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QJM: An International Journal of Medicine, 2022, 349–350

https://doi.org/10.1093/qjmed/hcac070
Advance Access Publication Date: 22 March 2022
Commentary

COMMENTARY

Long COVID syndrome and the lung: how long will it last?

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Summary

The prevalence and duration of the long-term respiratory complications of COVID-19 infection remains to be elucidated. This short commentary reports on recently published studies in patients post-acute COVID-19 infection in terms of symptom prevalence, physiological and radiological sequela and where only symptoms are present despite investigation. Pulmonary function testing, 6-min walk tests, computed tomography chest and more advanced imaging modalities have been incorporated to reveal the underlying pathophysiology that cause such disabling symptoms in patient with post-acute COVID-9 syndrome (PACS). PACS has a serious impact on people's ability to return to work, affecting the physical, mental, social sphere and with significant healthcare and general economic consequences for them, their families and society.

The prevalence and severity of the long-term respiratory complications of COVID-19 infection remains to be elucidated, but emerging data strongly indicates that many patients experience persistent respiratory symptoms for months after their initial illness or worsening of their pre-existing respiratory disease. This is not novel to COVID-19 infection. It has been reported that ∼30% of people with Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome had persisting lung abnormalities after their acute illness. Influenza infections are also responsible for long-term pulmonary complications.[1] Patients, especially ones with comorbidities, experience persistent or worsening dyspnoea, fatigue, body aches and brain fog for months after the acute COVID-19 infection for many months—'long COVID'.[2] One study of 327 people post-COVID infection (greater 3 months) reported 54% having persistent breathlessness, 34% persistent cough and 83% persistent fatigue.[3] In one of the largest published studies of 273 618 patient with COVID-19, 57% reported at least one long-term COVID symptom at 6 months.[4] In one early study from Wuhan, China, of 390 patients who had COVID-19 29% had a 6-min walk distance below the lower limit of normal, a lung diffusing capacity for carbon monoxide (D_{LCO}) below 80% predicted in 56% and abnormal chest computed tomography (CT) imaging in 45% between 6 and 12 months posted reported diagnosis.[5] Several studies have reported on post-COVID pulmonary function tests (PFTs). One study of 80 patients with both pre (mean 148 days before infection) and post (mean 77 days post-infection) PFTs demonstrated no difference in Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1) , FEV1/FVC ratio, and D_{LCO}. However, total lung capacity had a significantly worsened correlating with more severe disease (none of the patients were intubated in this study).[6] Another study evaluated 379 patients 4 months after severe COVID-19 infection and showed a reduction in respiratory function and exercise capacity secondary to severe acute respiratory syndrome coronavirus 2ARDS - Acute Respiratory Distress

Received: 25 January 2022; **Revised (in revised form):** 22 February 2022

Syndrome (SARS-CoV-2) pneumonia, mostly in patients who developed Acute Respiratory Distress Syndrome (ARDS) during the acute phase.[7] This same study also found 6-min walk test distance and SpO_2 values reduced and correlated to acute disease severity.[7] Other systematic reviews (seven studies) have shown that reduced D_{LCO}, restrictive pattern and obstructive pattern in 39%, 15% and 7% of patients 3 months post-COVID-19 infection, respectively.[8] Published studies of cardiopulmonary exercise testing in patients 3 months or longer post-acute COVID-19 infection have been highly suggestive of deconditioning and did not favour a cardiac or ventilatory limitation to exercise capacity.[9] In a follow-up CT chest study of patients post-COVID-19, evidence of fibrotic-like changes was observed in 40 of the 114 participants (35%), whereas the remaining 74 participants (65%) showed either complete radiologic resolution (38%) or residual ground-glass opacification or interstitial thickening (27%).[10] A significant number of patients in long COVID clinics with exertional dyspnoea have had negative CT pulmonary angiogram (CTPA) studies for emboli—however, small vessel thrombosis may have developed unnoticed by this modality. Evidence is emerging for a more specific, angiocentric signature of COVID-19, related to an *in situ* thrombotic microangiopathy and a complex immune inflammatory cascade, especially in the pulmonary vascular bed. Potentially modalities such as VQ Single-photon emission computed tomography (SPECT)-CT scintigraphy may allow us identify a subset of dyspnoeic patients post-COVID who have developed otherwise undetectable chronic microthromboembolism.[11] This throws another question into the mix—how do we manage microthromboemboli? This raises the spectra of undiagnosed pathologies such as pulmonary microthrombi—but how should they even be managed?

To summarize, persistent respiratory complications following COVID-19 are a cause of substantial morbidity and optimal management remains unclear. Prospective studies are under way to evaluate these complications further and to identify people at greatest risk. Advanced imaging studies coupled with physiological markers may reveal yet unknown or under recognized pathologies. Multidisciplinary teams in centres focused on managing these patients shall need significantly augmented support structures.

Conflict of interest. None declared.

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