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CT findings of COVID-19 pneumonia in ICU-patients

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Key words: CT; COVID-19; severity score; ICU.

Significance for public health

The major implication of our study is the differences in CT and laboratory findings in COVID-19 patients in ICU and non-ICU settings. Although the prospective impact of these findings was not assessed, recognition of these findings may help physicians anticipate the disease course and triage

the patient to early ICU management. Our study highlights the importance of structured and quantitative reporting format where radiologists explicitly describe the specific pattern of pulmonary opacities (such as GGO, consolidation, and mixed) as well as lung areas and the number of lung lobes involved with COVID-19 pneumonia. To our best knowledge, this is not practiced in most radiology department.

Abstract

Background: In December 2019, a cluster of unknown etiology pneumonia cases occurred in Wuhan, China leading to identification of the responsible pathogen as SARS-coV-2. Since then, the coronavirus disease 2019 (COVID-19) has spread to the entire world. Computed Tomography (CT) is frequently used to assess severity and complications of COVID-19 pneumonia. The purpose of this study is to compare the CT patterns and clinical characteristics in intensive care unit (ICU) and non-ICU patients with COVID-19 pneumonia.

Design and Methods: This retrospective study included 218 consecutive patients (136 males; 82 females; mean age 63 ± 15 years) with laboratory-confirmed SARS-coV-2. Patients were categorized in two different groups: (a) ICU patients and (b) non-ICU inpatients. We assessed the type and extent of pulmonary opacities on chest CT exams and recorded the information on comorbidities and laboratory values for all patients.

Results: Of the 218 patients, 23 (20 males; 3 females; mean age 60 years) required ICU admission, 195 (118 males; 77 females, mean age 64 years) were admitted to a clinical ward. Compared with non-ICU patients, ICU patients were predominantly males (60% versus 83% $p=0.03$), had more comorbidities, a positive CRP ($p=0.04$) and higher LDH values ($p=0.008$). ICU patients' chest CT demonstrated higher incidence of consolidation ($p=0.03$), mixed lesions ($p=0.01$), bilateral opacities ($p<0.01$) and overall greater lung involvement by consolidation ($p=0.02$) and GGO ($p=0.001$).

Conclusions: CT imaging features of ICU patients affected by COVID-19 are significantly different compared with non-ICU patients. Identification of CT features could assist in a stratification of the disease severity and supportive treatment.

Introduction

In December 2019, several viral pneumonia cases of unknown origin occurred in Wuhan, Hubei Province, China.^{1,2} The virus was named *Severe Acute Respiratory Syndrome Coronavirus 2* (SARS-CoV-2) and the subsequent disease COVID-19. In the following weeks, the virus spread quickly all over the world with dramatic consequences for global health. Different reports provide descriptions of the clinical signs associated with COVID-19 with disease expression ranging from mild infection to severe acute respiratory distress.²⁻⁵ In most of the cases, symptoms are mild, as reported by Wu *et al.*; however, in older patients and patients with comorbidities, COVID-19 tends to progress more severely.^{6,7}

The reference standard test in the diagnosis of COVID-19 is the reverse-transcription polymerase chain reaction (RT-PCR) to detect viral nucleotides from specimens obtained by bronchoalveolar lavage, nasopharyngeal swab, oropharyngeal swab, or tracheal aspirate.⁸ Computed Tomography

(CT) is considered as an important tool to diagnose COVID-19 infection in patients with false negative RT-PCR and in patients from high prevalence sites with limited RT-PCR as well as to assess disease severity and complications in those with confirmed COVID-19 pneumonia.^{9–11}

A key point in the management of inpatients with COVID-19 pneumonia is deciding whether patients require ICU admission and/or mechanical ventilation.¹² Although this decision relies on a multiple factors such as clinical conditions, co-morbidities, and disease severity, a delay in ICU admission and/or mechanical ventilation can affect the disease outcome.¹² For this reason, better strategies in decision-making-process are searched and CT imaging could play a role in this scenario.

The purpose of this study is to compare the CT patterns and clinical characteristics in intensive care unit (ICU) and non-ICU patients with COVID-19 pneumonia in order to better define the CT features of patients requiring ICU and non-ICU management.

Methods

Study population

In this single-center retrospective study, 218 patients (136 males; 82 females; mean age 63 ± 15 years) with confirmed RT-PCR of COVID-19 were enrolled from March 3 to April 28, 2020 at A.O.U. “Maggiore d.c.”, University of Eastern Piedmont, Novara, Italy. For each of the 218 patients a chest CT and laboratory test were performed at time of admission to the hospital. Patient characteristics including age, gender, clinical symptoms, time course of the symptoms, medical history and outcomes were recorded.

Patients were divided into two groups: (a) ICU and (b) non-ICU.^{13–15}

CT technique and feature analysis

All chest CT scans were performed during a single full inspiratory breath-hold in supine position on a 128-slice multidetector-row CT scanner (Philips Ingenuity Core, Philips Healthcare, Netherlands). No intravenous or oral contrast media were administered. The CT examinations were performed at 120 kV, 226 mAs (using automatic tube current modulation – Z-DOM, Philips), 1.08 spiral pitch factor, 0.5-second gantry rotation time and 64×0.625 detector configuration. One-mm thick images were reconstructed with soft tissue kernel using 512×512 matrix (mediastinal window) and with lung kernel using 768×768 matrix (lung window). CT images were reviewed on the Picture Archiving and Communication System (PACS) workstation equipped with two 35×43 cm monitors produced by Eizo, with 2048×1536 matrix.

Two radiologists (AC with 32 years and LS with 16 years of experience in chest radiology) assessed the type and extent of pulmonary opacities on chest CT images. Imaging was reviewed independently,

and final decision reached by consensus are reported. No negative control cases were examined. All 218 chest CT examinations were evaluated for the presence of ground glass opacity (GGO), consolidation, mixed GGO and consolidation, crazy paving, reverse halo sign, bilateral lung involvement, and lymph node enlargement (lymphadenopathy).

The severity on CT was estimated by visual assessment based on the areas of pulmonary opacities.^{16,17} The distribution of lung changes was also classified based on visual quantification of the percentage of lung parenchyma affected by COVID-19, as follow: 0, no lung involvement; 1 1-10%; 2 11-25%; 3 26-50%; 4 51-75%; 5 > 75%.¹⁸⁻²⁰ Mediastinal lymph nodes were considered enlarged when their short-axis diameter was greater than 1.0 cm. Radiological lesions were categorized based on the Fleischner Society's glossary of terms.²¹

Statistical analysis

Continuous variables are presented as mean \pm standard deviation or median (with interquartile range) values. Categorical variables were described as frequency rates and percentages, comparisons of continuous data were performed using the independent samples *t*-test or Mann-Whitney U test; Normality of distribution for continuous variable was tested using Kolmogorov-Smirnov before performing *t*-test or Mann-Whitney U test. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Correlation was assessed using the Pearson *r* and Spearman rho coefficient as appropriate. A *p*-value <0.05 was considered statistically significant. All statistical analysis was performed using IBM SPSS Statistics version 22 (SPSS Inc., Chicago, IL, USA).

Results

Overall study cohort

The mean (\pm SD) age of the patients was 63 \pm 15 years, 136 males, 82 females. The most common symptoms were cough (n=130/218; 59%), followed by dyspnea (n =113/218; 52%) Among the comorbidities, hypertension was the most common (n=99/218; 45%), followed by coronary heart disease (n=45/218; 21%) and diabetes (n=35; 11%). Forty patients (n=40/218; 18,3%) had fever on admission. The most common chest CT features of both groups included GGO (202/218, 92%) consolidation (184/218, 84%), mixed of GGO and consolidation (180/218, 82%). Less frequent CT findings were crazy paving pattern (60/218, 27%), reversed halo sign (22/218, 10%). In addition, 27% of patients had hilar and/or mediastinal lymphadenopathy

ICU versus non-ICU patients

ICU patients were 23 (20/23 [80%] were males, mean age 60 years) versus 195 who did not require ICU admission (118/195 [60%] were males, mean age 64 years) The proportion of ICU admissions represents 10.5% of the total cases (23/218).

Compared with non-ICU patients, ICU patients were predominantly males ($p=0.02$), had more underlying diseases, such as cancer ($p=0.02$). Therefore, patients with emphysema, which is more common in older patients ($p=0.01$), had correlation with mortality ($p=0.01$, $r=0.33$). The ICU group had a greater positivity of the c-reactive protein ($p=0.04$), LDH ($p=0.008$) and higher mortality ($p=0.01$). Baseline characteristics and laboratory findings are reported in Table 1.

Patients in the ICU had higher incidence of lung consolidation ($p=0.03$), mixed of GGO and consolidation ($p=0.01$) and a bilateral lung involvement ($p=0.03$) with a worse CT severity score and a greater number of lung lobar involvement compared with non-ICU patients, with statistically significant differences in GGO ($p=0.001$) and consolidation ($p=0.02$) (Figure 1). Distribution of chest CT findings are summarized in Tables 2 and 3.

In addition, the number of lung lobar involvement showed a positive correlation with duration of symptoms ($p=0.002$, $r=0.33$), cough ($p=0.01$, $r=0.31$), higher value of temperature ($p=0.01$, $r=0.23$), positive C-reactive protein (CRP) ($p=0.001$, $r=0.41$) and greater lymph node involvement in CT ($p=0.01$, $r=0.28$) (Supplemental Table 1).

Discussion

In this study we aimed at characterizing chest CT features of COVID-19 patients and to compare the clinical characteristics and CT patterns of inpatients in intensive care unit (ICU) with non-ICU COVID-19 patients, in order to better define the CT features of patients requiring ICU and non-ICU treatments. In our cases of SARS-coV-2 infection, we observed a greater number of men than women, as reported in other studies²² and a gender difference in ICU patients, with a predominance of males. The gender difference could be explained, as reported by Jaillon *et al.*, by a sexual dimorphism in the innate response with higher susceptibility to infections in males.²³

Cough was the most common presenting symptom followed by dyspnea, and the mean duration of symptoms was 1 week. Although 50% of patients had fever, there were no statistically significant differences in the presence of high temperature in the two groups under analysis; this suggests that fever was not a useful criterion to determine the severity of illness in our study cohort.²⁴ The median age of the patients admitted to the ICU was 60 ± 11 years, with no statistically significant difference in comparison to non-ICU patients, this might suggest that age alone is not a risk factor for ICU.²⁵

The proportion of ICU admissions represents 10.5% of the total cases, this percentage is higher than what was observed in prior studies from China;²⁶ though, these data are in agreement with other Italian studies.²⁷ This could be explained, as suggested by Grasselli *et al.*, by a demographic difference between the populations in two countries.²⁷

ICU patients had more comorbidities, such as chronic obstructive pulmonary disease. In particular, the presence of emphysema is associated with higher mortality, so an underlying lung disease affects the clinical outcome.^{28,29}

Compared with the non-ICU group, ICU patients had higher incidences of positive CRP and increased LDH values. CRP levels were positively correlated with lung lesions and disease severity, and CRP levels correlate well with the level of inflammation.³⁰ The baseline characteristics and laboratory findings of subjects enrolled in the study are summarized in Table 1.

To our knowledge, this is the first report of Italian patients that compared CT findings of ICU patients with non-ICU patients with COVID-19 pneumonia.

In this study, we found that the most common CT imaging features were GGO, consolidation, mixed of both and crazy-paving pattern. The CT findings are closely related to the physiological and pathological basis of the disease. According to Xu *et al.* pathological findings in COVID-19 patients resemble those seen in SARS and Middle Eastern respiratory syndrome (MERS) coronavirus infection.³¹ Moreover, COVID-19 shows CT similarities to SARS and MERS pneumonia^{32,33} and other lung disease.³⁴ Chest CT undoubtedly may play a key role in differential diagnosis. Specific CT features can help in the proper diagnosis, such as centrilobular nodules, mucoid impaction or unilateral involvement to diagnostic a bacterial or superinfection pneumonia. On the other hand, septal lines, large pulmonary vein suggest a pulmonary edema.³⁴

Li *et al.* assessed in their research the rate of misdiagnosis of COVID-19 at the CT admission. The authors reported a low rate of missed diagnosis (3,9%) based on CT features.³⁵ Furthermore, Fang *et al.* compared the sensitivity of chest CT with that of RT-PCR at the initial patient presentation, The authors reported that the sensitivity of chest CT was greater compared to RT-PCR (98 % vs 71%, $p<0.001$).³⁶

GGO were defined as hazy increased opacity of lung without obscuration of bronchial and vascular margins, its formation results in incomplete filling of the alveolar cavity and mild interstitial thickening.^{37,38} Consolidation was defined as an exudate or other product of disease that replaces alveolar air. In this scenario, it could be related to diffuse alveolar damage.³⁸ These findings are common in patients with COVID-19.^{18,39,40} Whereas crazy paving has not often been observed as GGO and consolidation,³⁹ and may be related to thickening of interlobular and intralobular interstitial.^{18,39,41} According to a recent study comprising 21 patients with COVID-19, crazy paving

pattern can be a marker of COVID-19 peak stage.⁴¹ Another CT finding present in our cohort of patients was reverse halo sign, this was described in several COVID-19 patients,⁴² which could be related to disease progression⁴³ and may reflect an organizing pneumonia pattern in COVID-19 cases.⁴⁴

Compared with non-ICU patients, ICU group has shown higher frequency of consolidation and mixed lesions. The pathological bases of these changes are not currently clear. Consolidation indicates that alveolar air is being replaced by inflammatory exudation, and in COVID-19 patients histological examination showed that consolidation may be referred to cellular fibromyxoid exudates.³¹ Moreover, ICU patients showed a greater bilateral lung involvement (Figure 2). The CT findings between the two groups are summarized in Table 2.

In our study, laboratory parameters and clinical characteristics, such as PCR, cough, fever, duration of symptoms and nodes involvement showed significant positive correlation with the number of lobes involved by pneumonia. These findings may be related to a gradual increase in lung involvement over time with the occurrence of severe inflammation and it could be considered as a marker of disease progression.^{18,43}

In addition, CT reports showed lymphadenopathy in 27% of the patients analyzed, a higher prevalence of nodal involved than in previous studies. This observation is not concordant with studies in Chinese populations.^{3,13} Lymphadenopathy could be considered as an uncommon feature of COVID-19, such as in viral pneumonia. Recent research of ICU patients reported increased lymph node involvement compared with the Chinese populations.^{18,40,43,45}

As reported by Sardanelli *et al.* lymphadenopathy may be considered a predictor of a worse outcome, and the differences in disease severity could probably explain this discrepancy in different studies.^{18,45} Furthermore, ICU-patients showed greater number of lung lobar involvement (Table 3) by consolidation and GGO, as reported in previous studies,^{41,46,47} and may help us make an early identification of patients that require ICU from patients who do not. Our results are in line with the current literature.^{20,48} Ruch *et al.* reported that quantification of CT lung lesion involvement is related to ICU admission, especially in patients with lung involvement >50%.²⁰

This study has several limitations. First the retrospective nature of our analysis. Secondly, the data of the two groups were not balanced, because too few ICU patients were included in this study, which decreased the reliability of the statistical results. Further studies with more patients, especially patients who require ICU, are warranted. Third, the quantitative method for measuring the pulmonary involvement may have subjectivity and we cannot rule out the possibility of concomitant superinfection due to bacterial pneumonias, aspiration, and pulmonary edema. In conclusion, the results of this study confirm that chest CT is important in the diagnosis and management of the SARS-

coV-2 infection. The CT features of the COVID-19 pneumonia were different in ICU patients compared with non-ICU patients, we found more consolidative lesions in critically ill patients and a greater pulmonary involvement. Our data suggest CT could be a useful tool for stratify patients who require ICU.

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Table 1. Baseline Characteristics and Laboratory Findings in ICU and non-ICU patients.

	ICU	Non-ICU	p	Size of effect
Age	60 ± 11	64 ±15	0.07	0.24
Male	19/23, 80%	117/195, 60%	0.02*	0.29
Height	172.2 ± 8	170±9	0.23	0.21
Weight	87.2 ± 14	80±17.7	0.07	0.04
CAD	4/23, 17%	41/195, 20%	0.56	0.07
Hypertension	11/23, 47%	88/195, 44%	0.56	0.02
Diabetes mellitus	5/23, 21%	30/195, 15%	0.69	0.05
Emphysema	2/23, 8%	6/195, 3%	0.66	0.08
Lung diseases (no COPD)	1/23, 4%	2/195, 1%	0.23	0.16
Cancer	2/23, 8%	19/195, 10%	0.02*	0.21
Neurovascular diseases	1/23, 4%	28/195, 14%	0.45	0.06
Chronic kidney diseases	1/23, 4%	17/195, 8%	0.54	0.08
Chronic liver diseases	0/23, 0%	7/195, 3%	0.41	0.12
Rheumatoid arthritis	1/23, 4%	1/195, 0,5 %	0.14	0.28
Smoke	2/23, 8%	28/195, 14%	0.38	0.12
Temperatures	37.66 (36.66-38.66)	37.56 (36.52-38.60)	0.38	0.11
Cough	14/23 60%	116/195, 58%	0.76	0.04
Sore Throat	1/23 4%	5/195, 2%	0.65	0.06
Dyspnea	15/23 65%	98/195, 49%	0.13	0.20
Days from symptoms onset to time of CT	6,23 ± 3,5	6.89±5.3	0.82	0.01
CRP +	23/23 100%	148/195, 74%	0.04*	0.17
LDH	1461 ± 394	905 ± 590	0.008*	0.85
Platelets	247.428 ± 141944	199.516±68650	0.66	0.10
Mortality	8/23 34%	24/195 12%	0.01	0.34

ICU: intensive care unit; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; CRP: c-reactive protein; LDH: lactate dehydrogenase. Mean ± SD. Data are n (%), or median (interquartile range). Size of effect: Cohen D or Was appropriate.

Table 2. Distribution of chest CT findings in ICU and non-ICU patients.

	ICU	Non-ICU	p	Size of effect
GGO	23/23, 100%	174/195, 89%	0.14	0.19
Consolidation	23/23, 100%	156/195, 80%	0.03*	0.28
GGO (lobes involved)	4.8±0.45	3.9±1.6	0.001*	0.41
Consolidation (lobes involved)	3.4±1.5	2.6±1.7	0.02*	0.29
Mixed GGO and consolidation	23/23 100%	152/195, 78%	0.01*	0.32
Bilateral involvement	23/23 100%	159/195, 81%	0.03*	0.28
Nodes involvement	6/23, 26%	49/195, 25%	0.79	0.03
Crazy paving	8/23, 35%	54/195, 27%	0.55	0.08
Reversed halo sign	2/23, 9%	19/195, 10%	0.73	0.04

GGO: ground-glass opacities; ICU: intensive care unit. Mean ±SD; Data are n (%). Size of effect, Cohen D or W as appropriate.

Table 3. Comparison of the number of affected lung lobes with require ICU.

Number of lobes involved	ICU	Non-ICU
0	0, 100%	29/195, 15%
1	3/23, 12,5%	21/195, 11%
2	6/23, 25%	38/195, 20%
3	2/23,8,5%	38/195, 20%
4	3/23 12,5%	28/195, 15%
5	10/23 41%	35/195, 18%

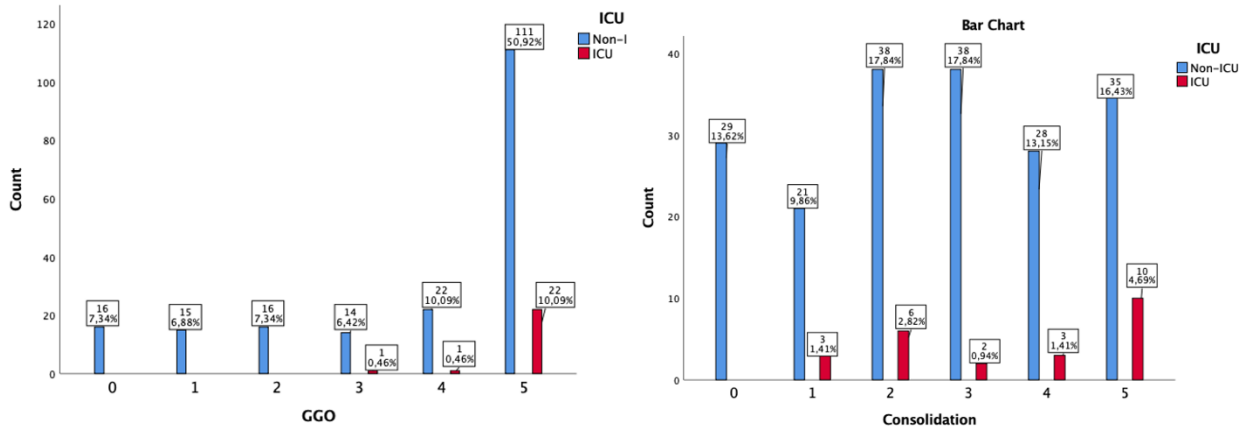


Figure 1. Number of lung lobes involved by GGO and by consolidation in ICU patients compared with non-ICU patients.

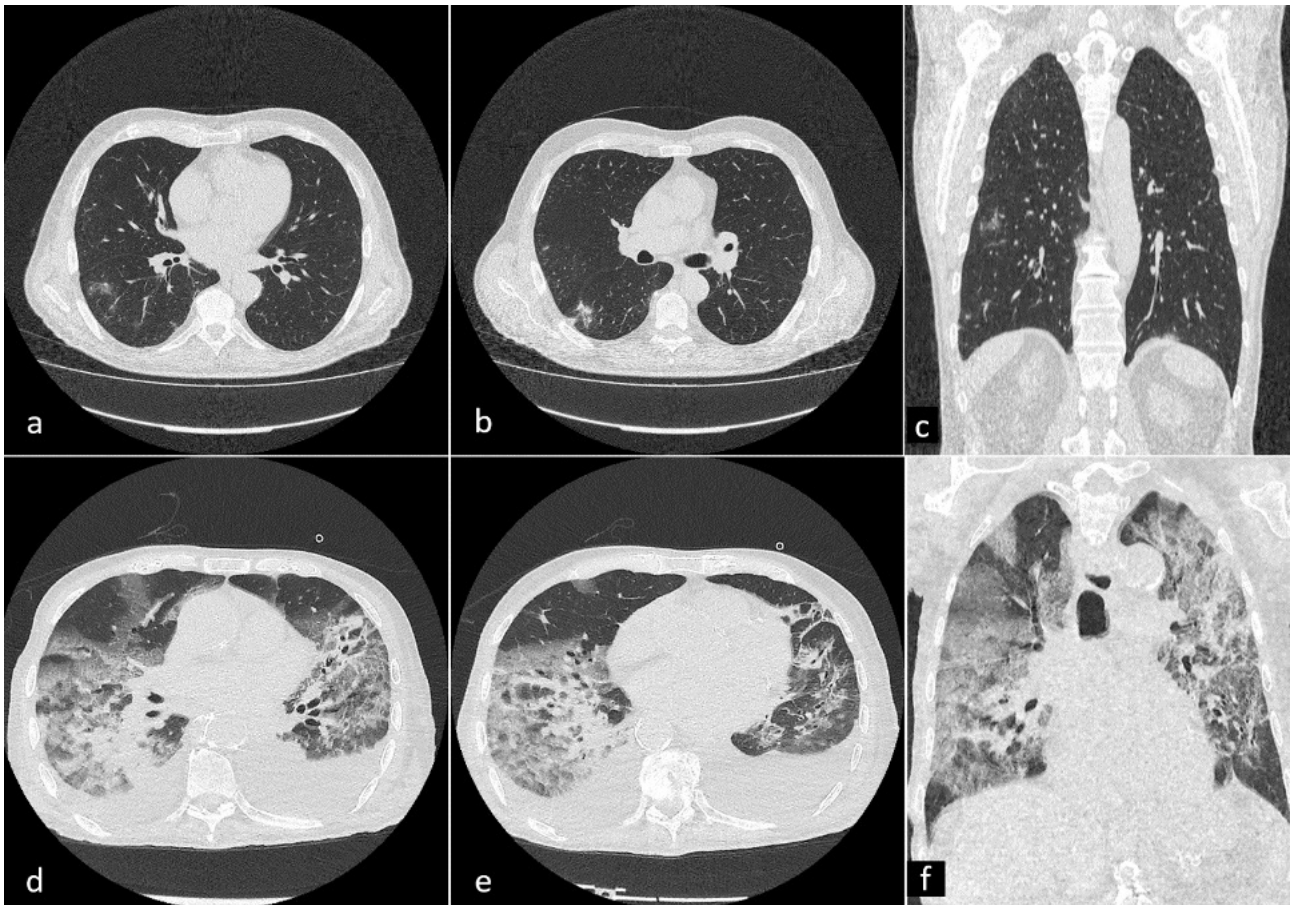


Figure 2. a-f) Chest CT of an 89-year-old man with ICU COVID-19 pneumonia (a). An axial and coronal CT image showed diffuse large regions of crazy-paving pattern with partial consolidation and bilateral pleural effusion. CT findings in a 54-year-old man with non-ICU COVID-19 pneumonia (b). An axial and coronal CT image showed bilateral multiple small regions of subpleural GGO and consolidation.