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CT follow-up of COVID-19 pneumonia in patients requiring hospitalization in the acute phase of the disease

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Abstract. – OBJECTIVE: There are studies discussing the lung CT abnormalities persisting 3-4 months after COVID-19 pneumonia. Very few studies have evaluated the radiological changes in longer perspective, especially in patients with a severe form of the disease.

The aim of our study was to show and qualify the persistent CT changes and to evaluate the dynamics of their evolution in convalescent patients after discharge from hospital post moderate and severe COVID-19 pneumonia.

PATIENTS AND METHODS: We retrospectively analyzed the lung involvement at acute phase and follow-up time of 6 months in 6 patients with COVID-19 pneumonia using high resolution computer tomography.

RESULTS: Radiological changes in the course of SARS-CoV-2 infection persisted in all patients 6 months after the first CT examination.

CONCLUSIONS: Our study confirms that the period of 3 months is too short for the follow-up CT examination in patients recovered after severe or moderate COVID-19 pneumonia.

Key Words:
COVID-19, Convalescence patients, Follow-up, 6 months, Lung CT, Chest CT features.

Introduction

Since the Coronavirus disease 19 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), spread worldwide, many studies have investigated lung abnormalities during acute and early to mid-term convalescence period. Chest computed tomography (CT) plays an important role in screening suspected patients, evaluating for signs of COVID-19 pneumonia and in assessing the residual lung changes during the follow-up of patients[1].

It has already been proved[2] that early follow-up lung CT changes are related to the course of the disease. Numerous studies[3-6] have also proved the existence of lung CT abnormalities persisting 3-4 months after the COVID-19 infection. Few studies[7-9], however, have evaluated long-term consequences visible on chest CT images, especially in seriously ill patients discharged from hospital.

Our report of case series shows the value of CT follow-up of hospitalized patients with COVID-19 pneumonia and helps both radiologists and clinicians understand the evolution of CT changes in patients with different severity of the disease.

In our retrospective, single-center 6-case study of convalescent patients after discharge from hospital post moderate and severe COVID-19 pneumonia, we aimed to qualify the persistent CT changes after 6 months and to study their dynamics with CT scores. We also aimed to analyze long-term residual lung CT abnormalities in comparison to the patients' medical history and the course of the acute phase of the disease.

Patients and Methods

Patients and CT Data Acquisition

We retrospectively analyzed the clinical data, lung involvement at admission and the dynamics of lung changes in the follow-up time of 5-7 months in 6 patients with COVID-19 pneumonia, hospitalized and then controlled during their convalescence in our center from October 10th, 2020 to June 30th, 2021. Medical records were reviewed for demographic data and medical history. Radiological examinations were available in the electronic records. The study was approved by Medical University Review Board (No. KE-0254/231/2021) with a waived informed consent

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of patients. Inclusion criteria for the study were as follows: SARS-CoV-2 infection confirmed with the RT-PCR test, adult age, symptomatic pneumonia requiring hospitalization, presence of at least 2 high-resolution CT examinations (at the acute infection and after 5-7 months from the onset of the disease).

Identification of SARS-CoV-2 infection in every patient was confirmed with the positive result by real-time reverse transcriptase polymerase chain reaction (RT-PCR) method for SARS-CoV-2 infection in respiratory material, obtained by the nasopharyngeal swab. All included patients were diagnosed and treated according to the current national recommendations for treatment of COVID-19 pneumonia, and classified into moderate and severe forms of the onset disease[10]. Exclusion criteria from the study involved the history of any chronic respiratory or psychotic diseases prior to SARS-CoV-2 infection.

CT Imaging

The high-resolution chest CT examinations from lungs apices to bases were performed in each patient using the standardized technique with the same CT equipment (supine position, in deepest inspiration and breath holding, without intravenous contrast using multi-spiral scanner, 120 kV, 650 mA, with automatic exposure control, pitch 1.375, tube rotation time 0.7 sec, matrix of 512 × 512 mm, slice thickness 1.25 mm). Obtained images were further reconstructed with slice thickness of 0.625 mm in lungs and mediastinum windows.

A specialist radiologist with 15 years of experience reviewed the images, described the radiological abnormalities and assessed the CT scores of lungs involvement[11]. The persistent pulmonary changes in each patient were classified as: (a) ground glass opacities (GGOs), (b) consolidations, (c) crazy-paving symptoms, (d) reticular patterns, (e) halo signs, (f) atoll signs, (g) fibrosis, (h) honeycombing, (i) air bronchograms, (j) bronchiectasis, (k) bronchial wall thickening, (l) pleural effusions, (m) pleural thickenings, (n) vascular enlargements, (o) air bubble signs/cavities, (p) nodules, (q) pericardial effusions and (r) lymphadenopathy.

To assess the extent of persisting lung changes after 6 months and to evaluate their dynamics of regression, well established semiquantitative CT scales were used: the total severity scale (TSS) and CT chest score, previously used by Li et al[12,13]. The TSS score ranges go from 0 (no involvement) to 20 (maximum involvement). Chest CT score is more detailed and ranges from 0 to 25.

Results

The analyzed group consisted of four men and two women. The age of the patients ranged from 37 to 77 years. After hospitalization, all patients had a check-up lung CT for medical indications during their convalescence, at the day between 147 and 198 from the onset of the disease. Demographic characteristics of the studied patients are presented in Table I.

In our study, GGO, reticular pattern and signs of fibrosis were observed on the initial CT in every patient. Frequent abnormalities in the acute phase involved vascular enlargement, consolidations, crazy paving, halo signs and mucous filling. No lymphadenopathy, pericardial effusion, air bubble sign, bronchiectasis, pleural effusion or honeycombing was observed in the acute phase (Table II).

In our case study on the group of 6 patients, radiological COVID-19 changes persisted in all patients even 6 months after the disease (Table

Table I. Characteristics of patients.

Patient	1	2	3	4	5	6
Age	55	54	69	65	37	77
Sex	Male	Male	Female	Female	Male	Male
Course of COVID-19 infection	Moderate	Moderate	Severe	Severe	Severe	moderate
Comorbidities	No	HTA	HTA	HTA obesity atherosclerosis heart failure	HTA liver steatosis	HTA obesity atherosclerosis heart failure
Time of the 1st chest CT during the acute phase of disease from the onset (in days)	15	14	10	15	10	15
Time of the last follow-up chest CT in the convalescence from the onset (in days)	147	162	175	177	183	198

Table II. Presence of radiological changes at baseline CT (Y-yes /N-no; TSS-total severity score).

Patient	1	2	3	4	5	6
Presence of changes at baseline CT	Y	Y	Y	Y	Y	Y
(a) ground glass opacities (GGOs)	Y	Y	Y	Y	Y	Y
(b) consolidations	Y	N	N	Y	Y	Y
(c) crazy-paving symptom	N	N	Y	Y	Y	N
(d) reticular pattern	Y	Y	Y	Y	Y	Y
(e) halo sign	N	Y	Y	N	Y	N
(f) atoll sign	Y	N	N	Y	N	N
(g) fibrosis	Y	Y	Y	Y	Y	Y
(h) honeycombing	N	N	N	N	N	N
(i) air bronchogram/mucous filling	N	Y	Y	Y	N	N
(j) bronchiectasis	Y	N	N	N	N	N
(k) bronchial wall thickening	N	N	N	N	Y	N
(l) pleural effusion	N	N	N	N	N	N
(m) pleural thickening	N	N	N	N	N	N
(n) vascular enlargement	Y	Y	Y	Y	Y	N
(o) air bubble sign / cavities	N	N	N	N	N	N
(p) nodules	Y	N	N	N	Y	N
(q) pericardial effusion	N	N	N	N	N	N
(r) lymphadenopathy	N	N	N	N	N	N
TSS Right upper lobe	2	2	3	4	2	1
TSS Right middle lobe	1	2	3	3	3	1
TSS Right lower lobe	2	2	4	4	3	2
TSS Left upper lobe	1	2	3	3	2	1
TSS Left lower lobe	1	2	3	3	3	1
TSS (Kunwei Li)	**7**	**10**	**16**	**17**	**14**	**6**
Chest CT score (Li)	**10**	**15**	**21**	**22**	**19**	**11**

III). Although GGOs were still observed in all patients during the follow-up period, a complete or at least partial regression of radiological changes in the lungs was described with CT scores. The changes that most often decreased in intensity were consolidations, reticular patterns, crazy pavings, halos and atoll signs (Figures 1-4). Honeycombing, bronchiectases, and air bubble signs appeared during the follow-up period, and each of these symptoms occurred in one, but not the same, patient. We also observed a considerable but not total reduction in scores of both TSS and chest CT score, compared to the baseline CT.

Discussion

Many previous studies[2,4,5,14] presented the evolution of radiological changes in much shorter time span compared to our research. Zhao et al[3] on the basis of their research, stated that the optimal time to perform a control lung CT examination after the onset of pneumonia in the course of SARS-CoV-2 infection is a period of 3 months. Our study proves, however, that changes in the CT examination may be visible even 6 months after the onset of the disease, so it can be assumed that this period should be extended to at least 6 months.

This is confirmed by the study of Stylemans et al[8] who observed a gradual decrease of CT score in patients 6 months after the recovery from COVID-19. However, many lung changes were still noticeable. As indicated by Pan et al[15], chest CT abnormal changes were still present in 25% of patients a year after COVID-19 diagnosis. Persistence of chest CT abnormalities existed more often in older patients after severe pneumonias, acute respiratory distress syndromes and lymphopenias.

Many observations indicate that the presence of persistent radiographic changes in follow-up examinations may be related to pulmonary interstitial fibrosis[16,17]. Risk factors for pulmonary fibrosis after COVID-19 pneumonia include advanced age, severity of disease, mechanical ventilation, length of hospitalization in intensive care unit, smoking, and alcoholism[18]. In the prospective research of Han et al[7], the follow-up examination was performed after 175±20 days from the onset of symptoms: only 38% of patients showed complete resolution of radiological changes, 27% showed residual GGOs and 35% of patients still

Table III. Presence of radiological changes after 6 months and the change direction (0-no change between first and follow-up CT, (-)-regression/disappearance of changes, in blue, (+)-progression or the appearance of changes, in red). In the case of numerical scales, the value of the change along with its direction are given in parentheses.

Patient	1	2	3	4	5	6
Presence of changes at baseline CT	Y	Y	Y	Y	Y	Y
Presence of changes in 6-month-follow-up CT	Y(0)	Y(0)	Y(0)	Y(0)	Y(0)	Y(0)
(a) ground glass opacities (GGOs)	Y(0)	Y(0)	Y(0)	Y(0)	Y(0)	Y(0)
(b) consolidations	N(-)	N(0)	N(0)	N(-)	N(-)	N(-)
(c) crazy-paving symptom	N(0)	N(0)	N(-)	N(-)	N(-)	N(0)
(d) reticular pattern	N(-)	Y(0)	Y(0)	Y(0)	Y(0)	N(-)
(e) halo sign	N(0)	N(-)	N(-)	N(0)	N(-)	N(0)
(f) atoll sign	N(-)	N(0)	N(0)	N(-)	N(0)	N(0)
(g) fibrosis	Y(0)	N(-)	Y(0)	Y(0)	N(-)	Y(0)
(h) honeycombing	Y(+)	N(0)	N(0)	N(0)	N(0)	N(0)
(i) air bronchogram / mucous filling	N(0)	N(-)	N(-)	N(-)	N(0)	N(0)
(j) bronchiectasis	Y(0)	N(0)	N(0)	Y(+)	N(0)	N(0)
(k) bronchial wall thickening	N(0)	N(0)	N(0)	N(0)	N(-)	N(0)
(l) pleural effusion	N(0)	N(0)	N(0)	N(0)	N(0)	N(0)
(m) pleural thickening	N(0)	N(0)	N(0)	N(0)	N(0)	N(0)
(n) vascular enlargement	N(-)	N(-)	Y(0)	N(-)	N(-)	N(0)
(o) air bubble sign / cavities	N(0)	N(0)	N(0)	N(0)	N(0)	Y(+)
(p) nodules	Y(0)	N(0)	N(0)	N(0)	Y(0)	N(0)
(q) pericardial effusion	N(0)	N(0)	N(0)	N(0)	N(0)	N(0)
(r) lymphadenopathy	N	N(0)	N(0)	N(0)	N(0)	N(0)
TSS Right upper lobe	1(-1)	1(-1)	2(-1)	2(-2)	1(-1)	0(-1)
TSS Right middle lobe	1(0)	0(-2)	1(-2)	2(-1)	1(-2)	1(0)
TSS Right lower lobe	1(-1)	1(-1)	2(-2)	3(-1)	1(-2)	1(-1)
TSS Left upper lobe	1(0)	1(-1)	2(-1)	2(-1)	1(-1)	1(0)
TSS Left lower lobe	1(0)	1(-1)	3(0)	2(-1)	1(-2)	0(-1)
TSS (Kunwei Li)	5(-2)	4(-6)	10(-6)	11(-6)	5(-9)	3(-3)
Chest CT score (Li)	7(-3)	5(-10)	15(-7)	16(-6)	7(-12)	3(-8)

had fibrotic-like changes. The authors proved that total CT score ≥ 18 on the initial CT, apart from the age, acute respiratory distress syndrome and mechanical ventilation, could be used as the independent predictor for lung fibrotic-like changes at 6-month follow-up.

Fibrosis was diagnosed in all our patients after 6 months from the recovery. It is worth noting that our patients required hospitalization, suffering from the moderate or severe type of the disease.

Since the cases of COVID-19 pneumonia have been observed only for the past two years, further studies are needed to complete observations in patients with developed pulmonary fibrosis and other lung changes, due to this disease. It should also be noted that in the COVID-19 era, the diagnostics of idiopathic pulmonary fibrosis (IPF) might be impaired, due to the limited access to health care. On the other hand, many patients have never had a CT examination before COVID-19, so patients with undiagnosed IPF could be revealed in this group.

There is currently no effective therapy to reverse the fibrotic pulmonary changes. However, antifibrotic drugs have been already tried not only in pulmonary fibrosis of other origins, but also in the course of COVID-19[17-19].

Persistence of radiological changes, often associated with pulmonary dysfunctions, may become an element for the diagnosis of the long COVID-19 lung disease. Currently, many studies[9,20-22] are investigating factors that predispose to prolonged COVID-19 disease.

Dysregulation of the immune system and long-term inflammation in the course of COVID-19 can also potentially lead to the development of other diseases, which will require longer observations and population studies.

Our study shows that CT lung examination performed 6 months after developing COVID-19 pneumonia still shows numerous lung lesions. Apart from subsiding residual changes of a decreasing extent, new changes appear, the progression of which in the future may have far-reaching clinical consequences. In addition, there are assumptions that post-COVID-19 changes, which are an expression of long-term inflammation in

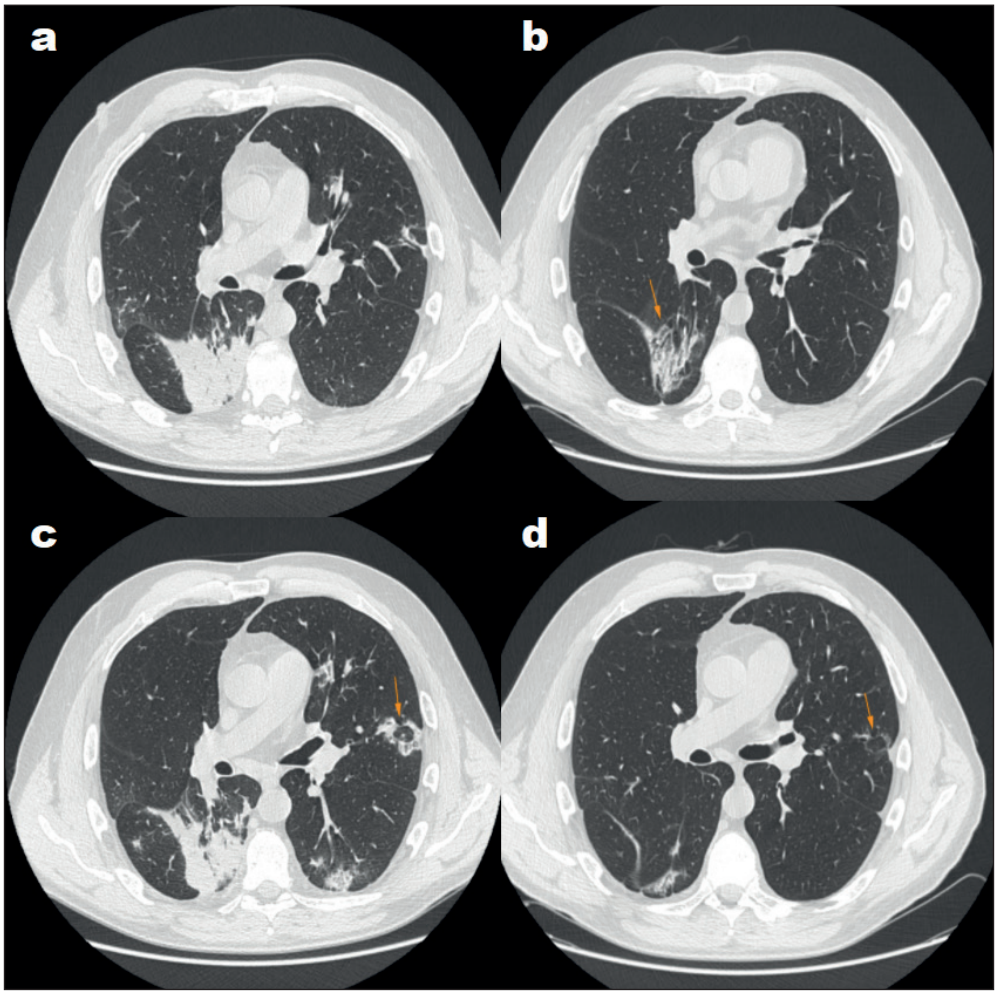

Figure 1. Patient 1. Corresponding CT changes seen at baseline (**a**, **c**) and after 146 days from onset (**b**, **d**). The regression of consolidations is observed with persistence of GGO, bronchiectasis and fibrosis. Red arrow shows the regression of the atoll sign and consolidations.

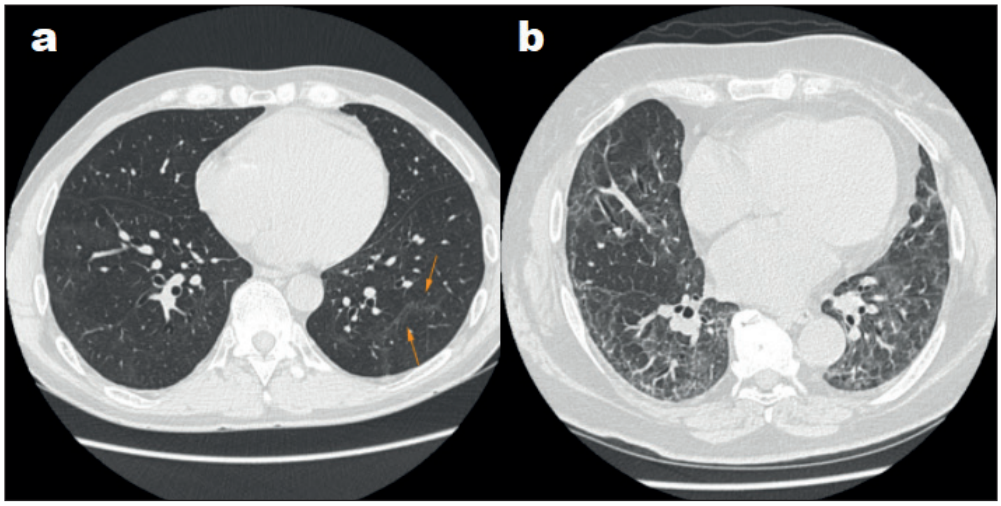

Figure 2. Persistent GGOs and fibrotic lines (arrows) after 6 months in patients 2 (**a**) and 3 (**b**).

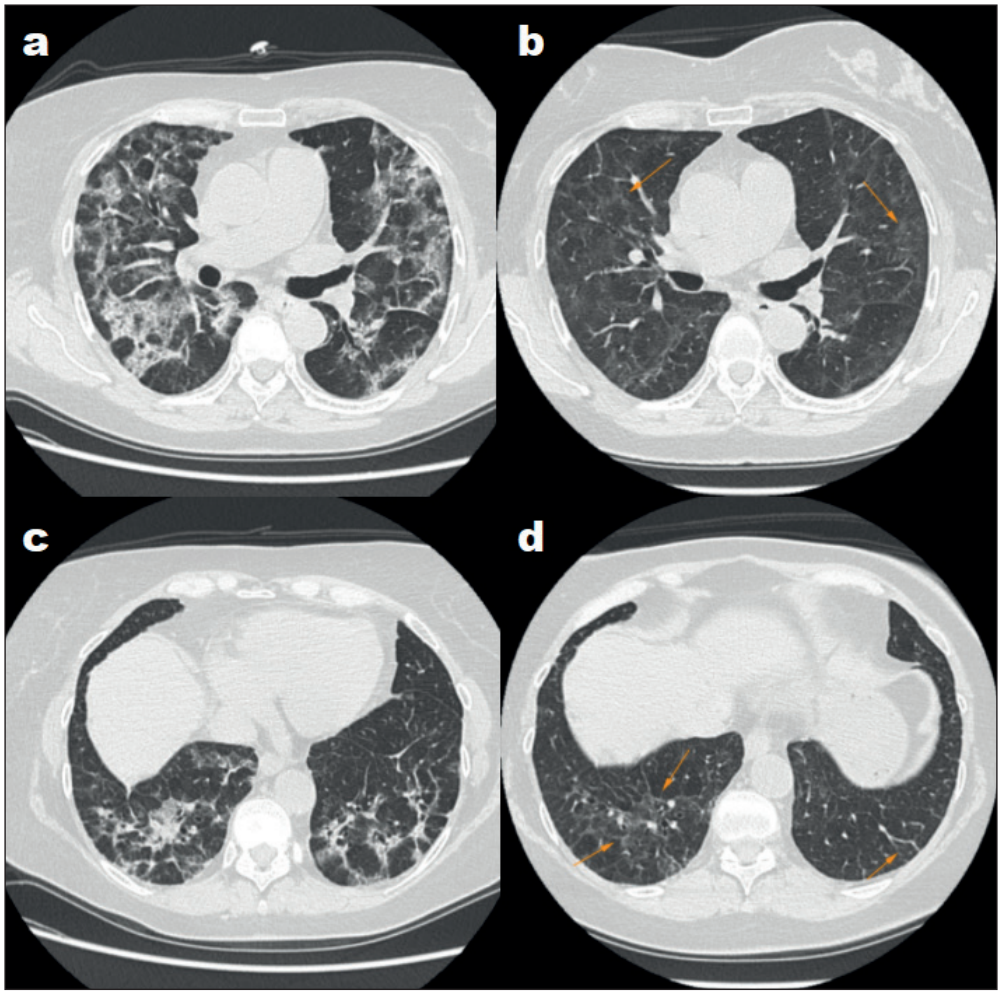

Figure 3. Patient 4. Important regression of extensive, diffused crazy paving signs, halo signs and consolidations at baseline CT (**a**, **c**), in a female patient with obesity and comorbidities. Persistence of important residual GGOs and fibrotic lines (arrows) in the follow-up CT (**b**, **d**).

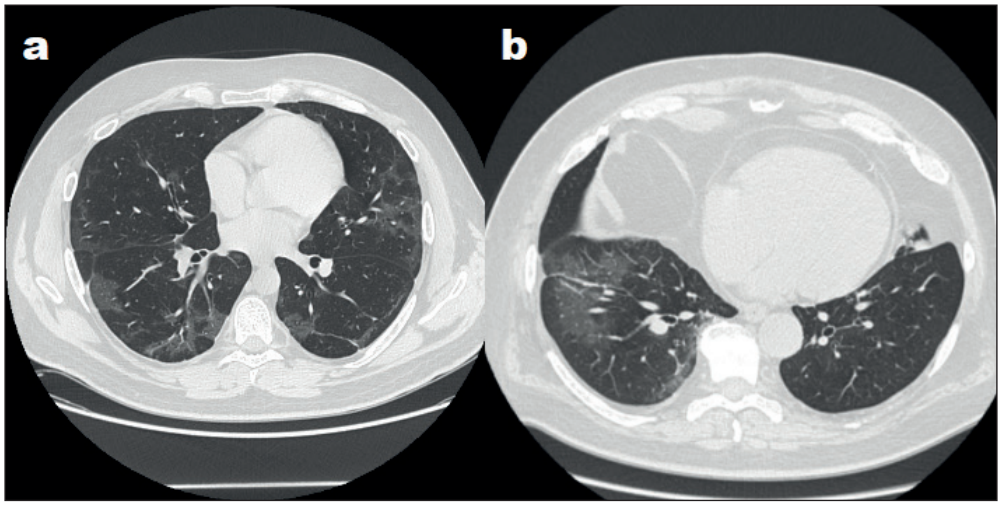

Figure 4. Persistent GGOs and fibrotic lines after 6 months in patients 5 (**a**) and 6 (**b**).

the pulmonary parenchyma, may in the future become the starting point for other previously known diseases, including lung cancer[23].

Despite the interesting observations constituting the results of our research, this study has some limitations. Undoubtedly, the main limitation is the small group of patients. Nevertheless, the conclusions of our study indicate the importance of conducting similar studies on larger groups of patients. Moreover, most reliable results could be obtained if the control CT examination was performed at exactly the same time point from the onset of the disease. It was difficult to achieve during this study because our patients had a CT scan just for medical indications, not only for the purpose of this research. We retrospectively used the data of real patients who came to the follow-up visits at different times, which was in part due to the long waiting time for the scheduled outpatient examinations.

Conclusions

Our study confirms that CT is a useful tool in the diagnosis of persistent radiological changes in patients in long follow-up after pneumonia in the course of COVID-19. So far, the conducted observations have not found a final time point to stop controlling convalescents, because many studies, the ones performed after a long time from the infection, indicate that changes are still visible in a significant percentage of patients.

Ethics Approval

Medical University of Lublin Ethical Board, Poland (No. KE-0254/231/2021).

Informed Consent

Waived informed consent, according to the Medical University of Lublin Ethical Board document.

Availability of Data and Materials

Anonymized data were collected for medical purposes and then retrospectively used for this study.

Conflict of Interest

The authors declare that they have no conflict of interest.

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None.

Authors' Contributions

EKD: conception and design of the study, acquisition of data, analysis and interpretation of data, making critical revisions related to relevant intellectual content of the manuscript, supervision, validation and final approval of the version of the article to be published.
AGC: analysis and interpretation of data, making critical revisions related to relevant intellectual content of the manuscript, final approval of the version of the article to be published.
RC: analysis and interpretation of data, making critical revisions related to relevant intellectual content of the manuscript, final approval of the version of the article to be published.

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