

South African Thoracic Society position statement on post-acute sequelae of SARS-CoV-2 infection

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Executive summary

- Post-acute coronavirus disease-19 (COVID-19) respiratory symptoms are common and may be caused by a variety of factors including, among others, cardiac and respiratory dysfunction.
- A detailed history and examination with appropriate investigations is imperative to define the exact nature of the dysfunction.
- Limited data exist to guide evidence-based approaches to treatment.
- Injudicious use of corticosteroids is cautioned against as well as indiscriminate use of off-label drugs.

Background and nomenclature

The COVID-19 pandemic caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) has caused significant mortality and morbidity in South Africa. The initial clinical focus was on the waves of acute disease and the focus has now shifted to those with post-COVID-19 symptoms and impairments. It is anticipated that COVID-19 will have a long-term impact on the physical, emotional, mental, cognitive, and social status of survivors.

Most patients have mild COVID-19, while a minority of those with acute symptoms require hospitalisation (~10 - 15% depending on age and comorbidities), and only a fraction of these require intensive care support (~3 - 5% of those hospitalised). COVID-19 is responsible for considerable mortality in hospitalised patients, and those that survive may have significant ongoing health issues after discharge.^[1-4] It is also now well recognised that many patients who did not require hospitalisation or intensive care support, may also have ongoing symptoms for weeks or months after the acute illness.^[1-4]

The spectrum of pulmonary involvement in COVID-19 is extensive, and the clinical and radiological presentation of severe COVID-19 pneumonia is variable. It is not yet known to what extent acute infection results in long term respiratory impairments nor the time course to potential resolution.^[5-7] These are often referred to as post-COVID-19 lung disease, long-COVID, or COVID-19 pulmonary fibrosis/ post-COVID-19 organising pneumonia. More recently, the term post-acute sequelae of SARS-CoV-2 infection (PASC) has been used as an umbrella term to collectively describe these effects.

There are currently no clinical trials to provide high-quality data to guide the clinical care of this growing patient population^[8]. The

South African Thoracic Society position statement on post-COVID lung disease is to assist clinicians in managing patients with persistent respiratory symptoms following proven or suspected COVID-19.

Recommendations

We recommend the following:

1. Patients who required intensive care or ventilatory support (including high flow nasal oxygen) may have residual respiratory symptoms and deficits.^[5,7] Follow-up with a specialist physician or pulmonologist is advised.
2. Post-acute respiratory distress syndrome pulmonary fibrosis is a well-recognised condition and responds poorly to available medical therapies.^[9] Follow-up with a specialist physician or pulmonologist is advised.
3. Organising pneumonia is a clinical entity usually diagnosed on histology, together with compatible radiology, and upon the exclusion of an ongoing infectious process. This condition generally responds well to oral corticosteroids but is diagnosed by exclusion and should not be made using radiology alone.^[10,11] Patients with radiological features of organising pneumonia should be referred to a pulmonologist for further investigation, multidisciplinary team discussion, and consideration of therapeutic interventions.
4. SARS-CoV-2 infection may result in prolonged cardiovascular, neurocognitive, and psychiatric problems. Patients with persistent symptoms (>3 months) should be referred to the appropriate specialist for further investigation.^[12]
5. Fatigue is a common symptom following both mild and severe COVID-19 and may be multifactorial in aetiology. Patients with persistent fatigue (>3 months) should be investigated broadly before attributing fatigue to respiratory deficits.^[12,13] A referral to a specialist physician is advised.
6. There are no proven therapies for post-COVID-19 lung disease. Referral of patients to specialist units or to units undertaking clinical trials is advised. The use of experimental/unproven therapies should only be considered by specialist respiratory units, those doing clinical trials, or multidisciplinary teams.
7. Evidence for the use of corticosteroids is limited but their use may be appropriate in a subset of patients with persistent, non-improving

symptoms, in the presence of a multidisciplinary team-confirmed interstitial lung disease and objective impairment in lung function.^[14]

8. Clinical details should be comprehensively recorded, decision-making should be rational and carefully documented, and patients should be closely monitored. The injudicious use of high-dose prolonged courses of corticosteroids, immunomodulatory drugs such as azithromycin, or antifibrotic agents such as pirfenidone, is discouraged.

Workup

Suggestions for initial workup:

1. A detailed history of pre-COVID-19 clinical status, comorbidities, effort tolerance, functional status, in addition to medication and smoking history should be ascertained.
2. A SARS-CoV-2 PCR should ideally be performed and confirmed to be negative prior to physiological testing (lung function/6-minute walk/exercise test etc.) in accordance with infection prevention and control policies and guidelines. Patients may have persistent positive PCR of uncertain significance and while ongoing infectiousness is unlikely, staff/patient safety must be prioritised^[15].
3. Stress-testing, sub-maximal exercise testing, and maximal exercise testing should be used with caution within 3 months of the acute illness due to the risk of exacerbating fatigue, myositis, and myocarditis.
4. A thorough clinical and laboratory evaluation should be performed for common causes of fatigue, including an evaluation of sleep and mental health changes, haemoglobin, thyroid function, renal function, creatinine kinase, and glycated haemoglobin A1C.^[1,16]
5. An electrocardiogram, spirometry, pulse oximetry and chest radiograph are recommended for the initial investigation of persistent respiratory or cardiovascular symptoms.^[12-14]
6. Specialised investigation with high resolution computerised tomography (CT), CT pulmonary angiography, echocardiography, coronary angiography, and neurocognitive studies should be considered for patients with persistent symptoms (>3 months) who are not on an improving clinical trajectory, or in whom initial testing (as above) warrants further specialist investigation. Bronchoscopy with lavage and biopsies should also be considered where indicated.^[10,11,17]

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