EDITORIAL

Coronavirus Disease 2019 (COVID-19) and the Heart—Is Heart Failure the Next Chapter?

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Multiple data sets now confirm the increased risk for morbid and mortal complications due to coronavirus disease 2019 (COVID-19) in individuals with preexisting cardiovascular diseases including hypertension, coronary artery disease, and heart failure.[1,2] These salient observations have strengthened preventive strategies and undoubtedly have resulted in lives saved. Although episodes of clinical myocarditis have been suspected and a few cases have been reported in the literature,[3] direct cardiac involvement due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been difficult to confirm.

In this issue of *JAMA Cardiology*, Linder and colleagues[4] report on 39 autopsy cases of patients with COVID-19 in whom pneumonia was the clinical cause of death in 35 of 39 (89.7%). While histopathologic evaluation did not meet criteria seen in acute myocarditis, there was evidence of virus present in the heart in 24 of 39 patients (61.5%) with a viral load more than 1000 copies per microgram of RNA in 16 of 24 patients (66.7%). Evidence of active viral replication was also noted. In situ hybridization suggested that the most likely localization of the viral infection was in interstitial cells or macrophages infiltrating the myocardial tissue rather than localization in the myocytes themselves. Further using a panel of 6 proinflammatory genes, the investigators demonstrated increased activity among hearts with evidence of viral infection compared with hearts with no SARS-CoV-2 viral infection detected.[4] These new findings provide intriguing evidence that COVID-19 is associated with at least some component of myocardial injury, perhaps as the result of direct viral infection of the heart.

The discoveries highlighted in this issue of *JAMA Cardiology* by Puntmann and colleagues[5] are also informative. In 100 recovering patients included in the study, 67% of whom recovered at home, evaluated a mean of 71 days after confirmed COVID-19 diagnosis, 78% had demonstrable cardiac involvement via cardiac magnetic resonance imaging, 76% had detectable high-sensitivity troponin, and 60% had evidence of active myocardial inflammation by abnormal native T1 and T2. Compared with controls including those with a similar profile of preexisting conditions, left ventricular ejection fraction was lower and volumes higher, as well as 32% manifesting late gadolinium enhancement and 22% with pericardial involvement. There are important residual questions about potential selection bias and generalizability and not all of the patients may have recovered, but the observations cannot be dismissed. Months after a COVID-19 diagnosis, the possibility exists of residual left ventricular dysfunction and ongoing inflammation, both of sufficient concern to represent a nidus for new-onset heart failure and other cardiovascular complications. Moreover, we cannot dismiss important other clinical pathophysiological observations, including clinical syndromes consistent with acute myocarditis, the cascade of immunologic responses, a prothrombotic milieu with microvascular clot formation, and/or myocardial injury due to supply-demand mismatch. When added to the postmortem pathological findings from Linder et al,[4] we see the plot thickening and we are inclined to raise a new and very evident concern that cardiomyopathy and heart failure related to COVID-19 may potentially evolve as the natural history of this infection becomes clearer.

We wish not to generate additional anxiety but rather to incite other investigators to carefully examine existing and prospectively collect new data in other populations to confirm or refute these findings. We hope these findings represent that of a select cohort of patients. Yet, if this high rate of risk is confirmed, the pathologic basis for progressive left ventricular dysfunction is validated, and especially if longitudinal assessment reveals new-onset heart failure in the recovery phase of COVID-19, then the crisis of COVID-19 will not abate but will instead shift to a new de novo incidence of heart failure and other chronic cardiovascular complications.

Given the pressing burden of the ongoing COVID-19 crisis, as well as the initiation of longitudinal care models for those recovering from COVID-19, the concerns we are raising are not theoretical but instead practical and require our due diligence to study and prepare for what may be another dimension of the COVID-19 crisis.

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