should be designed to prospectively define whether or not wide QRS complex and LV lateral ECG abnormalities play an important role in predicting worse clinical outcome in patients with significant elevation of cardiac injury biomarkers in COVID-19. These handy, fast, unexpensive, easily obtainable and reliable ECG parameters may help identifying a group of patients with possible cardiac injury in order to make rapid and appropriate clinical maneuvers to prevent progression and complications of this fearsome viral disease.

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