

A Key to Unlocking the Mysteries of COVID-19 Pulmonary Sequelae: Are We There?

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Coronavirus disease 2019 (COVID-19) pneumonia is a progressive disease with a variable clinical course. Nearly 50% of COVID-19 survivors experience long-lasting sequelae after the acute phase of illness with the persistence of pulmonary and extrapulmonary symptoms [1]. One of the foremost consequences of severe acute respiratory syndrome (SARS)-CoV-2 infection is the development of a persistent restrictive ventilatory defect and radiological findings consistent with interstitial lung disease [2–5].

The mechanism underlying the chronic respiratory sequelae and precipitating factors of post-acute COVID-19 are not well understood, but long-term pulmonary effects have been similarly shown in patients with SARS [6] and Middle East respiratory syndrome [7]. Moreover, given the high number of SARS-CoV-2-infected patients, early prediction of post-acute progression of clinical abnormalities may be fundamental in delivering appropriate health care for COVID-19 survivors that are likely to develop persistent lung abnormalities.

Patient characterization and risk assessment for the development of pulmonary sequelae in individuals previously hospitalized for COVID-19 pneumonia are crucial to optimize follow-up and treatment as well as to design

a dedicated clinical pathway for delivery of care when managing outpatient with long-lasting respiratory involvement. Factors predicting the evolution of pulmonary sequelae after COVID-19 pneumonia were first reported in the literature by Marvisi et al. [8], and then further reports explored different variables associated with pulmonary sequelae and radiological fibrosis-like changes in survivors of COVID-19 [9–12].

In this issue of *Respiration*, Aiello et al. [13] reported the results of a prospective, observational, single-center study of a large cohort of subjects who suffered from COVID-19 pneumonia during their follow-up post-hospital admission. They collected changes in clinical and functional data to identify risk factors for high-resolution computer tomography (HRCT) sequelae in COVID-19 patients after hospitalization and to test the usefulness and clinical relevance of the COSeSco score (COVID-19 Sequelae Score), which includes age, body mass index, comorbidities, and D-dimer at the time of hospitalization, as well as exercise capacity and dyspnea at follow-up, for the prediction of developing pulmonary sequelae at HRCT.

In a cohort of 121 patients recovering from COVID-19 pneumonia, they found that 63% of patients showed radiological and lung function impairment in terms of diffusing lung capacity and lung volumes with an average HRCT score of 11.22% after 4 months from hospitalization. Moreover, examining the cluster of patients with a re-

duced diffusing lung capacity (<80%), they found six dependent variables characterizing subjects with radiological pulmonary sequelae, which were analyzed, pooled together, and synthesized in the COSeSco score. The COSeSco score, ranging from 0 to 15, was able to significantly discriminate COVID-19 patients with radiological sequelae (HRCT score >10%) at follow-up, with a high prediction accuracy of the model (AUC of 0.94) with high sensitivity and specificity (sensitivity: 100%; 95% CI: 67.54%–86.44% and specificity: 76.86; 95% CI: 68.32%–84.04%, respectively). The authors acknowledged the main limitations of the study. The absence of a control cohort implies the need to validate the COSeSco on an external population, and the lack of baseline data on pulmonary function and exercise capacity does not allow to attribute with certainty to COVID-19 the abnormal findings. Since the COVID-19 pandemic is continuing to threaten and overwhelm the healthcare system during both the acute phase of the disease and the chronic phase for the persistent long-term pulmonary impairment triggered by the SARS-CoV-2 infection, this score might represent a key for unloading the healthcare system of unnecessary exams and outpatient visits of the COVID-19 survivors.

The importance of assessing a predictive score for pulmonary sequelae at HRCT in COVID-19 patients arises from the need to promptly recognize symptoms and diagnose chronic respiratory sequelae in patients recovering

from COVID-19, thus reducing adverse outcomes. Indeed, routinely performing HRCT scans on all the patients with a history of COVID-19 would be costly, time-consuming, and poorly feasible, given the high number of infected patients. Moreover, the COSeSco scoring systems require few, easily measurable, and routinely collected variables; thus, it may be valuable even in resource-limited settings, allowing clinicians worldwide to identify subjects at risk for pulmonary complications and offer the best available clinical management strategy to the patients at risk. Further validation studies of the COSeSco score in a larger cohort of individuals remain fundamental to confirm its external validity and its routine use in clinical practice.

Conflict of Interest Statement

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Author Contributions

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References

- Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. Six-month consequences of COVID-19 in patients discharged from hospital: a Cohort Study. *Lancet*. 2021 Jan 16; 397(10270):220–32.
- Spagnolo P, Balestro E, Aliberti S, Cocconcelli E, Biondini D, Casa GD, et al. Pulmonary fibrosis secondary to COVID-19: a call to arms? *Lancet Respir Med*. 2020 Aug;8(8): 750–2.
- Guler SA, Ebner L, Aubry-Beigelman C, Bridevaux PO, Brutsche M, Clarenbach C, et al. Pulmonary function and radiological features 4 months after COVID-19: first results from the National Prospective Observational Swiss COVID-19 Lung Study. *Eur Respir J*. 2021 Apr;57(4).
- Mylvaganam RJ, Bailey JI, Sznajder JI, Sala MA. Northwestern comprehensive CCC. Recovering from a pandemic: pulmonary fibrosis after SARS-CoV-2 infection. *Eur Respir Rev*. 2021 Dec;30(162):30.
- Crimi C, Impellizzeri P, Campisi R, Nolasco S, Spanevello A, Crimi N. Practical considerations for spirometry during the COVID-19 outbreak: Literature review and insights. *Pulmonology*. 2021;27(5):438–47.
- Hui DS, Wong KT, Ko FW, Tam LS, Chan DP, Woo J, et al. The 1-year impact of severe acute respiratory syndrome on pulmonary function, exercise capacity, and quality of life in a cohort of survivors. *Chest*. 2005 Oct;128(4):2247–61.
- Park WB, Jun KI, Kim G, Choi JP, Rhee JY, Cheon S, et al. Correlation between pneumonia severity and pulmonary complications in middle east respiratory syndrome. *J Korean Med Sci*. 2018 Jun 11;33(24):e169.
- Marvisi M, Ferrozzi F, Balzarini L, Mancini C, Ramponi S, Uccelli M. First report on clinical and radiological features of COVID-19 pneumonia in a Caucasian population: factors predicting fibrotic evolution. *Int J Infect Dis*. 2020 Oct;99:485–8.
- Lerum TV, Aalokken TM, Bronstad E, Aarli B, Ikdahl E, Lund KMA, et al. Dyspnoea, lung function and CT findings 3 months after hospital admission for COVID-19. *Eur Respir J*. 2021 Apr;57(4):2003448.
- Myall KJ, Mukherjee B, Castanheira AM, Lam JL, Benedetti G, Mak SM, et al. Persistent post-COVID-19 interstitial lung disease. An Observational Study of corticosteroid treatment. *Ann Am Thorac Soc*. 2021 May;18(5): 799–806.
- Sonnweber T, Sahanic S, Pizzini A, Luger A, Schwabl C, Sonnweber B, et al. Cardiopulmonary recovery after COVID-19: an observational prospective multicentre trial. *Eur Respir J*. 2021 Apr;57(4).
- Wu X, Liu X, Zhou Y, Yu H, Li R, Zhan Q, et al. 3-month, 6-month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalisation: a Prospective Study. *Lancet Respir Med*. 2021 Jul;9(7):747–54.
- Aiello M, Marchi L, Calzetta L, Speroni S, Frizzelli A, Ghirardini M, et al. Coronavirus disease 2019: COSeSco – a risk assessment score to predict the risk of pulmonary sequelae in COVID-19 patients. *Respiration*. 2021 Oct 21;1–9.