RESEARCH LETTER

A comprehensive study of persistent changes on lung computed tomography scans of convalescent patients 3 months after recovery from severe and moderate COVID-19 pneumonia

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Introduction Since the outbreak of the coronavirus pandemic in Wuhan, China, there has been growing evidence about the evolution of chest computed tomography (CT) abnormalities in SARS-CoV-2 pneumonia.[1] However, relatively few studies focused on residual radiological changes found in convalescent patients in the long term.[2-4] There are even fewer studies that used CT scores to classify particular radiological changes observed after different courses of SARS-CoV-2 infection.

The aim of our study was to classify and determine the incidence of particular residual radiological lung changes in convalescent patients 2 to 4 months (mean, 3 months) after moderate and severe COVID-19 pneumonia. We also aimed to assess the progression of the persisting disease using the total severity score (TSS) by Kunwei Li et al[5,6] and the chest CT score by Kunhua Li et al.[7] Finally, we aimed to analyze the changes visible on the chest CT scans in association with the severity of the disease on admission to the hospital, age, sex, and duration of convalescence.

Patients and methods We retrospectively analyzed chest CT scans of 107 convalescent patients after SARS-CoV-2 infection who were hospitalized between September 1, 2020 and April 15, 2021. The patients were managed according to the current treatment recommendations for COVID-19 pneumonia. At the time of leaving the hospital, they met the standard discharge criteria (normal body temperature for >3 days, improved laboratory, clinical, and respiratory parameters, and negative results of 2 consecutive SARS-CoV-2 tests). The exclusion criteria comprised chronic respiratory or psychotic diseases prior to hospitalization for COVID-19. The study group was divided into 2 subgroups of patients with moderate (n = 67) and severe / critical disease (n = 40), according to the recommendations of the Polish Association of Epidemiologists and Infectiologists.[8] All the patients were hospitalized during the acute phase of the disease, 28 of them were treated with mechanical ventilation, and all had a control chest CT scan performed after discharge in the period between December 15, 2020 and July 31, 2021.

CT imaging from the apices to the bases of the lungs was performed in each patient in the supine position during deepest inspiration and breath holding, without intravenous contrast administration, using a General Electric 64-row scanner (GE Healthcare, Waukesha, Wisconsin, United States). The extent of radiological changes and the degree of involvement of each lobe were assessed with the well-established semiquantitative scales: the TSS by Kunwei Li et al[5,6] and the chest CT score by Kunhua Li et al.[7] Further, we analyzed the frequency of persistent changes on chest CT imaging and their association with the initial clinical severity of the disease. All the baseline and follow-up images were assessed by a radiology specialist with 15 years of experience, who was blinded to the clinical data of the patients.

Ethics The study was approved by the Institutional Review Board (KE-0254/231/2021), and

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Received: December 28, 2021.
Revision accepted: April 8, 2022.
Published online: April 14, 2022.
Pol Arch Intern Med. 2022; 132 (5): 16242
doi:10.20452/pamw.16242
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the requirement for written informed consent was waived because it involved a retrospective analysis of existing medical records of the participants. However, written informed consent for performing a chest CT scan was obtained from all patients in adherence to the national regulations on medical treatment.

Statistical analysis Continuous variables were presented as means (SDs), whereas categorical variables were expressed as frequencies and percentages. Ordinal variables were presented as medians and interquartile ranges (IQRs). To analyze the association between ordinal variables, the nonparametric Spearman rank correlation was used. The rank correlation coefficient equal or greater than 0.19 was considered significant for our sample size (>100). The comparison between abnormalities on CT or sex and the CT scores was assessed with the Mann–Whitney test. Nominal variables were compared between the groups using the Fisher exact test. A 2-tailed *P* value below 0.05 was considered significant. Statistical analyses were performed with the SPSS software (SPSS Inc., IBM, Armonk, New York, United States).

Results A total of 107 hospitalized patients (52 men and 55 women) were enrolled in the study. The mean (SD) age of the participants was 60.2 (12.7) years (median [IQR], 63 [33–86] years). They underwent a follow-up CT examination during their convalescence period, at a mean (SD) of 87.3 (16.1) days and a median of 82 days after the onset of the disease (min–max, 65–130 days). Among them, 67 patients (62.6%) developed moderate symptoms and 40 patients (37.4%) had severe disease.

On follow-up CT images, only 1.9% of the patients showed complete resolution of pulmonary changes. We found that the most frequent changes on the control CT scans were ground-glass opacities (GGOs) (79.4%), reticular pattern (77.6%), fibrotic changes (67.3%), nodules (18.7%), cavitation or air bubble signs (11.2%), and bronchiectasis (7.5%) with bronchial and pleural thickening (7.5% and 9.4%, respectively). The detailed distribution of radiological changes in different groups, together with the clinical characteristics of the patients are presented in TABLE 1. No significant differences were observed between the sexes. However, a significant difference was noted between the frequencies of residual pulmonary changes in the patients after severe and moderate disease. Patients after severe COVID-19 had a higher prevalence of fibrosis, reticular pattern, honeycombing, and vascular enlargement ($P < 0.05$).

Computed tomography score classifications High TSS and CT scores were observed in all the convalescent patients. The median TSS was 5 points (IQR, 2–7; min–max, 0–19) and the median chest CT score was 6 points (IQR, 2–10; min–max, 0–24). The obtained radiological scores were further analyzed in relation to the clinical data of the patients and their initial disease severity. We observed a significant difference in the number of days between the onset of the disease and the control CT in the subgroups with different severity of COVID-19 ($P = 0.037$). Age was strongly positively linked with both radiological scores—TSS and chest CT score ($R = 0.47$; $P < 0.001$ and $R = 0.4$; $P < 0.001$, respectively). However, it was not associated with the severity of the initial disease ($P = 0.12$). Male sex was linked with both TSS and chest CT score ($P = 0.04$ and $P = 0.049$, respectively), whereas it did not show any association with the disease severity at the onset ($P = 0.33$). Both TSS and chest CT score were associated with the severity of the initial disease ($P = 0.01$ and $P = 0.01$, respectively), indicating that, in patients with severe COVID-19, pulmonary abnormalities resolved slower than in individuals with a moderate infection. The duration of convalescence showed an inverse correlation with the radiological scores (TSS, $R = –0.22$; $P = 0.02$; chest CT score, $R = –0.22$; $P = 0.02$), indicating that the pulmonary changes were subsiding with time in all patients.

Discussion Computed tomography is a confirmed method of diagnosis and follow-up of pulmonary consequences in patients with COVID-19. To our best knowledge, there are limited data in terms of complex radiological analysis of pulmonary abnormalities in convalescent COVID-19 patients 3 months after hospitalization for moderate and severe disease.

Pan et al[9] analyzed changes on lung CT over time during an acute infection and in the early recovery period (up to 2 weeks). They found extensive GGOs and subpleural bands persisting at 2 weeks post COVID-19 pneumonia to be an already well-developed healing response. However, the study analyzed only a small number of patients with mild or moderate infection, who did not need oxygen supplementation during the disease and had no respiratory distress, unlike patients in our study group.

In the study by Tabatabaei et al,[10] 42.3% of its 51 participants had residual abnormalities visible on control CT scans after 3 months. The most frequent changes on the follow-up CT scans were GGOs (54.5%), whereas 31.8% of the cases showed GGOs coexisting with subpleural parenchymal bands, and 13.7% showed pure subpleural parenchymal bands. This study included patients at all stages of acute infection. In our study, we observed more pulmonary changes during a 3-month period of convalescence; however, we included only patients with moderate and severe disease with distress syndrome, who needed prolonged hospitalization and oxygen supplementation.

Han et al[11] assessed pulmonary changes on follow-up CT scans of patients with severe COVID-19 pneumonia 6 months after discharge from the hospital. In that study, fibrotic changes

TABLE 1 Characteristics of the study participants, computed tomography scores, and the frequency of radiological changes observed in convalescent COVID-19 patients

Parameter	Total (n = 107)	Men (n = 52)	Women (n = 55)	*P* value	Severe (n = 40)	Moderate (n = 67)	*P* value
Severe disease, %	37.4	42.3	32.7	–	–	–	–
Age, y, mean (SD; min–max)	60.2 (12.7; 33–86)	59.4 (12.4; 35–82)	60.9 (13.1; 33–86)	–	62.1 (14.7; 33–86)	59.0 (11.3; 35–80)	–
Time from disease onset to control CT, d, mean (SD; min–max)	87.3 (16.1; 65–130)	85.1 (15.6; 65–130)	89.5 (16.5; 66–130)	–	91.0 (16.1; 65–119)	85.1 (15.9; 66–130)	–
TSS, points, median (IQR; min–max)	5.0 (2–7; 0–19)	5.0 (2–7; 0–19)	5.0 (3–5.5; 1–11)	–	5.5 (3.5–10; 1–19)	5.0 (2–5; 0–11)	–
Chest CT score, points, median (IQR; min–max)	6.0 (2–10; 0–24)	8.0 (2–11.25; 0–24)	5.0 (3–9; 1–16)	–	10.0 (2.75–15; 0–24)	5.0 (2–8.5; 0–14)	–
CT abnormalities, n (%)							
Presence of radiological symptoms	105 (98.1)	50 (96.2)	55 (100)	0.35	40 (100)	65 (97.0)	0.56
GGO	85 (79.4)	38 (73.1)	47 (85.5)	0.15	34 (85)	51 (76.1)	0.33
Consolidations	12 (11.2)	6 (11.5)	6 (10.9)	1.00	4 (10)	8 (11.9)	>0.99
Crazy paving	6 (5.6)	4 (7.7)	2 (3.6)	0.43	2 (5)	4 (6.0)	>0.99
Reticular pattern	83 (77.6)	36 (69.2)	47 (85.5)	0.06	36 (90)	47 (70.1)	0.02
Halo sign	2 (1.9)	2 (3.8)	0	0.35	0	2 (3.0)	0.56
Atol sign	4 (3.7)	2 (3.8)	2 (3.6)	1.02	0	4 (6.0)	0.3
Fibrosis	72 (67.3)	34 (65.4)	38 (69.1)	0.84	20 (50)	52 (77.6)	0.005
Honeycomb sign	6 (5.6)	4 (7.7)	2 (3.6)	0.43	6 (15)	0	0.005
Air brochogram	6 (5.6)	4 (7.7)	2 (3.6)	0.43	2 (5)	4 (6)	>0.99
Brochiectasis	8 (7.5)	6 (11.5)	2 (3.6)	0.15	4 (10)	4 (6.0)	0.47
Bronchial wall thickening	8 (7.5)	8 (15.4)	0	0.003	6 (15)	2 (3)	0.054
Pleural effusion	2 (1.9)	2 (3.8)	0	0.35	2 (5)	0	0.25
Pleural thickening	10 (9.3)	6 (11.5)	4 (7.3)	0.52	2 (5)	8 (11.9)	0.31
Vascular enlargement	8 (7.5)	4 (7.7)	4 (7.3)	1.00	8 (20)	0	<0.001
Air bubble sign/cavitation	12 (11.2)	8 (15.4)	4 (7.3)	0.23	6 (15)	6 (9)	0.36
Nodules	20 (18.7)	8 (15.4)	12 (21.8)	0.47	10 (25)	10 (14.9)	0.21
Pericardial effusion	0	0	0	–	0	0	–
Lymphadenopathy	2 (1.9)	2 (3.8)	0	0.35	0	2 (3)	0.56

Differences were considered significant at $P < 0.05$.

Abbreviations: CT, computed tomography; GGO, ground-glass opacities; IQR, interquartile range; TSS, total severity score

were observed in 35% of the cases, complete resolution in 35%, and GGOs or interstitial thickening in 27%. This was an interesting observation, and we also continue to monitor our patients to collect the data from their next CT scans with the aim to assess the sequelae of COVID-19 pneumonia 6 months after hospitalization.

In our study, after a mean of 3 months from discharge, the intensity of radiological changes measured with the chest CT score and TSS was still high. The incidence of radiological changes was different for patients with severe and moderate disease. Our 3-month observational study showed that recovery occurs at a different stage in patients from these 2 groups. After 3 months of convalescence, in patients with severe/critical disease, there were still many active lesions, such as GGOs, consolidations, vascular enlargement, reticular patterns, or other serious pulmonary complications. On the other hand, in patients with a milder course of the disease, the observed changes were frequently in the later phase of evolution (ie, fibrosis or pleural thickening).

Our analysis, in accordance with all the studies cited herein, showed that radiological changes in the course of COVID-19 pneumonia last much longer than in the case of most pneumonias with a different infectious etiology. It is important to evaluate the impact of such long-term changes on the risk for other severe lung diseases, including lung cancer.[12]

Limitations to our study include a relatively small number of patients, and the lack of exhaustive clinical data that could be gathered in this retrospective radiological analysis.

Conclusions Our study confirms the high incidence of pulmonary abnormalities persisting up to 4 months after COVID-19 in the hospitalized patients with a history of moderate and severe

disease. After a mean convalescence period of 3 months, 98.1% of patients still had a median TSS of 5 points. The most frequently observed abnormalities were GGOs, reticular pattern, fibrotic changes, nodules, cavitation, and bronchiectasis with bronchial and pleural thickening. The extent and forms of the residual pulmonary sequelae were strongly linked with the severity of the initial disease as well as the patients' age, sex, and duration of convalescence.

The results of our study highlight the need for further monitoring, especially with regard to the patients with initial severe SARS-CoV-2 infection in whom the lung changes did not fully resolve within 3 months of recovery, and possibly after that time.

ARTICLE INFORMATION

ACKNOWLEDGMENTS None.

FUNDING None.

CONFLICT OF INTEREST None declared.

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HOW TO CITE Kurys-Denis E, Grzywa-Celińska A, Kawa M. A comprehensive study of persistent changes on lung computed tomography scans of convalescent patients 3 months after recovery from severe and moderate COVID-19 pneumonia. Pol Arch Intern Med. 2022; 132: 16242. doi:10.20452/pamw.16242

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