ISSN 2515-8260 Volume 10, Issue 04, 2023

Original Research Article

Follow up study of the high-resolution computed tomography (HRCT) of COVID-19 patients having CT severity score of more than 10 at 6 months after recovery

Dr. Sangeeta Saxena[1] (Senior Professor & Head), Dr. Sanju Palsania[2] (Post Graduate Resident) & Dr. Megha Kakkar[3] (Senior Resident)

Department of Radio diagnosis, Government Medical College, Kota[1,2&3]

Corresponding Author: Dr. Sanju Palsania

ABSTRACT

Background – Novel Corona Virus disease, or popularly known as COVID-2019, is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). HRCT plays a crucial role in the diagnosis and follow-up of patients with COVID-19 pneumonia.

Aims- The main objective of this study was to determine the computed tomography findings in the covid survivors at 6 months after being discharged and to study the potential acute and chronic post Covid chest complications like lung fibrosis

Material and Methods- 100 Cases who were referred for follow up of CT scan after COVID -2019 positive report on RT-PCR test 6 months back in a tertiary care centre were included in this study.

Results- Patients older than 50 years, who were hospitalized, patients with acute respiratory distress syndrome and other co- morbidities, who were on mechanical ventilation, and a total chest CT score of 18 or greater on initial CT scans were more prone to fibrotic-like changes in the lung after 6-month follow-up.

Conclusion- Follow-up CT scans obtained within 6 months of disease onset showed fibrotic-like changes in the lung in one-third of patients who survived severe coronavirus disease 2019 pneumonia. These patients were older and had more severe disease during the acute phase. The younger patients showed normal follow up scans or only ground glass opacities.

1. INTRODUCTION

Since the discovery of coronaviruses in the 1960s, there have been three outbreaks of a severe acute respiratory syndrome (SARS) caused by novel coronaviruses (1–3). Novel Corona Virus disease, or popularly known as COVID-2019, is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In December 2019, a series of COVID-19 pneumonia cases emerged in Wuhan, China. Thereafter, the disease rapidly spread worldwide. Accordingly, based on the WHO declaration, it became a pandemic on March 11, 2020. Pandemic has led to travel restrictions and nationwide lockdowns in many countries. With this effect, the scientific community across the world has found itself in a race against time to control the spread of the disease.

Though the gold standard test / most specific test for COVID-19 diagnosis is reverse transcription–polymerase-chain-reaction (RTPCR), the sensitivity is low as compared to HRCT of the chest. Chest radiography (CXR) helps in excluding the need for patient transfer and restricted use of PPE (personal protective equipment); however, CXR is not very sensitive in the detection of early disease. The usefulness of CXR is limited just only to establish a baseline survey. Despite the fact that imaging is not considered the most specific diagnostic tool for COVID- 19 and that most radiology professional organizations and societies unanimously oppose using computed tomography (CT) to screen COVID-19 pneumonia, a large number of chests computed tomography (CT) scans have been performed worldwide to assess the severity and extent of the lower respiratory tract (Zhaom et al, 2020) [4]. The scope of medical imaging has further extended in determining the course of illness and potential complications, which plays a vital role in patient management. With the advancement in techniques of Computed Tomography (CT) scanners, there has been significant improvement in the spatial resolution, which can help in detecting even minute parenchymal lung lesions. The CT scan results of COVID-19 pneumonia and the differential diagnosis should be more familiar to radiologists.

In the original SARS-CoV outbreak in 2003, which had 8,000 confirmed cases and a 9% mortality rate (5), reticular abnormalities were first noticed at 2 weeks when CT abnormalities were most severe (6). While the GGOs and consolidations slowly improved, fibrosis was seen in 50 to 60% of patients on follow-up scans after discharge (6,7). Fibrosis was more common in the elderly, those with a longer length of stay, those with a higher lactate dehydrogenase (LDH) in the acute phase (8) and those with notable exercise intolerance after recovery and those with high oxygen dependency (9). In 2012, Middle East Respiratory Syndrome (MERS), caused by the coronavirus MERS-CoV, was first identified in Saudi Arabia. As of January 2020, there were 2,519 confirmed cases with just over a 34% mortality rate (10). A study of 36 patients who had follow up chest X-rays (median of 43 days) after recovering from MERS showed that 33% had residual reticular opacities suggestive of fibrosis (11). Similar to the SARS data, these patients also had significantly longer ICU stays, higher peak LDH levels, and were older compared to those without reticulations. Post-acute fibrosis has also been reported in other viral infections with lower morbidity and mortality. In H1N1 influenza infection, which was benign in most cases and had an overall 0.5% mortality, there are reports of post-infection fibrosis (12-14) though the exact incidence is unknown. A recent meta-analysis in preprint of 60 studies looking at follow-up imaging after inpatient admissions for SARS-CoV, SARS-CoV-2, MERS or influenza pneumonia found inflammatory changes (ground glass opacity or consolidation) in 56% of scans and "fibrosis" (reticulation, lung architectural distortion, interlobular septal thickening, traction bronchiectasis, or honeycombing) in 40% (15). Given the known association between other viral pneumonias and fibrosis as well as the incidence of pulmonary involvement in COVID-19 during the acute illness and persistent respiratory symptoms after recovery, there has been a focus on the post-acute lung disease in COVID-19 (16).

In the evaluation of subjects with post-covid lung disease, clinical phenotypes have emerged. The majority of patients with significant radiographic abnormalities will have accompanying symptoms (i.e., breathlessness with or without cough) or abnormalities on lung physiology. However, it is recognized that a subset of patients will have symptoms suggestive of lung involvement without imaging abnormalities; conversely significant imaging abnormalities may be present without attributable symptoms.

The present study was designed to study the spectrum of computed tomography findings in chest in COVID-2019 infection, and the post covid sequalae at 6-month follow-up scans in order to provide a reliable basis for management at every point of disease. This study also evaluated the potential acute and chronic chest complications of the disease.

2. MATERIALS AND METHODS

A prospective observational study has been carried out between April 1,2021 to March 31,2022 on patients who were referred to Department of Radio-diagnosis for follow up of CT scan after COVID - 2019 positive report on RT-PCR and /or rapid antigen (True Nat) test 6 months back in tertiary care centre after obtaining informed written consent. 100 Cases who fulfilled the selection criteria during the study period were included. Selection of the cases was based on convenience sampling.

INCLUSION CRITERIA: -

1) All the patients of age more than 18 years diagnosed as COVID positive by RT PCR 6 months before.
2) Patients who were having CT severity score of more than 10.
3) Patients fulfilling the above criteria consenting to participate in the study

EXCLUSION CRITERIA: -

1) Patients who did not give consent to participate in the study.
2) Patients having CT severity score less than 10.
3) Patients of age less than 18 years.
4) Pregnant females

Methodology:

- After approval by the ethical committee of the Institute, the detailed information about the study was explained to the patients found eligible for inclusion in the study. Informed consent was taken from all of them.

- Demographic profiles of the patients were noted and complete details about the clinical diagnosis and laboratory diagnosis was noted in the study proforma.
- CT of thorax was done on GE CT BRIGHTSPEED 16 SLICE CT SCANNER (GE HEALTHCARE, USA).
- Patient questionnaires were completed during each screening visit.
- **GE CT Scan Bright speed slice CT scanner (GE Healthcare, USA). CONFIGURATION**

Software version	VA44
Scan mode	Spiral
Tube Voltage	120Kv
Qual.Ref.mAs(QRM)	210/150
Rotation time (sec)	0.5
Acquisition (detector configuration)	16x 0.6
Pitch	0.6
Dose modulation	CARE Dose4D

SCANNING PARAMETERS: -

- Position - Supine
- Scanner settings - kVP – 120
- mAS – 250
- Collimation - 1 mm
- Scan time - 1 to 2 sec
- Matrix Size - 512 x 512
- Superior extent - Lung apices
- Inferior extent - Domes of diaphragm
- Reconstruction algorithm: - High spatial frequency bone algorithm.
- Window level - - 550 to - 700 HU
- Window width - 1000 to 1650 HU
- For mediastinal viewing - 50 / 400 HU
- **HRCT Technique:**
- The purpose of HRCT is to increase the spatial resolution of the lung. Following protocol is used to acquire the images:
- - CT scan was performed according to a standard single breath hold protocol in supine position with full inspiration. Sections of 1 mm slice thickness were obtained using high spatial frequency volumetric reconstruction algorithm.
- - Collimation was adjusted and field of view (FOV) of 350 mm was taken. It is adjusted according to the size of the lung which reduces the anatomic dimensions of the picture elements (pixel), reducing volume averaging and increasing spatial resolution.
- - Reconstruction algorithms were used which sharpen images of the lung resulting in improved spatial resolution and definition of pulmonary parenchymal details without causing degradation of the overall visual acuity of images.
- - For viewing the lungs, a window level of 600 to 700 and width of 1000 to 1500 HU were adjusted and used.
- - Few of the patients with unexplained clinical deterioration were referred to our department for CT pulmonary angiography (CTPA). CTPA was performed as per standard technique. 30ml of OMNIPAQUE 350 contrast media was administered IV with rate of 4ml/sec and at 300 psi pressure. Pulmonary arterial phase images were acquired in 6-10 sec interval.
- - The CT chest images thus obtained were studied by a radiologist for presence of ground glass opacities, consolidation, septal thickening, fibrosis and other findings as described.
- - Follow up CT scans were taken after 6 months of COVID-19 positive result.

3. RESULTS

Present study was done to study HRCT findings in patients who came for follow up scan at 6 months of being COVID-19 positive. We studied the findings in follow up HRCT scan and the various complications that occurred after COVID-19 infection. The study was conducted among 100 patients.

In this study, 6 months follow up HRCT scan was completely normal in 28% of the patients. GGO's were found in 72% of the patients in our study and consolidation with GGO's were found in 10% of the patients. The scans in which, GGO was the only finding, were mainly young patients or patients of age less than 50 years. 30 of 100 participants (30%) who recovered from severe coronavirus disease 2019 pneumonia developed fibrotic like changes (traction bronchiectasis, reticulations and septal thickening) in the lung within 6 months. Honey combing was found in 5% of the patients and reverse halo sign was found in 3% of the total patients. Patients with age more than 50 years, who were hospitalized and on mechanical ventilation, and with co-morbidities like diabetes and hypertension, a total chest CT score of 18 or greater on initial CT scans were independent predictors of the subsequent development of fibrotic-like changes in the lung after 6-month follow-up. Patients with covid score of more than 15 at the time of Covid infection; they were found to have more lung fibrotic like changes. (TABLE 1. TABLE 2, TABLE3, TABLE 4, CASE 1)

TABLE 1 : Association between age and CT severity score

Age Group	CT Score		
	Mild (1-8)	Moderate (9-14)	Severe (15-25)
20-30	0	4	5
30-40	0	6	13
40-50	0	4	8
50-60	0	3	26
60-70	0	4	18
≥70 Years	0	0	9
p-value			0.002*

TABLE 2 : Association between mechanical ventilation during COVID Infection & CT scan parameters at six months follow up scan

Traction Bronchiectasis	**Positive**	**Negative**	**p-value**
Non-invasive	19	2	0.393
Invasive	2	0	
Reticulations			
Non-invasive	19	2	0.393
Invasive	2	0	
Septal thickening			
Non-invasive	19	2	0.393
Invasive	2	0	
Honey combing			
Non-invasive	3	18	0.596
Invasive	0	2	
Reverse halo sign			
Non-invasive	1	20	0.134
Invasive	0	2	

ISSN 2515-8260 Volume 10, Issue 04, 2023

TABLE 3 : Association between admission status at the time of COVID & CT scan parameters at six months follow up scan

Traction Bronchiectasis	Positive	Negative	p-value
Home	1	57	<0.0001*
Hospitalisation	29	13	
Reticulations			
Home	1	57	<0.0001*
Hospitalisation	29	13	
Septal Thickening			
Home	1	57	<0.0001*
Hospitalisation	29	13	
Honey combing			
Home	0	58	0.060
Hospitalisation	4	38	
Reverse halo			
Home	2	56	0.777
Hospitalisation	1	41	

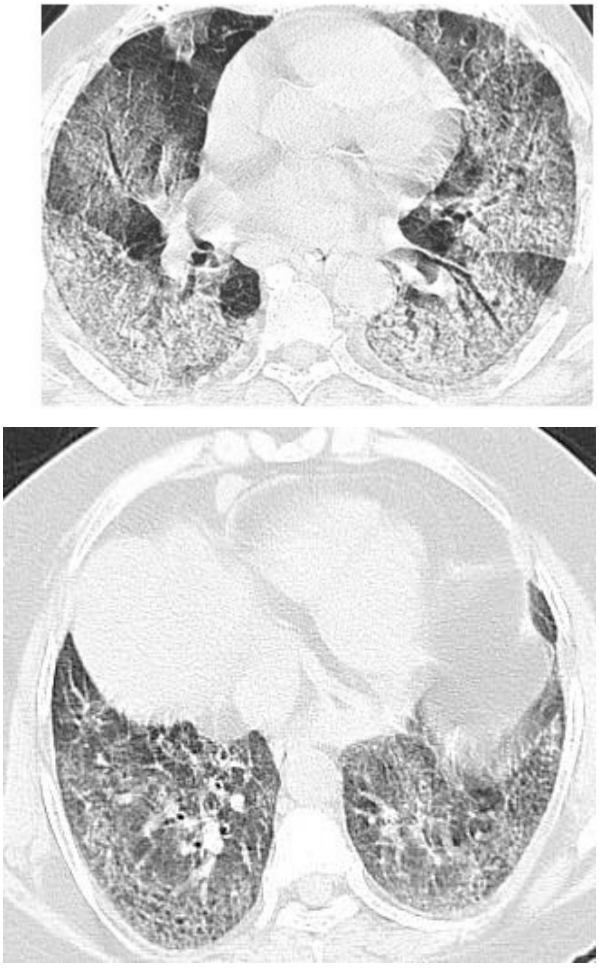
TABLE 4 : Association between co-morbidities & CT scan parameters at six months follow up scan

Traction Bronchiectasis	Positive	Negative	p-value
Diabetes	8	3	0.121
HTN	18	16	
Respiratory	13	3	
ARDS	22	4	
Reticulations			
Diabetes	8	3	0.121
HTN	18	16	
Respiratory	13	3	
ARDS	22	4	
Septal thickening			
Diabetes	8	3	
HTN	18	16	
Respiratory	13	3	0.121
ARDS	22	4	
Honey combing			
Diabetes	1	10	0.136
HTN	2	32	
Respiratory	4	12	
ARDS	4	22	
Reverse halo			
Diabetes	3	8	0.006*
HTN	0	34	
Respiratory	1	`15	
ARDS	1	25	

CASE 1-

(A) Axial HRCT Chest image in patient with severe covid 19 pneumonia showing extensive ground glass opacities involving bilateral lung parenchyma with septal thickening.

(B) Serial axial HRCT chest image after 6 months shows interlobular septal thickening and reticulations predominantly in postero-basal distribution.



(A)

(B)

4. DISCUSSION

The present study was conducted on patients who were RT-PCR COVID-19 positive patients and who came for follow up HRCT scan after 6 months. The study was conducted between April 1, 2021 to March 31, 2022 with aims to determine the computed tomography findings in the covid survivors at 6 months and the potential acute and chronic post Covid chest complications like lung fibrosis. A total of 100 patients were enrolled for this study.

In our study, 6 months follow up HRCT scan was completely normal in 28% of the patients. The main spectrum which we found on HRCT was GGO's. GGO's was found in 72% of the patients in our study and consolidation with GGO's was found in 10% of the patients. The scans in which, GGO was the only finding, were mainly young patients or patients of age less than 50 years. 30 of 100 participants (30%) who recovered from severe coronavirus disease 2019 pneumonia, developed fibrotic like changes (like traction bronchiectasis, reticulations and septal thickening) in the lung within 6 months. Honey combing was found in 5% of the patients and reverse halo sign was found in 3% of the total patients. We found that age of more than 50 years, who were hospitalized, patients with acute respiratory distress syndrome, mechanical ventilation, and a total chest CT score of 18 or greater on initial CT scans were independent

predictors of the subsequent development of fibrotic-like changes in the lung after 6-month follow-up. Participants with fibrotic-like changes in the lung showed a higher frequency of ARDS (22 of 30 [73.3%]), which was also a predictor of fibrotic-like changes. Previous studies (17,18) have demonstrated that a substantial proportion of patients who survive ARDS may develop progressive fibrotic-like changes on CT scans. Nevertheless, it remains uncertain whether the fibrotic-like changes observed in this study represent true fibrotic lung disease (e.g., at pathologic examination or longer-term follow- up CT). Whether or not these fibrotic-like changes, found at 6 months, reflect permanent change in the lung remains to be investigated. Furthermore, fibrotic like changes are more found in patients with other co-morbidities like diabetes and hypertension. 8% of the diabetic patients and 18% patients who had HTN, 13% patients with respiratory problems and 22% patients with ARDS, were found to have typical post covid findings on CT like traction bronchiectasis, reticulations, septal thickening and 1 diabetic & 2 patients with HTN, had honey combing and 3 diabetic patients had reverse halo in their follow up CT scans. Additionally, the high frequency of mechanical ventilation is another risk factor for the development of fibrotic-like changes at 6 months. On the basis of previously published data (18), mechanical ventilation is strongly related to fibrotic-like changes observed after ARDS. Likewise, the fibrotic-like changes in the lung in our patients may also be associated with ventilator-induced lung injury. In our study, 21 patients developed fibrotic like changes who were on mechanical ventilation at the time of covid infection. We found that a higher CT score (>15) at the initial CT examination led to the fibrotic like changes at the 6-month follow-up examination. According to a previous study on idiopathic pulmonary fibrosis (19), CT score is correlated with the degree of pulmonary fibrosis in pathologic specimens. Moreover, a recent publication revealed an association between a CT score of 15 or greater and an increased mortality risk in patients with COVID-19 (20). In our study, 53 patients had covid score of more than 15. Therefore, a greater extent of lung injury in the acute phase may be associated with a higher mortality rate and more severe pulmonary sequelae in survivors. In addition, the correlations of scores for fibrotic-like changes with the above-mentioned risk factors were also confirmed in our study. At 6-month follow-up, a few patients still reported ongoing respiratory symptoms, which more frequently occurred in patients with fibrotic-like changes. Thus, both structural and functional lung impairments may simultaneously occur in patients who survive severe COVID-19 pneumonia. Significant decreases in CT scores for total lesions, GGO, and consolidation were observed at follow-up CT compared with the initial CT. Although the predominant CT pattern at follow- up CT was still GGO, the densities had visually decreased. Two studies (20,21) reported an increased extension of the GGO or consolidation and a decreased attenuation at follow-up CT of COVID-19 pneumonia, which may indicate the gradual regression of the inflammation and re-expansion of the alveoli. GGO in the acute phase of COVID-19 pneumonia may represent the inflammatory infiltrates, edema, or haemorrhaging (22,23). The pathophysiology underlying GGO in the convalescent phase of COVID-19 pneumonia and the correlation with fibrosis is worthy of further investigation.

5. CONCLUSION-

We concluded that follow-up CT scans obtained within 6 months of disease onset showed fibrotic-like changes in the lung in one-third of patients who survived severe coronavirus disease 2019 pneumonia. These patients were older and had more severe disease during the acute phase. The younger patients show normal follow up scans or only ground glass opacities.

However, the long-term lung sequelae of these CT findings are still largely unknown. This report serves as a basis for new, prospective, large-scale, long-term investigations analysing these high-risk patients.

6. REFERENCES: -

1. Stadler K, Masignani V, Eickmann M , Becker S , Abrignani S , Klenk HD , et al. . SARS--beginning to understand a new virus. Nat Rev Microbiol . 2003.; 1 (3): 209 – 18 . 10.1038/nrmicro775 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
2. Mackay IM, Arden KE . MERS coronavirus: diagnostics, epidemiology and transmission. Virol J . 2015.; 12 : 222 . 10.1186/s12985-015-0439-5 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

3. Jin Y, Yang H , Ji W , Wu W , Chen S , Zhang W , et al. . Virology, Epidemiology, Pathogenesis, and Control of COVID-19 . Viruses . 2020. ; 12 (4 . 10.3390/v12040372 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
4. Zhaom W, Zhon Z et al. Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: a multicenter study AJR 2020; 215:1 –6
5. Cherry JD , Krogstad P . SARS: The First Pandemic of the 21st Century . Pediatric Research . 2004. ; 56 (1): 1 – 5 . 10.1203/01.pdr.0000129184.87042.fc [PMC free article] [PubMed] [CrossRef] [Google Scholar]
6. Ooi GC KP , Muller NL , Yiu WC , Zhou LJ , Ho JC , Lam B , Nicolaou S , Tsang KW . Severe acute respiratory syndrome: temporal lung changes at thin-section CT in 30 patients . Radiology . 2004. ; 230 : 836 – 44 . 10.1148/radiol.2303030853 [PubMed] [CrossRef] [Google Scholar]
7. Antonio GE , Wong KT , Chu WC , Hui DS , Cheng FW , Yuen EH , et al. . Imaging in severe acute respiratory syndrome (SARS) . Clin Radiol . 2003. ; 58 (11): 825 – 32 . 10.1016/s0009-9260(03)00308-8 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
8. Antonio GE WK , Hui DS , Wu A , Lee N , Yuen EH , Leung CB , Rainer TH , Cameron P , Chung SS , Sung JJ , Ahuja AT . Thin-Section CT in Patients with Severe Acute Respiratory Syndrome Following Hospital Discharge: Preliminary Experience . Radiology . 2003. ; 228 : 810 – 5 . 10.1148/radiol.2283030726 [PubMed] [CrossRef] [Google Scholar]
9. Chan KS ZJ , Mok YW , Li YM , Liu YN , Chu CM , Ip MS . SARS: prognosis, outcome and sequelae . Respirology . 2003. ; 8 : S36 – S40 . 10.1046/j.1440-1843.2003.00522.x [PMC free article] [PubMed] [CrossRef] [Google Scholar]
10. Da Costa VG , Moreli ML , Saivish MV . The emergence of SARS, MERS and novel SARS-2 coronaviruses in the 21st century . Archives of Virology . 2020. ; 165 (7): 1517 – 26 . 10.1007/s00705-020-04628-0 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
11. Das KM , Lee EY , Singh R , Enani MA , Al Dossari K , Van Gorkom K , et al. . Follow-up chest radiographic findings in patients with MERS-CoV after recovery . Indian J Radiol Imaging . 2017. ; 27 (3): 342 – 9 . 10.4103/ijri.IJRI_469_16 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
12. Mineo G , Ciccarese F , Modolon C , Landini MP , Valentino M , Zompatori M . Post-ARDS pulmonary fibrosis in patients with H1N1 pneumonia: role of follow-up CT . Radiol Med . 2012. ; 117 (2): 185 – 200 . 10.1007/s11547-011-0740-3 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
13. Singh V , Sharma BB , Patel V . Pulmonary sequelae in a patient recovered from swine flu . Lung India . 2012. ; 29 (3): 277 – 9 . 10.4103/0970-2113.99118 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
14. Shieh W-J BD , Denison AM , DeLeon-Carnes M , Adem P , Bhatnagar J , Sumner J , Liu L , Patel M , Batten B , Greer P , Jones T , Smith C , Bartlett J , Montague J , White E , Rollin D , Gao R , Seales C , Jost H , Metcalfe M , Goldsmith CS , Humphrey C , Schmitz A , Drew C , Paddock C , Uyeki TM , Zaki SR . 2009 Pandemic Influenza A (H1N1) Pathology and Pathogenesis of 100 Fatal Cases in the United States. American Journal of Pathology. 2010.; 177: 166 – 75 . 10.2353/ajpath.2010.100115 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
15. Fabbri L, Moss S , Khan F , Chi W , Xia J , Robinson K , et al. . Post-viral parenchymal lung disease of COVID-19 and viral pneumonitis: A systematic review and meta-analysis. medRxiv . 2021.: 10.1101/2021.03.15.21253593 [CrossRef] [Google Scholar]
16. 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. . 10.1016/S2213-2600(20)30222-8 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
17. Meduri GU, Headley S, Kohler G, et al. Persistent elevation of inflammatory cytokines predicts a poor outcome in ARDS. Plasma IL-1 beta and IL-6 levels are consistent and efficient predictors of outcome over time. Chest 1995;107(4):1062–1073.

18. Desai SR, Wells AU, Rubens MB, Evans TW, Hansell DM. Acute respiratory distress syndrome: CT abnormalities at long-term follow-up. Radiology 1999;210(1):29–35.
19. Kazerooni EA, Martinez FJ, Flint A, et al. Thin-section CT obtained at 10-mm increments versus limited three-level thin-section CT for idiopathic pulmonary fibrosis: correlation with pathologic scoring. AJR Am J Roentgenol 1997;169(4):977–983.
20. Francone M, Iafrate F, Masci GM, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. Eur Radiol 2020;30(12):6808–6817.
21. Pan Y, Guan H, Zhou S, et al. Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): a study of 63 patients in Wuhan China. Eur Radiol 2020;30(6):3306–3309.
22. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020;8(4):420–422.
23. Liu J, Zheng X, Tong Q, et al. Overlapping and discrete aspects of the pathology and pathogenesis of the emerging human pathogenic coronaviruses SARS-CoV, MERSCoV, and 2019-nCoV. J Med Virol 2020;92(5):491–494.