Radiology

Residual Lung Lesions at 1-year CT after COVID-19

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As of September 14, 2021, there were nearly 220 million confirmed cases of severe acute respiratory syndrome coronavirus 2, with almost 4.6 million deaths worldwide. Although unprecedented efforts have focused on the sequencing, diagnosis, treatment, and prevention of COVID-19, the long-term sequelae of COVID-19 have not yet been fully elucidated. Ongoing studies have reported that the effects of long-term sequelae of COVID-19 include fatigue, muscle weakness, dyspnea, mental disorders, and decreased quality of life.

Systematic evaluation of long-term CT features from the initial diagnosis to the convalescent period at 1 year after symptom onset in patients with COVID-19 is lacking. Thus, in this issue of *Radiology*, Pan and Yang et al (1) performed an observational study to assess the dynamic chest CT manifestations of COVID-19 over a follow-up period of 1 year. The authors concluded that chest CT showed abnormal findings in 25% (53 of 209 study participants) of participants with COVID-19 at 1-year follow-up CT. The abnormalities are comprised of chronic fibrotic-like lesions (linear lesions, 25 of 209 participants [12%] or multifocal reticular or cystic lesions, 28 of 209 participants [13%]). Older patients with severe COVID-19 or adult respiratory distress syndrome (ARDS) are more likely to develop lung sequelae. At 3-month follow-up CT, 61% of participants (128 of 209) had no remaining lesions, and at 12-month CT, 75% of participants (156 of 209) had resolution. Therefore, resorption of lung abnormality is much slower at CT performed more than 3 months after symptom onset.

It is difficult to obtain serial CT studies in patients with COVID-19 pneumonia because follow-up evaluations are usually not performed on a routine basis, and most patients have mild symptoms and are discharged without disease progression. In this context, Pan and Yang et al (1) should be commended for their judicious review of 209 consecutive patients regarding serial CT findings of the disease at 3, 7, and 12 months after symptom onset. In addition, the authors found that being aged 50 years or older, having peripheral blood lymphopenia, and having severe pneumonia and/or ARDS were independent risk factors for residual abnormality at 1 year (odds ratio = 15.9, 18.9, and 43.9, respectively; $P < .001$ for each comparison). Prioritization of follow-up care may be considered for these patients at high risk for the long-term sequelae of COVID-19.

To date, two previous studies described the 1-year long-term respiratory complications of COVID-19 using CT scans and lung function test results (2,3). In one study of 83 patients with severe COVID-19 pneumonia who were not intubated, impaired pulmonary function was observed in one-third of patients 12 months after discharge (2). In that study, 65 of the 83 patients (78%) had residual changes at CT at 3 months, and 40 of the 83 patients (48%) had residual changes at CT at 6 months. CT changes were not completely resolved in 27% of patients (22 of 83), predominantly in those with ground-glass opacity (n = 20, 24%) without development of definitive fibrosis or progressive interstitial changes.

In the second 12-month follow-up study (3), 1276 hospital survivors of COVID-19 were included to show the dynamic recovery of health outcomes within 12 months of symptom onset. The lung diffusion impairment and radiographic abnormalities persisted for up to 12 months in some patients. At 1 year, ground-glass opacities and interlobular septal thickenings were present in 76% (29 of 38) and 11% (four of 38), respectively, of 38 patients who received oxygenation by means of a high-flow device, ventilator, or extracorporeal membrane oxygenation therapy. Meanwhile, in 28 patients who did not require oxygenation, ground-glass opacities and interlobular septal thickenings remained at 1 year in 39% (11 of 28) and 0%, respectively. Ground-glass opacity and irregular lines were associated with lung diffusion impairment.

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Conflicts of interest are listed at the end of this article.

See also the article by Pan and Yang et al in this issue.

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Post–COVID-19 pulmonary fibrosis may be defined as the persistent presence of fibrotic CT changes identified at follow-up study, often combined clinically with declined pulmonary function. Histopathologic patterns identified in post–COVID-19 pulmonary fibrosis, even though not fully determined, are presumed to be those of an organizing and fibrotic phase of diffuse alveolar damage, fibrosing nonspecific interstitial pneumonitis, and organizing pneumonia patterns. CT features potentially identified in pulmonary fibrosis secondary to COVID-19 pneumonia have been suggested to include the presence of architectural distortion, reticular lesions, traction bronchiolectasis, ground-glass opacity, mosaic attenuation, and honeycombing in consideration of presumed histopathologic patterns (4). However, according to the study by Pan and Yang et al (1), the CT features seen at 1-year follow-up studies were those of fibrotic-like linear or multifocal reticular or cystic lesions. Typical features of diffuse alveolar damage at CT, fibrosing nonspecific interstitial pneumonitis, or organizing pneumonia patterns could not be seen. These results are similar to those of follow-up CT features of severe acute respiratory syndrome–associated coronavirus (SARS-CoV) infection. Interestingly, in SARS-CoV infection, ground-glass opacity and interstitial opacity in the convalescent phase usually resolve over time, and only air trapping persists (5). Conversely, patients with underlying interstitial lung disease are at an increased risk of death from COVID-19, particularly those with poor lung function and obesity (6).

Some limitations should be noted. First, although Pan and Yang et al (1) succeeded in enrolling 209 patients for serial CT evaluation, selection bias may have been present. Patients with severe disease and/or ARDS may have self-discharged or may have been admitted to the intensive care unit and treated longer, thus evading study enrollment. Therefore, patients with rather milder diseases may have been selectively included.

Second, COVID-19 pneumonia can be differentiated into three patterns, namely bronchopneumonia, organizing pneumonia, and diffuse alveolar damage. Patients showing a diffuse alveolar damage pattern at CT have clinically severe disease, thus requiring oxygen therapy or mechanical ventilation therapy (7). If the patients with a diffuse alveolar damage pattern at CT were consecutively included, different patterns of remaining disease could have been encountered in more cases than in those of the authors' case series. Then, follow-up CT may have included the cases of oxygen toxicity related to the ventilator therapy. The consequent patterns of oxygen toxicity and ventilation therapy include areas of reticular and ground-glass opacity in addition to pulmonary cysts of varying sizes and bullae, particularly in the anterior parts of the lungs, which probably developed as a result of prolonged ventilation (8).

Finally, in patients with a diffuse alveolar damage pattern at CT, a condition of prolonged stay in the intensive care unit, early and inappropriate use of corticosteroids, virus-induced immune dysregulation, and concurrent use of immunomodulatory drugs may have led to pulmonary fungal infections. These include COVID-19–associated pulmonary aspergillosis (9) and COVID-19–associated pulmonary mucormycosis (10). Such ongoing pulmonary fungal infections or healing status of these infections may have changed the features on CT scans obtained at 1-year follow-up.

In conclusion, 1-year follow-up CT scans in patients who recovered from COVID-19 pneumonia showed chronic fibrotic-like linear or multifocal reticular or cystic lesions. However, the features are different from classic diffuse alveolar damage patterns at CT, fibrosing nonspecific interstitial pneumonitis, or organizing pneumonia. Independent risk factors for these fibrotic-like lesions include being aged 50 years or older, having peripheral blood lymphopenia, and having severe pneumonia and/or ARDS. However, those features at CT may vary according to the presence of confounding variables such as a history of intensive care with ventilation therapy or the concurrent presence of a pulmonary fungal infection such as COVID-19–associated pulmonary aspergillosis or COVID-19–associated pulmonary mucormycosis.

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