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Commentary

Long-Term COVID-19 and Cardiac Complications Over the Pandemic Timeline

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DESCRIPTION

The COVID-19 pandemic has resulted in profound effects on education, economies, and health on a global scale. Many survivors of acute SARS-CoV-2 infection are now suffering from new or persistent sequelae involving nearly every organ system. This diverse constellation of symptoms has been termed long COVID. Significant ischemic, inflammatory, dysrhythmias, and thrombotic cardiovascular sequelae have been reported after acute infection, though significant knowledge gaps remain. Clinically, patients suffering from long COVID may present with cardiovascular symptoms, however, objective evidence of true cardiovascular disease with current diagnostics is often not found. For decades it has been recognized that viruses can cause post-acute sequelae or chronic adverse outcomes following acute infection. The pandemic has brought notoriety to this observation and significant work is now being done to learn more about the pathophysiology, natural history, new diagnostics, and treatment options for long COVID. Severity of initial infection has brought increased risk for adverse cardiovascular outcomes, but it is unclear how heart-related events and spectrum of long-term sequelae may be changing over the COVID-19 pandemic timeline. We plan to study this question utilizing a large community sample in Minnesota and Wisconsin in the hopes that the data would better our understanding of long-term COVID-19 effects on the cardiovascular system.

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has not only emerged as a global health crisis with significant deleterious impacts on education and economies, but has also posed considerable challenges to our understanding of its multi-faceted impacts on human health. Many survivors of acute infection have noted symptoms affecting almost every organ system including neurologic, gastrointestinal, and pulmonary, among others [1]. Long-term COVID-19 is defined as symptoms persisting or starting one month after initial laboratory-confirmed acute infection [2,3]. Estimates for prevalence of long COVID have been as high as 65 million patients in a review article from 2023, but whether this represents the true prevalence remains unclear [4,5]. Among its various manifestations, COVID-19 has been increasingly recognized for its intricate interplay with the cardiovascular system leading to multiple heart-related complications, many of which remain incompletely understood.

Late cardiovascular manifestations are diverse, with increased risk among patients who had severe initial illness requiring hospitalization or intensive care unit admission, although patients with mild initial infection can also be affected [6,7]. Cardiac complications have also increased from many other pandemic-related factors including lengthened time from symptom onset to presentation, delayed door-to-balloon times, and impacts on mental health including marked rises in depression and anxiety. These factors have been described as "collateral damage" that will likely continue to result in COVID-19-related cardiovascular complications for years to come [8]. As an example, larger infarct area of the left ventricle has been linked to increased mortality [9]. Survivors of acute coronary syndrome during the pandemic may have larger infarcts from delayed presentation which could lead to increased mortality among other complications in the future.

In the clinic, patients with long-term COVID-19 often present with cardiovascular symptoms including chest pain, dyspnea, fatigue, palpitations, and syncope [10-13]. Whether these findings represent a true cardiovascular process has been unclear. Objective evidence of cardiovascular disease on subsequent testing is often not found [14]. In our recent pragmatic study involving 40,462 unique patients diagnosed with COVID-19, 363 patients diagnosed with long COVID referred to the division of cardiovascular disease for ongoing cardiovascular symptoms were identified. From this sample, a little over 10% were found to have new cardiovascular disease related to COVID-19. Each patient in the cohort was manually validated in contrast to prior studies using large databases. Our data argues for a more conservative approach to utilization of our current available diagnostics while we learn more about the natural history of the cardiovascular involvement in survivors of acute COVID-19 infection.

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Our understanding of long COVID continues to evolve and new diagnostic and therapeutic approaches are under investigation [15]. Recently, a study identified ischemia of non-obstructive origin in 80% of patients with long COVID presenting with chest pain at a center in Spain [16]. Patients presumably improved after diagnosis of endothelial abnormalities (epicardial spasm and microvascular abnormalities) was confirmed and patients were started on physiologic guided medical management. Patients with post-COVID conditions receive care through a multidisciplinary approach at our center [17]. Our approach will continue to evolve as we gain further insights into the natural history and underlying pathophysiology of long COVID. Many randomized trials are underway in an effort to guide management moving forward [15].

Current knowledge gaps include the natural history of post-COVID conditions, diagnostics, and treatment options [15]. Another knowledge gap that remains is how spectrum and severity of cardiovascular events may be changing over the pandemic timeline. We plan to investigate this question by utilizing the Rochester Epidemiology Project database to study multiple composite outcomes during pre-Delta, Delta, and Omicron phases of the pandemic, similar to our prior study [18]. The dominant circulating strain of COVID-19 at the time of initial infection could prove to be an important consideration along with severity of initial infection and total number of infections. These various factors taken together could change how clinicians approach patients with persistent cardiac symptoms after COVID-19 infection in the future.

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