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Post-COVID Care Untying the Covidian Knot

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Since its first appearance at the end of 2019, infection due to SARS-CoV-2 has resulted in a significant burden on health care. Although the cost of acute illness is generally appreciated and obvious in terms of hospitalization and loss of work and school productivity, we are only just beginning to understand what the health care cost may be of patients developing long-term health problems from SARS-CoV-2 infection.

Although most patients recover from their SARS-CoV-2 infection without lasting symptoms, a significant proportion report ongoing health issues. These prolonged symptoms are often split into two categories: the ongoing symptomatic phase after resolution of the acute infection and the post-COVID-19 syndrome.¹ The former is considered in patients with signs and symptoms from 4 to 12 weeks from initial infection, and the consensus definition of the latter is symptoms usually 3 months from the onset with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis.² Longer-term symptoms are a mixture of psychological or physical complaints without identifiable pathologic roots, typical post-critical illness myopathies and neuropathies, and identifiable organ damage from SARS-CoV-2.^{3,4}

The exact proportion of patients who will complain of post-COVID-19 symptoms remains unclear. A prospective follow-up of patients with COVID-19

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showed that 13.3% reported symptoms lasting more than 28 days and 2.3% longer than 12 weeks; however, follow-up studies, reviews, and meta-analyses show a much higher prevalence of post-COVID-19 syndrome, ranging from 30% to 87.4%, with persistent complaints being more prevalent in patients who needed hospitalization.⁵⁻⁷ Reports identified a total of 55 long-term effects associated with COVID-19, the most common being fatigue, headache, attention disorder, hair loss, and dyspnea. Nonetheless, other symptoms such as cough, chest discomfort, sleep apnea, pulmonary fibrosis, dementia, depression, anxiety, arrhythmias, myocarditis, and night sweats should be highlighted as well.⁴ Prospective data of a population at low risk of COVID-19 mortality and only a 19% hospitalization rate identified that in those with ongoing symptoms 70% had evidence of impairment in one or more organs 4 months after initial COVID-19 symptoms.⁸

Increasingly, health care workers and governments realize that after several waves of the COVID-19 pandemic, we are facing waves of post-COVID-19 morbidity that will continue to be a significant health care burden. Increased presentations will be a mixture of delayed health care for non-COVID-19 related matters in which assessment and treatment were postponed because of overwhelmed health care providers and the needs of patients with post-COVID-19 syndrome.

In the face of a likely epidemic of patients requiring assessment and management of post-COVID illness, health care providers worldwide are scrambling to create the clinical pathways required in an environment where the best approach from both clinical and economic standpoints is decidedly unclear. In this issue of *Chest*, Valley and colleagues⁹ present the results of a survey of 47 respondents from the 51 hospitals in the Prevention and Early Treatment of Acute Lung Injury (PETAL) Clinical Trials Network, representing a broad collection of hospitals across the United States. Unsurprisingly, they found a very broad range of the extent of information provided to patients post-COVID as well as the extent of multidisciplinary assessment for post-COVID-19 problems and the range of services currently set up to deal with post-COVID-19 related disease.

Significant concerns were also raised regarding potential inequities in access to health care for post-COVID-19 assessment based on socioeconomic factors, although this of course is not unique to this disease.^{10,11}

What then are the key questions that we need answers to so as to design appropriate, evidence-based post-COVID-19 care pathways in our health systems? First, are there any interventions in the acute phase of COVID-19 that reduce the risk of long-term complications? A recent analysis by Antonelli and colleagues¹² showed that patients who had received two doses of vaccination had lower odds of developing post-COVID-19 syndrome (OR, 0.51; 95% CI, 0.32-0.82; $P = .006$). Because no other acute therapy has been shown to reduce post-COVID complications, this further emphasizes the need for vaccination campaigns. There is an urgent need to look at the impact of all current acute therapies on the long-term effects of COVID-19, including steroids, anti-IL-6 agents, anti-spike protein monoclonal antibodies, and the newer antivirals.

What is the most cost-effective and accurate diagnostic pathway to detect chronic organ damage from COVID-19, and does detection make a difference to therapy? Aside from long COVID-19 prevention, further research on its pathophysiology, identification, risk factors, diagnosis, treatment, and management is needed. As pointed out by Valley and colleagues,⁹ because there are a wide array of presentations with and without obvious organ pathology, multidisciplinary teams are crucial to address post-COVID-19 syndrome.

Does early intervention based on early diagnosis make a difference in patient outcomes or should we wait for patients to self-refer? Data from a broad group of patients with COVID-19 showed that patients who experienced more than five symptoms in the first week were more likely to develop post-COVID-19 syndrome (OR, 3.95; CI, 3.10-5.04). They also found that individuals with post-COVID-19 syndrome were more likely to have required hospital assessment.⁵ Looking further into the hospitalized patients, the recent PHOSP-COVID study found that factors associated with post-COVID-19 syndrome were female sex, two or more comorbidities, and more severe acute illness (WHO classes 7-9), whereas age groups < 30 and > 70 years had a better recovery. They also found four clusters of severity, with differences in severity regarding mental and physical health impairment.⁷ Although validating risk factors for post-COVID-19 syndrome is potentially useful, without effective interventions shown to improve

outcomes, they remain an academic exercise rather than a clinically useful one.

A few attempts have already been made to formulate practical recommendations to tackle post-COVID-19 syndrome care, suggesting a multidisciplinary one-stop clinic to screen, diagnose, and treat patients with specialist expertise and interdisciplinary collaboration.¹³ Models have been developed and put into practice, such as the Multidisciplinary NHS COVID-19 service, with the establishment of a three-tier model.¹⁴ These approaches need confirmation and validation but provide a great basis to start further research. In the post-COVID world, the extent to which these clinics could be delivered virtually while achieving the same or better outcomes will undoubtedly be a major focus of study.¹⁵

We also should not forget lessons already learned in other analogous conditions. Post critical-illness syndrome is well recognized, and there has been extensive research into its pathology, diagnosis, and avenues of treatment.¹⁶ Although there is certainly a larger variety of pathologies and symptomatology reported post-COVID-19, lessons already learnt around the importance of exercise, nutrition, and psychological support should not have to be rediscovered.

In summary, specific guidelines are needed for all what entails post-COVID-19 care, but the evidence base for such recommendations is scant. In the absence of evidence, not surprisingly, a broad range of approaches are being taken across the United States (Valley et al⁹) and indeed the world. Although we are approaching some understanding of who is most at risk, the best approach to screening for pathology and which treatments (if any) modify long-term outcomes remains to be defined. Further well-designed research studies are urgently required for what is already a major health problem and likely to be so for some years to come.

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