

Editorial



Understanding and Addressing Long COVID, the Lingering Shadow of COVID-19

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► See the article “Characteristics and Prevalence of Sequelae after COVID-19: A Longitudinal Cohort Study” in volume 57 on page 72.

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The declaration of the World Health Organization announcing the end of the coronavirus disease 2019 (COVID-19) public health emergency did not indicate that the virus, *i.e.*, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), would end impacting our lives. The research efforts presented in the recent study "Characteristics and Prevalence of Sequelae after COVID-19: A Longitudinal Cohort Study" highlights the significant and persistent burden of long COVID. This study underscores the urgent need for comprehensive and multifaceted approaches to understand, manage, and ultimately mitigate the long-term consequences of SARS-CoV-2 infection.

Long COVID is defined by the Infectious Diseases Society of Korea guidelines as the persistence of symptoms for more than 12 weeks [1]. Moreover, disease phenotypes are also distinguished based on the presentation of clinical symptoms [2]. Long COVID pathogenesis is proposedly multifactorial, with the persistence of SARS-CoV-2 viral antigens, systemic and tissue-specific inflammation, the reactivation or dysbiosis of other microbiota in the body of the host (*e.g.*, microbiome, human herpesvirus, *etc.*),

microvascular dysfunction, or the proposed contribution of autoreactive immune responses [3].

Long COVID displays several risk factors. A retrospective analysis of health insurance data from the United Kingdom identified female sex, ethnic minorities, socioeconomic deprivation, smoking, obesity, and multiple comorbidities as the main long COVID-related risk factors [4]. A prospective cohort study from 17 countries, published in *BMJ Global Health* in 2024, described that long-term COVID was more likely to occur in patients who were hospitalized with severe symptoms of acute COVID-19 as well as obesity and comorbidities, such as hypertension, diabetes, HIV infection, asthma, chronic obstructive pulmonary disease, and chronic heart disease [5].

The hereby-presented investigation represents a longitudinal study involving a two-year follow-up at six medical centers in Korea [6]; providing valuable insights into the evolving nature of long COVID. Notably, the authors discovered that a significant proportion (*i.e.*, 34.6%) of the patients were still experiencing persistent symptoms 18 months post-infection. This result challenges the notion

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that long COVID is a transient condition and calls for a shift to more ongoing monitoring and treatment. This study highlights symptom persistence, such as that of fatigue, forgetfulness, and shortness of breath, revealing the breadth of the clinical presentation. Persistent abnormalities identified on chest computed tomography scans confirmed the significant physiological impact of the virus months after the resolution of acute infection.

The results of the study also raise crucial questions concerning the risk factors and long-term consequences of various COVID-19 severities. While the study indicates a strong association between male sex and older age with persistent long COVID, it raises the question of whether other factors, including comorbidities, lifestyle choices, and healthcare access, could also significantly contribute to the discussed complications. Further investigation would be necessary concerning the underlying mechanisms of the observed long-term complications to guide the development of tailored prevention and treatment strategies.

The limitations of the study, acknowledged by the authors themselves, including the pre-omicron timeframe and relatively small sample size, highlight the need for further research. Future studies should include larger, more geographically diverse populations and patients infected with different SARS-CoV-2 variants, such as Omicron. Focusing on preexisting health conditions, vaccination status, and detailed follow-up over longer timeframes would further enhance our understanding.

In conclusion, this study provides compelling evidence for the significant and prolonged impact of long COVID. Persistent symptoms and detected physiological abnormalities necessitate concerted multidisciplinary efforts. Such efforts would involve not only continued research to delineate the mechanisms, risk factors, and long-term outcomes, but also the development of integrated, patient-centered management strategies tailored to diverse long COVID manifestations. Only through this combined effort could we hope to chase away the lingering shadows of the pandemic.

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Conflict of Interest

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