



## Evaluation of pulmonary function in post-COVID-19 patients - when and how should we do it?

Ana Fonseca<sup>1</sup>, Ricardo Lima<sup>1,2</sup>, Inês Ladeira<sup>1,2,3</sup>, Miguel Guimarães<sup>1,2</sup>

### TO THE EDITOR:

In December of 2019, initial reports regarding a novel respiratory virus, later designated SARS-CoV-2, emerged from Wuhan, China. This highly transmissible virus spread rapidly. On March 11, 2020, the WHO declared COVID-19 to be a global pandemic, marking the beginning of a new world era. Given the possible clinical consequences of this infection—such as the development of SARS and the high infection and mortality rates—countless investigations and studies were conducted. In 2020, a great deal of knowledge was generated at light speed about the virus itself and its transmission, as well as on the applicability of various drugs/procedures as potential therapeutic approaches. Now, after one year from the beginning of the pandemic and more than 100 million cases of SARS-CoV-2 infection, the majority of whom surviving, we are posed with a new challenge: how and when ought we to follow up these patients?

Looking back, the outbreak of SARS, a novel coronavirus infection that started in southern China and was identified in March of 2003, became a global public health crisis. In the years that followed, various studies regarding the follow-up of survivors were published. The assessment included spirometry and determination of lung volumes and DL<sub>CO</sub> at 3, 6, 12, 18, and 24 months after the disease onset.<sup>(1-3)</sup> Significantly impaired DL<sub>CO</sub> was the most commonly reported lung abnormality, present in 15-50% of the survivors. Low exercise capacity was also reported, measured by the six-minute walk test (6MWT)<sup>(1-3)</sup> and cardiopulmonary exercise testing (CPET),<sup>(4)</sup> the latter suggesting extrapulmonary causes for the functional outcomes in those patients. Respiratory muscle strength was measured in two studies,<sup>(2,3)</sup> using MIP and MEP. It is also important to point out that health status was evaluated using the Medical Outcomes Study 36-item Short-Form Health Survey, whose scores showed a positive correlation with pulmonary function abnormalities.<sup>(1-3)</sup>

Most recently, a systematic review and meta-analysis<sup>(5)</sup> on respiratory function in post-COVID-19 patients reported altered DL<sub>CO</sub> in approximately 40% of the patients. However, the results must be analyzed with caution, because respiratory comorbidities and different timing of evaluations should be considered. It is still unclear whether interstitial abnormalities or pulmonary vascular abnormalities contributed to the decrease in DL<sub>CO</sub> in those patients.<sup>(6)</sup> Initial results from the national prospective observational Swiss COVID-19 lung study,<sup>(7)</sup> after a

4-month follow-up of COVID-19 survivors, identified that low DL<sub>CO</sub> was the single most important factor associated with previous severe/critical disease, which translated to reduced six-minute walk distance and oxygen desaturation during exercise.

An important aspect to consider is the ideal timing to perform pulmonary function tests. The British Thoracic Society guidelines, regarding patients with COVID-19 pneumonia, recommended that pulmonary function tests be performed at 3 months after discharge if chest X-ray changes have not satisfactorily resolved or if the patient has ongoing respiratory symptoms.<sup>(8)</sup> Similar recommendations have been made by the Spanish Society of Pulmonology and Thoracic Surgery.<sup>(9)</sup> That society suggests that simple spirometry and determination of DL<sub>CO</sub> should be used as a first approach; if interstitial lung disease is suspected, body plethysmography should be included, whereas if symptoms persist, exercise tests, such as 6MWT or CPET, should be carried out. Measuring respiratory muscle strength (MIP, MEP, and sniff nasal inspiratory pressure) may also be considered in such patients.<sup>(9)</sup>

In the United States, the Yale School of Medicine at New Haven has developed a program to provide a comprehensive evaluation of post-COVID-19 complications, characterize and mitigate pulmonary sequelae, and address persistent symptoms experienced by survivors.<sup>(10)</sup> There is also an ongoing multicenter prospective observational cohort study in Brazil<sup>(11)</sup> involving post-COVID-19 patients during a one-year follow-up by means of extensive pulmonary function assessment (spirometry, lung volumes, DL<sub>CO</sub>, 6MWT, and CPET), CT of the chest, and administration of quality of life questionnaires.

In summary, there are currently a great number of post-COVID-19 patients who ought to be followed up so that respiratory and nonrespiratory complications can be identified. It is of utmost importance that clinical follow-up protocols be established and adapted to the reality of every country for recommending which, when, and how often ancillary tests should be performed. On the basis of the information available so far, survivors of COVID-19 pneumonia should be evaluated at 3 months after discharge. That evaluation should include investigation of respiratory symptoms, X-ray of the chest, spirometry, and determination of DL<sub>CO</sub>. In the presence of altered or persistent symptoms, whole body plethysmography, exercise testing, and evaluation of muscle strength should be carried out. In addition, patients with a previous

1. Departamento de Pneumologia, Centro Hospitalar Vila Nova de Gaia e Espinho, Porto, Portugal  
2. Laboratório de Função Pulmonar, Centro Hospitalar Vila Nova de Gaia e Espinho, Portugal  
3. Departamento de Medicina, Faculdade de Medicina, Universidade do Porto, Porto, Portugal

diagnosis of respiratory disease who get infected with SARS-CoV-2, even without developing pneumonia, should be reevaluated 3 months after the infection being detected, or earlier if there is worsening of symptoms.

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