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Post-acute conditions of patients with COVID-19 not requiring hospital admission



As of early April, 2021, more than 2.8 million individuals have died globally from COVID-19. However, tens of millions of patients have survived COVID-19 and returned to everyday life. Increasing evidence has shown that a considerable proportion of patients did not recover fully and had lasting sequelae, described by various terms without consensus, including long COVID, post-COVID condition or syndrome, postacute (or late) sequelae of COVID-19, and post-acute COVID syndrome.^{1,2} Studies have mainly focused on patients with COVID-19 after hospital admission.^{3,4} One study with a small sample size and without a control group of people without COVID-19 described the long-term outcomes of patients with COVID-19 who did not require hospital admission.⁵

In *The Lancet Infectious Diseases*, Lars Christian Lund and colleagues⁶ did a population-based cohort study in Denmark and reported the medical outcomes of patients with COVID-19 not requiring hospital admission, within 6 months after testing SARS-CoV-2 positive. The authors should be commended because the study introduced a control group of SARS-CoV-2-negative individuals, had a large cohort (8983 SARS-CoV-2-positive and 80 894 negative individuals), and adopted a reasonable propensity score matching analysis. Compared with SARS-CoV-2-negative participants during the study period, they found that SARS-CoV-2-positive individuals had an increased risk of receiving the diagnosis of dyspnoea and venous thromboembolism, and initiating bronchodilating agents (particularly short-acting β 2-agonists) and triptans. SARS-CoV-2-positive individuals had higher risk of visiting a general practitioner and outpatient clinic than negative individuals, but no difference was noted for emergency department visits and inpatient hospital admissions.

In the study, the authors only investigated six persisting symptoms, which did not cover the whole potential clinical spectrum. In addition, the prevalence of the persistent symptoms in patients with COVID-19 was about 1%, which was lower than that in a previous study, which showed a rate of 5–15%.⁵ Given the inherent nature of this type of registration study, there is the possibility of greatly underestimating the actual

prevalence, because there are many reasons that patients with persistent symptoms might not visit the health-care service, such as symptoms being mild, not having health insurance or access to health care, and the risk of reinfection when visiting a health-care facility during the COVID-19 pandemic. Although the number might be underestimated, SARS-CoV-2-positive individuals still more frequently developed dyspnoea than SARS-CoV-2-negative individuals, supporting the finding of greater prescription of bronchodilating agents in SARS-CoV-2-positive individuals. These findings will prompt health-care workers to focus on those patients who have recovered from COVID-19 who already have potential risk factors for dyspnoea, such as chronic pulmonary disease, heart failure, and pulmonary hypertension. Monitoring respiratory rate and oxygen saturation at home were simple and practicable ways for these patients to assess their respiratory function and health status.

SARS-CoV-2 could impair function of multiple organs, including the coagulation system. Venous thromboembolism has always been a key concern in patients with COVID-19. Patients admitted to COVID-19 frequently developed venous thromboembolism during their hospital stay, especially in critically ill patients.⁷ A prospective study in China of patients discharged after a hospital stay due to COVID-19 reported that no deep vein thrombosis of lower limbs occurred in 390 participants by ultrasonography 6 months after illness onset.³ Another prospective follow-up study of patients admitted to hospital due to COVID-19 showed that at 6 weeks after discharge, one (1%) of 102 patients developed a symptomatic venous thromboembolism event by venous ultrasound.⁸ Hence, the incidence of post-acute venous thromboembolism in patients with COVID-19 after admission to hospital is very low. This finding is supported by the study by Lund and colleagues,⁶ in which 20 (0.2%) of 8785 SARS-CoV-2-positive individuals not requiring hospital admission had a venous thromboembolism. However, considering the possibility of an underestimate, the short follow-up time, and the huge numbers of SARS-CoV-2 infections worldwide, venous thromboembolism could be a potential concern. Endothelialitis, caused by SARS-CoV-2 direct damage



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or immunological damage, could be associated with thrombotic complications,^{9,10} but it is unknown how long endothelialitis persists. The conclusive evidence of thromboprophylaxis for patients with COVID-19 not requiring hospital admission is not yet available, but some clinical studies addressing this area have been registered at ClinicalTrials.gov (NCT04498273 and NCT04508023). Regarding the issue of post-acute thrombosis, older age, elevated D-dimers, and comorbidities such as cancer and immobility might help to risk stratify patients.²

Most SARS-CoV-2 infections will remain asymptomatic and mild for the foreseeable future, so understanding the long-term consequences of COVID-19 in these populations is crucial to the natural history of the emerging disease. Despite the limitations of this type of cohort study, the results of Lund and colleagues⁶ provide evidence of the increased risk of lasting sequelae for a population that should not be ignored—patients with COVID-19 who are not admitted to hospital. In the future, follow-up clinics are needed to establish longer-term outcomes in this population and explore strategies to prevent and mitigate sequelae of COVID-19.

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Lixue Huang, Bin Cao
caobin_ben@163.com

Department of Pulmonary and Critical Care Medicine, Capital Medical University, Beijing, China (LH); Department of Pulmonary and Critical Care Medicine, National Center for Respiratory Medicine, Center of Respiratory Medicine, National Clinical Research Center for Respiratory Diseases, China-Japan Friendship Hospital, Beijing, China (LH, BC); Institute of Respiratory Medicine, Chinese Academy of Medical Science, Beijing, China (BC); Tsinghua University-Peking University Joint Center for Life Sciences, Beijing, China (BC)

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