

EDITORIAL

Considering the long-term respiratory effects of Covid-19

The Covid-19 pandemic arrived in Western Europe in the early spring of 2020. It has had a devastating effect on almost every aspect of our lives. There have been immediate impacts on those most affected with significant loss of life and prolonged periods of illness. So many families are unable to be with loved ones and the immediate effect of their loss can be seen in those most affected. The virus has significant ramifications on all aspects of our society which will continue for the foreseeable future. The consequences for societal norms, career and employment opportunities, both physical and mental health remain have yet to fully unfold.

While there have been many deaths from Covid-19, the majority of patients survive. As many as 80% of those who contract the virus will remain asymptomatic or only have mild symptoms. The remaining sufferers may require admission to hospital with ~5% of patients requiring mechanical respiratory support of varying levels of intensity.

Those patients who do require invasive ventilation often need it for many weeks. The disease imitates Adult Respiratory Distress Syndrome (ARDS). Post-mortem studies indicate exudative diffuse alveolar damage with hyaline membrane formation, organizing micro-thrombi, organizing pneumonia and advanced proliferative phases of diffuse alveolar damage but little in the way of early fibrotic changes [1]. The treatment of the disease is similar to standard treatment of ARDS albeit the lungs do not seem to develop the same problems with compliance and the inflammatory process has a greater degree of thrombogenic inflammation than might be seen in other forms of ARDS.

Patients requiring prolonged ventilation for ARDS may be subject to complications not just from the disease itself but may develop tracheal complications such as tracheomalacia or stenosis, pulmonary complications related to barotrauma, oxygen toxicity, ventilator-associated pneumonia and pleural fibrosis. Many patients may develop multi-organ failure and almost all develop forms of critical illness myopathy and/or neuropathy. In such patients the path to recovery is inevitably slow and arduous [2]. The degree of any disability will depend on the severity of the condition and the complications of the treatments needed to keep the patient alive. It is too early to speculate even now as to what

the long-term complications of the most severe manifestations of Covid-19 will be because of the prolonged time to achieve optimal recovery.

Several recent studies in patients with Covid-19 infection with both moderate and severe disease show residual changes on chest scans with varying degrees of reductions in lung function 3 months post-discharge [3–5] with ground glass changes, atelectasis and varying degrees of obstructive or restrictive pulmonary dysfunction. Previous studies on patients with Middle East Respiratory Syndrome (MERS) and Severe Adult Respiratory Syndrome (SARS-CoV-1), both RNA viruses, may provide some insight looking forward.

Ahmed and colleagues [6] reviewed the data on 28 studies which followed up patients who were hospitalized with MERS and SARS-1 and noted persistent reductions in respiratory function and exercise tolerance at 6 and 12 months post-discharge with noted reductions in diffusion capacity and total lung capacity. As many as 35% of patients had significant mental health issues identified including post-traumatic stress disorder, depression and anxiety identified using varying scales. Those patients affected had significantly lower scores in quality of life outcomes using the Short Form 36 health survey and the Health-Related Quality of Life questionnaire.

Hui *et al.* [7] noted significant impairment in SARS-1 survivors specifically diffusion capacity in 23.7% of patients after 12 months. A reduction in exercise capacity and well-being compared to a normal population was also noted. Batawi *et al.* [8] compared quality of life indices in MERS and SARS-1 survivors and found little difference between the two groups although perhaps not surprising those requiring ICU care reported lower quality of life scores. In patients with SARS followed up over a 15-year period, pulmonary function recovered much later than changes on CT scanning. Long-term studies have only been described in the most seriously affected patients. The demographic profile and history of co-morbidities was similar for patients with MERS and SARS-1 as we have noted for Covid-19 with older patients with ischaemic heart disease, type 2 diabetes, obesity and chronic lung diseases faring worst.

Those with mild pneumonitis who required oxygen support only may present with a number of symptoms. These might include persisting dyspnoea,

prolonged cough, asthma like symptoms and sleep-related symptoms. Data on viral chest infections pre-COVID show that patients may develop post-viral cough syndromes and those who with previous airway hyper-responsiveness, asthma maybe a temporary or permanent sequelae. A number of patients may present with undiagnosed respiratory conditions such as chronic obstructive pulmonary disease (COPD) or early idiopathic pulmonary fibrosis (IPF). Persisting fatigue and dyspnoea may be due to de-conditioning but may relate to parenchymal scarring or milder forms of post-infective myopathy.

Many post-Covid-19 patients experience persistent symptoms of anxiety with dysfunctional breathing, palpitation, asthenia and headaches. In many these will be superimposed on other symptoms related to co-morbidities which made them more susceptible to the effects of the Covid-19 virus. These patients should receive appropriate follow-up with early intervention which should include access to clinical, radiological and physiological assessment with referral to pulmonary rehabilitation and psychological support. In many centres virtual early discharge pulmonary rehabilitation programmes have already been initiated with apparent success. The British Thoracic Society [9] have issued guidelines on the follow-up of patients with post-Covid-19 pneumonia emphasizing the risk of pulmonary embolus and persistent parenchymal disease. While it acknowledges the need for a holistic approach this is not specifically included in its protocol.

The larger group of patients with few or no symptoms may have concerns about the future presenting with various symptoms which are likely to be varying manifestations of anxiety. It is too early to dismiss these symptoms as not reflecting ongoing pathophysiology. The effects of the social restrictions imposed by government and the response by and effect of family and colleagues is likely to impact on this process. There are now reports of 'long' COVID occurring in patients even after mild episodes of the infection but its exact nature remains unknown and probably will form a heterogeneous group who may require a multidisciplinary approach to diagnosis and management. The National Institute for Health Research [10] recently outlined four variants of 'Long Covid'. While useful it is unlikely to be helpful to label the wide variation in physical and psychological complications under the same umbrella. Greenhalgh and colleagues [11] have outlined an approach which integrates post-infection physical symptoms, co-morbidities and the psychosocial impact on the overall health and well-being of the patient.

Returning to the workplace may be an unnerving experience. The workplace will have changed and the restrictions required may impact heavily on normal work dynamics. Although disadvantageous for many, some will welcome the new arrangements. The NHS has

recently updated its advice on those with medical conditions or treatments which it considers to be at high or moderately high vulnerability risk. The advice remains that they should work from home if at all possible. Some patients may not be aware of the immunosuppressive effect of their medication. Although some data suggest a lower-than-expected prevalence of Covid-19 in those with asthma and COPD, they are still at greater risk from the effects of infection. Risk assessments for patients with chronic asthma and chronic obstructive airways disease will depend on the severity of the disease and the need for medication to maintain a well patient. Those on biologic therapies are considered to be particularly at risk. For patients with cystic fibrosis, pulmonary fibrosis and history of lung cancer return to work needs some reflection and specialist advice may be sought. Patients with sleep apnoea [12] are likely to be at greater risk due to the many risk factors and co-morbidities that these patients share with those related to poor outcome from the infection. The Society of Occupational Medicine [13] was early in publishing guidelines on advising the need for ensuring a safe working environment and appropriate risk assessment of individual workers. This guideline on emerging from lockdown will remain relevant for the foreseeable future.

The National Institute for Clinical Excellence (NICE) aims to publish a strategy in the near future to provide a national framework for assessing and managing patients with ongoing symptoms. The development of effective therapies such as remdesivir, dexamethasone and others as well as improved clinical management and organizational strategies has resulted in improved outcomes for many patients. The announcement of an effective vaccine(s) gives hope for the future. The challenge will be to provide the energy, resources and infrastructure to help the increasing number of post-Covid symptomatic patients.

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