

Severe coronavirus disease 2019: CT changes based on prognosis

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Abstract

Purpose: To determine the characteristics of CT changes in patients with severe coronavirus disease 2019 (COVID-19) based on prognosis.

Method: Serial CT scans in 47 patients with severe COVID-19 were reviewed. The patterns, distribution and CT score of lung abnormalities were assessed. Scans were classified according to duration in weeks after onset of symptoms. These CT abnormalities were compared between discharged and dead patients.

Results: Twenty-six patients were discharged, whereas 21 passed away. Discharged patients were characterized by a rapid rise in CT score in the first 2 weeks followed by a slow decline, presence of reticular and mixed patterns from the second week, and prevalence of subpleural distribution of opacities in all weeks. In contrast, dead patients were characterized by a progressive rise in CT score, persistence of ground-glass opacity and consolidation patterns in all weeks, and prevalence of diffuse distribution from the second week. CT scores of death group were significantly higher than those of discharge group ($P < .05$). Significant differences were also noted in abnormality pattern ($P < .05$) and opacity distribution ($P < .05$) between groups.

Conclusions: The severe COVID-19 patients presented with characteristic CT changes and the CT changes varied with prognosis.

Authors Bin Liang, Lingli Xie contributed equally to this work.

Background

An outbreak of coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China in December 2019¹, and the pandemic has accelerated recently, with a considerable number of cases now confirmed in multiple countries and territories. This disease is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and has been regarded as a life-threatening respiratory infection². By April 15th, 2020, 50008 cases had been confirmed, with 2579 deaths in Wuhan, China³. Although COVID-19 may present with mild, moderate or severe illness, a minority of patients with severe illness may deteriorate rapidly and even die, and these patients will require accurate assessment and aggressive treatment⁴.

CT is currently the main imaging modality employed for patients with COVID-19 in China, and it has played an important role in the diagnosis and treatment of the novel coronavirus pneumonia⁵⁻⁸. A recent study has shown that CT assists in the early diagnosis for patients with a high clinical suspicion of COVID-19 but a negative real-time RT-PCR test⁶. Another recent study evaluating the change of CT findings in patients with mild and moderate COVID-19 found that the abnormality on CT can be divided into 4 stages in the natural history of the disease, with the maximal abnormality being noted at 10 days after onset of symptoms⁷. However, there is little information regarding the chest CT changes in patients with severe illness. Knowledge of CT features in severe COVID-19 can be helpful to assess severity of

illness. Therefore, the aim of this study was to determine the characteristics of CT changes of severe COVID-19 based on prognosis.

Materials And Methods

Patients. The Medical Ethics Committee of Wuhan Union Hospital, Tongji Medical College, Huazhong University of Science and Technology and General Hospital of the Yangtze River Shipping (Wuhan, China) approved this study and waived informed consent. The study was carried out in accordance with the principles embodied in the Declaration of Helsinki. A retrospective analysis was conducted of all patients who had been hospitalized for COVID-19 infection at the Wuhan Union Hospital and the General Hospital of the Yangtze River Shipping from December 25 2020 to March 12 2020. The criteria for patient selection included 1) patients aged >18 years, 2) patients whose pharyngeal swab specimen tested positive for COVID-19 by real-time RT-PCR, 3) patients who presented with severe illness, 4) patients who had been discharged from hospital or had died of the disease, and 5) patients who underwent at least two serial chest CT scans. Patients were excluded if they had been transferred to other hospitals, had mild or moderate illness, or had incomplete CT or clinical data.

According to the WHO guidance⁴, severe COVID-19 infection includes severe pneumonia and the relevant clinical syndromes, including acute respiratory distress syndrome (ARDS), sepsis and septic shock. The severe pneumonia is defined as fever or suspected respiratory infection, plus one of respiratory rate >30 breaths/min, severe respiratory distress, or SpO₂ <90% on room air. The definition of the other 3 clinical syndromes, which developed based on the pneumonia, are also referenced in the WHO guidance⁴.

The criteria for patient discharge include being afebrile for greater than 3 days, significant improvement in respiratory symptoms and radiological abnormalities, and two consecutive pharyngeal swab specimens testing negative for COVID-19 at least 24 hours apart⁹.

CT imaging. Chest CT examinations were performed using multidetector CT scanners (Somatom Perspective; Somatom Spirit; Somatom Definition AS+, Siemens Healthineers, Germany; Aquilion one, Toshiba, Japan). The patients received non-contrast enhanced CT scanning on breath-hold in the supine position and the scan ranged from the level of the thoracic inlet to the costophrenic angles. The CT parameters were as follows: tube voltage, 120 kV; tube current, regulated by an automatic exposure control system. Images were reconstructed at 1.5-mm slice thickness and interval, and then transmitted to picture archiving and communication systems (PACS) for interpretation or additional post-processing⁵.

Image evaluation. The serial thin-section CT images of the patients during hospitalization were reviewed in consensus by two radiologists (B. L. and F. Y., with 26 and 12 years of experience in diagnostic radiology, respectively), who were blinded to the patients' demographic, clinical and laboratory data.

Each lobe of the lung was reviewed for possible abnormal findings in accordance with the glossary of terms for thoracic imaging recommended by Fleischner Society¹⁰. The predominant patterns of

abnormality on CT scans were categorized as ground-glass pattern, consolidation pattern, reticular pattern and mixed pattern 11. Ground-glass opacity pattern appeared as ground-glass opacities alone or with superimposed interlobular and intralobular septal thickening and irregular linear opacities. Consolidation pattern appeared as consolidation alone or predominant consolidation without architectural distortion. Reticular pattern consisted of either coarse linear or curvilinear opacities or fine subpleural reticulation without substantial ground-glass opacities. Mixed pattern appeared as a combination of consolidation, ground-glass opacities, and reticular opacities in the presence of architectural distortion 11. Pleural thickening, pleural effusion, mediastinal lymphadenopathy, pneumothorax, pneumomediastinum and other possible findings were also recorded.

The distribution of opacities was evaluated according to the previous method 11 with minor modifications. Opacities were noted as being subpleural (abutting the pleural surface, including interlobar pleura), random (without predilection for subpleural or central regions), or diffuse (continuous involvement without respect to lung segments).

The extent of lung lesion was also quantified according to a CT scoring system 12. Each lobe of the lung was visually scored on a scale of 0–5, depending on the percentage of each lobe involved: 0, no involvement; 1, <5%; 2, 5%–25%; 3, 26%–49%; 4, 50%–75%; 5, >75%. The sum of scores of the 5 lobes provided total lung involvement, with a range of 0–25.

Collection of clinical data. Data for demographic, clinical and laboratory parameters, including age, sex, symptoms, comorbidities, clinical syndromes, lymphocyte count, C-reactive protein (CRP), lactate dehydrogenase (LDH), alanine aminotransferase (ALT), and pulse oxygen saturation (SpO₂) levels were collected by one of four clinicians (L. L. X., R. P., and P. D.) for evaluating severity of illness. Patient prognosis, either discharge or death, was also documented.

Statistical Analysis. Statistical analyses were performed using IBM SPSS Statistics (version 22; SPSS, Chicago, Ill). The data were expressed as Mean \pm SD and median and range unless otherwise stated. Differences in CT parameters between discharged and dead patients were tested using Chi-square test and Mann-Whitney *U* test. Two-sided $P < 0.05$ was considered statistically significant.

Results

Patient characteristics. A total of 498 patients had been hospitalized for COVID–19 by the end of March 20 2020. 451 patients were excluded due to transfer to other hospitals (204 patients), mild or moderate illness (222 patients), or incomplete data (25 patients). Consequently, 47 patients were included in this study.

Of the included 47 patients, 26 patients were discharged after treatment, whereas 21 patients died from the severe illness. Time from onset of symptoms to discharge or death was 27.4 ± 8.3 (27, 12–50) days or 17.9 ± 7.3 (16, 8–33) days, respectively. Initial symptoms included fever, fatigue, dry cough, expectoration, pharyngalgia, dyspnea, anorexia, myalgia, diarrhea, nausea and vomiting. Table 1

summarizes the baseline characteristics and clinical syndromes of patients with severe COVID-19 based on prognosis. The dead patients showed significant increases in age, comorbidities (cerebrovascular disease, diabetes mellitus and chronic kidney disease) and clinical syndromes (sepsis and septic shock) compared with the discharged patients ($P < .05$). In addition, the dead patients showed significant decreases in lymphocyte count ($P < .001$), CRP ($P < .001$), ALT ($P < .001$) and SpO₂ level ($P < .001$) compared with the discharged patients at baseline. *Changes of CT abnormalities.* The indications for serial scans included initial diagnosis, clinical deterioration and requirement of a change in treatment. The mean number of CT scans was 3.3 ± 1.2 (3, 2-6) per patient. The mean time from onset of symptoms to the first CT scan was 4.9 ± 3 (5, 0-13) days, and the mean time from the last CT scan to discharge or death was 3.3 ± 2.3 (3, 0-10) and 5.6 ± 4 (5, 0-18) days, respectively.

There were apparent changes of CT abnormalities in patients with severe COVID-19 during the hospitalization. In the 26 discharged patients, the total CT score markedly increased during the first two weeks after onset of symptoms, with a median peak CT score of 10 (range, 5-21), and then it dropped slowly to a median CT score of 8 (range, 3-15) in the fourth week or longer (Fig. 1).

The predominant abnormalities were ground-glass opacity and opacification within the first week, followed by coexistence of 4 patterns during the second week, after which the pattern appeared as ground-glass, reticular or mixed patterns (Fig. 2A). The frequency of the ground-glass pattern (Figs. 3 and 4) was highest in the first week (79.2%, 19/24) and maintained a high proportion in the second week (45.5%, 15/33), after which it decreased. Superimposed interlobular and intralobular septal thickening (Fig. 4B) were frequently observed in the first 2 weeks and superimposed irregular linear opacities (Fig. 4C) became more common thereafter. Consolidation pattern was not common, with a frequency of 16.7% (4/24), 15.2% (5/33) and 4% (1/25) in the first, second and third week, respectively, although consolidation was frequently noted in combination with other abnormalities. Reticular pattern (Fig. 3C) was found from the second week (6.1%, 2/33) and became more common in the third (20%, 5/25) week and fourth week or longer (45.8%, 11/24). Mixed pattern (Fig. 4D) was noted from the second week and maintain high proportions in the second (33.3%, 11/33) week and the third week (44%, 11/25), after which it decreased (29.2%, 7/24). In terms of the longitudinal changes of abnormalities, the initial CT scans demonstrated predominant ground-glass opacities, consolidation, mixed pattern and normal findings in 20, 4, 1 and 1 patients, respectively. Of the 20 patients with ground-glass opacities on the initial scans, 10 developed a reticular pattern, 8 developed a mixed pattern, and 2 decreased in extent before discharge. Of the 4 patients with consolidation on the initial scans, 2 developed a ground-glass opacity pattern, 1 developed a reticular pattern, and 1 developed a mixed pattern. The patient with mixed pattern on the initial scan revolved completely, and the patient with normal findings developed a reticular pattern. Of note, the reticular and mixed pattern generally occurred in the background of the original ground-glass opacities or consolidation and may persist until discharge (Figs. 3 and 4).

The distribution of opacities also varied with time (Fig. 5A). Subpleural distribution (Fig. 4A) was predominant in all the weeks, with proportions of 42.4%-66.7%. Random distribution (Fig. 3A) was noted with a low frequency in all the weeks. Diffuse distribution (Fig. 4B) was occasionally noted in the first

week (8.3%, 2/24) and become more common in the second week (39.4%, 13/33), after which it decreased. Thirteen patients presented with pleural thickening adjacent to the lung abnormalities. Seven patients developed mild to moderate pleural effusion, one of whom developed concomitant pericardial effusion. Two patients developed subsegmental atelectasis, which appeared as parenchymal bands and was reversed with inflammation resolution. No pneumothorax, pneumomediastinum or mediastinal lymphadenopathy was noted.

In contrast, the 21 dead patients showed different CT features (Fig. 6). The median CT score was progressively increased from 9 (rang, 1–19) in the first week to 19.5 (rang, 19–20) in the fourth week (Fig. 1). The predominant patterns of abnormality only included ground-glass opacity and consolidation. Ground-glass opacity pattern was more common than consolidation pattern during the first 3 weeks, and thereafter the two patterns were found in equal proportions (Fig. 2B). Opacities were predominantly distributed in the subpleural regions (48.3%, 14/29) during the first week and became more diffuse (69.2%, 9/13) in the second week, after which opacities were only found displaying a diffuse pattern (Fig. 5B). Pleural thickening and pleural effusion were found in 4 and 7 patients, respectively. Pneumomediastinum was noted in 1 patient late in the course (Fig. 6C).

Comparison of CT changes in discharged and dead patients. Given the length of hospital stay, the distribution of time to CT scan and the CT findings, the CT changes was compared in discharged and dead patients on the bases on scans of three time periods: within the first week, within the second week, and from the third week onwards. Table 2 summarizes the temporal change in CT score, abnormality pattern and opacity distribution between the two groups of patients. CT scores of the death group were significantly higher than those of the discharge group within the first week (9 vs. 6, P

= .014), the second week (14 vs. 10, P = .042) and from the third week (19 vs. 9, P < .001). There were significant differences in abnormality pattern between two groups within the second week (P = .029) and from the third week (P < .001). Mixed and reticular patterns were noted in discharged patients during the second week or longer, whereas they were not found in dead patients. Significant differences were also noted in opacity distribution between the two groups from the third week (P < .001). Subpleural and random distribution were more prevalent in discharged patients, whereas diffuse distribution achieved a dominant proportion in death group from the third week onwards.

Discussion

Management of patients with severe COVID–19 currently represents a challenge. Since the natural history of COVID–19 is not clearly understood, identification and assessment of severely ill patients is considerably based on the combination of clinical, laboratory and imaging findings⁹. To our knowledge, this is the first study to report the CT changes of severe COVID–19 during hospitalization based on prognosis. Our results demonstrated that the severely ill patients presented with characteristic CT changes and the CT changes varied with prognosis.

Our study found that the discharged patients were characterized by a rapid rise in CT score in the first 2 weeks followed by slow decline in it, presence of reticular and mixed patterns from the second week, and prevalence of subpleural and random distribution of opacities in the first and from the third week. These findings provide a supplement to those observed in mild and moderate illness. Pan et al⁶ investigated CT changes of non-severe COVID-19 from diagnosis until recovery of disease and revealed four stages of CT characteristics. Abnormalities included ground-glass opacities and superimposed crazy-paving pattern, with mean CT scores of 2 and 6 on stage I (0-4 days) and II (5-8 days), respectively, and became more consolidative on stage III (9-13 days), with a mean peak CT score of 7, after which the consolidation resolved gradually, with a mean CT score of 6 before discharge (stage IV, ≥ 14 days). In this study, the discharged patients also showed a rapid increase in CT score and abnormality patterns of ground-glass opacities and consolidation within the first 2 weeks. However, the CT score seemed higher, with a median peak CT score of 10 in the second week, which then decreased more slowly, with median CT scores of 9 and 8 in the third and fourth week, respectively. In addition, reticular and mixed patterns were noted in the second week and became more prevalent thereafter. Diffuse distribution was also more common, particularly in the second week. Extrapulmonary abnormalities including pleural thickening, pleural effusion, subsegmental atelectasis and pneumomediastinum, were also found in this study. The discrepancies between our findings and previous findings are most likely due to differences in severity of illness.

A surprising finding was that the CT changes of our discharged patients greatly resembled those seen in SARS patients¹¹. One possible explanation for this is that SARS-CoV-2 exhibits 79.5% sequence identity to SARS-CoV that causes SARS¹³. Both the coronavirus-associated respiratory infections are also similar in pathological features^{14,15}. Xu et al¹⁵ performed histological examination on a patient who died from COVID-19 on illness day 14 and this showed bilateral diffuse alveolar damage with cellular fibromyxoid exudates, which was accompanied by pulmonary edema, pneumocyte desquamation and hyaline membrane formation. Interstitial mononuclear inflammatory infiltrates, dominated by lymphocytes, were also noted in both lungs. These pathological findings indicate ARDS, and they also explain the pattern of ground-glass opacities or consolidation seen on CT within the first 2 weeks. Like the findings noted in SARS patients [11], we found that the ground-glass opacities and consolidation on the initial scans generally either resolved completely or reduced in extent or transformed into the other patterns during hospitalization. The reticular and mixed patterns were found from the second week, and they generally developed in the background of the original ground-glass opacities or consolidation and may persist for a long period. The reticular pattern probably represents residual interstitial disease, and the mixed pattern probably represents mixed disease of parenchyma and interstitium during the improvement of the severe pneumonia. Precise interpretation of these CT abnormalities in COVID-19 awaits the results of further postmortem.

More importantly, our study revealed the CT changes in the dead patients. They were characterized by a progressive rise in CT score, persistence of ground-glass opacities and consolidation patterns in all weeks, and prevalence of diffuse opacity distribution from the second week. By comparison of CT findings in discharged and dead patients, we found several crucial differences between the two groups,

which may be helpful in the assessment of prognosis. Firstly, the extent of parenchymal abnormalities was significantly higher in the death compared with discharge group in all weeks, which suggests that the dead patients presented with a more intense inflammation storm in lungs. Accordingly, more clinical syndromes, such as sepsis and septic shock, developed and the patients deteriorate rapidly. Secondly, neither the mixed nor reticular pattern was noted in the death group, particularly from the second week. As discussed earlier, the mixed and reticular patterns probably represent improvements of pneumonia. The absence of the two patterns implies a poor prognosis. Finally, diffuse distribution of opacities achieved a dominant proportion in death group from the third week. Given the fact that the interval between onset of symptoms and death was short, with a median of 16 (8–33) days, the assessment of CT abnormalities should focus on the first 2 weeks.

Like recent results^{16,17}, our observations showed statistically significant increases in age, comorbidities (cerebrovascular disease, diabetes mellitus and chronic kidney disease) and clinical syndromes (sepsis and septic shock) in the dead patients compared with the discharged patients. These finding supports the belief that age, comorbidity and secondary clinical syndromes may be risk factors for poor outcomes. In terms with laboratory parameters, although the dead patients showed significant decreases in lymphocyte count, CRP, ALT and SpO₂ level compared with the discharged patients at baseline, dynamic profile of laboratory findings merits further studies.

One of the major limitations of this study was that the number and time points of CT scans were not uniform because some severely ill patients could not be weaned from mechanical ventilation, which may affect the assessment of CT changes in individuals. In addition, residual abnormalities persisted on the last CT scan in discharged patients. Further CT follow-up is necessary to assess the long-term lung sequelae.

In conclusion, this study found that the severe COVID–19 presented with characteristic CT changes and the CT changes differed between the discharged and dead patients. An understanding of these differences can be of clinical significance in the assessment of the prognosis of severely ill patients. Whether these CT changes can be used as independent predictors of prognosis awaits the results of further studies.

Declarations

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None.

Author contributions

B.L. and L.X. contributed to conception, design, data acquisition, analysis, interpretation and draft of the manuscript; F.Y., J.M., L.Z., R.P., P.D. and W.F contributed to data acquisition, analysis and interpretation;

B.L., L.X. and J.M. contributed to data interpretation and editing of the manuscript. C.Z. contributed to technical support and design of the research.

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Competing interests

The authors declare no competing interests.

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Tables

TABLE 1: Baseline characteristics and clinical syndromes of patients with severe COVID-19

Parameters	Discharge Patients (n = 26)	Dead Patients (n = 21)	<i>P</i> value
Age	61.7 ± 14.8 (60, 24–90)	77 ± 12.5 (78, 56–99)	.001
Sex (man/woman)			.770
Female	11 (42.3%)	8 (38.1%)	
Male	15 (57.7%)	13 (61.9%)	
Comorbidities	19 (73.1%)	20 (95.2%)	.044
Hypertension	15 (57.7%)	12 (57.1%)	.970
Cardiovascular disease	7 (26.9%)	11 (52.4%)	.074
Cerebrovascular disease	0	4 (19%)	.020
Diabetes mellitus	2 (7.7%)	9 (42.9%)	.005
COPD	1 (3.8%)	2 (9.5%)	.429
Chronic kidney disease	1 (3.8%)	6 (28.6%)	.018
Chronic hepatic disease	7 (26.9%)	6 (28.6%)	.900
Others	4 (15.4%)	3 (14.3%)	.916
Lymphocyte count (× 10 ⁹ /L)	1.1 ± 1.3 (0.7, 0.4–7.5)	0.9 ± 0.4 (1, 0.2–2)	<.001
CRP level (mg/L)	36.1 ± 41.4 (27.5, 4.7–187.8)	30.8 ± 15.5 (31.3, 4.2–83.6)	<.001
LDH level (U/L)	330 ± 129.5 (301, 172–641)	312.2 ± 98.6 (302, 134–550)	.323
ALT level (U/L)	33.4 ± 25.3 (26, 8–116)	24.6 ± 16.4 (21, 8–70)	<.001
SpO ₂ level (%)	91.6 ± 7.3 (94, 64–99)	88.1 ± 8.2 (89, 69–98)	<.001
Clinical syndromes			
Severe pneumonia	26	21	–
ARDS	21 (80.8%)	20 (95.2%)	0.139
Sepsis	11 (42.3%)	19 (90.5%)	.001
Septic shock	3 (11.5%)	20 (95.2%)	<.001

Except where otherwise indicated, data are mean ± SD (median and range) of age or number (%) of patients. COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; LDH = lactate dehydrogenase; ALT = alanine aminotransferase; SpO₂ = pulse oxygen saturation; ARDS = acute respiratory distress syndrome.

TABLE 2: Comparison of CT Findings in Discharge and Death Groups Based on CT Scans

Parameters	Within the First Week			Within the Second Week			From the Third	Week onwards	<i>P</i>
	Discharge (scans = 24) = 29)	Death (scans	<i>P</i> value	Discharge (scans = 33) (scans= 13)	Death	<i>P</i> value	Discharge (scans = 49)	Death (scans = 11)	
CT score	6, 0–11 (5.7 ± 3) ± 5.3)	9, 1–19 (9.5	.014	10, 5–21 (11.2 ± 4) ± 5.1)	14, 6–23 (14.4	.042	9, 3–17 (9.2 ± 3.4)	19, 16–22 (18.9 ± 2.0)	<.001
CT Pattern			.460			.029			<.001
Ground-glass	19	26		15	12		14	8	
Consolidation	4	3		5	1		1	3	
Reticular pattern	0	0		2	0		16	0	
Mixed pattern	0	0		11	0		18	0	
CT Distribution			.133			.110			<.001
Subpleural	16	14		14	4		25	0	
Random	5	6		6	0		11	0	
Diffuse	2	9		13	9		13	11	

Except where otherwise indicated, data are mean ± SD (median and range) of CT score or number of CT scans. One patient showed no any abnormalities on CT scan within the first week.

Figures

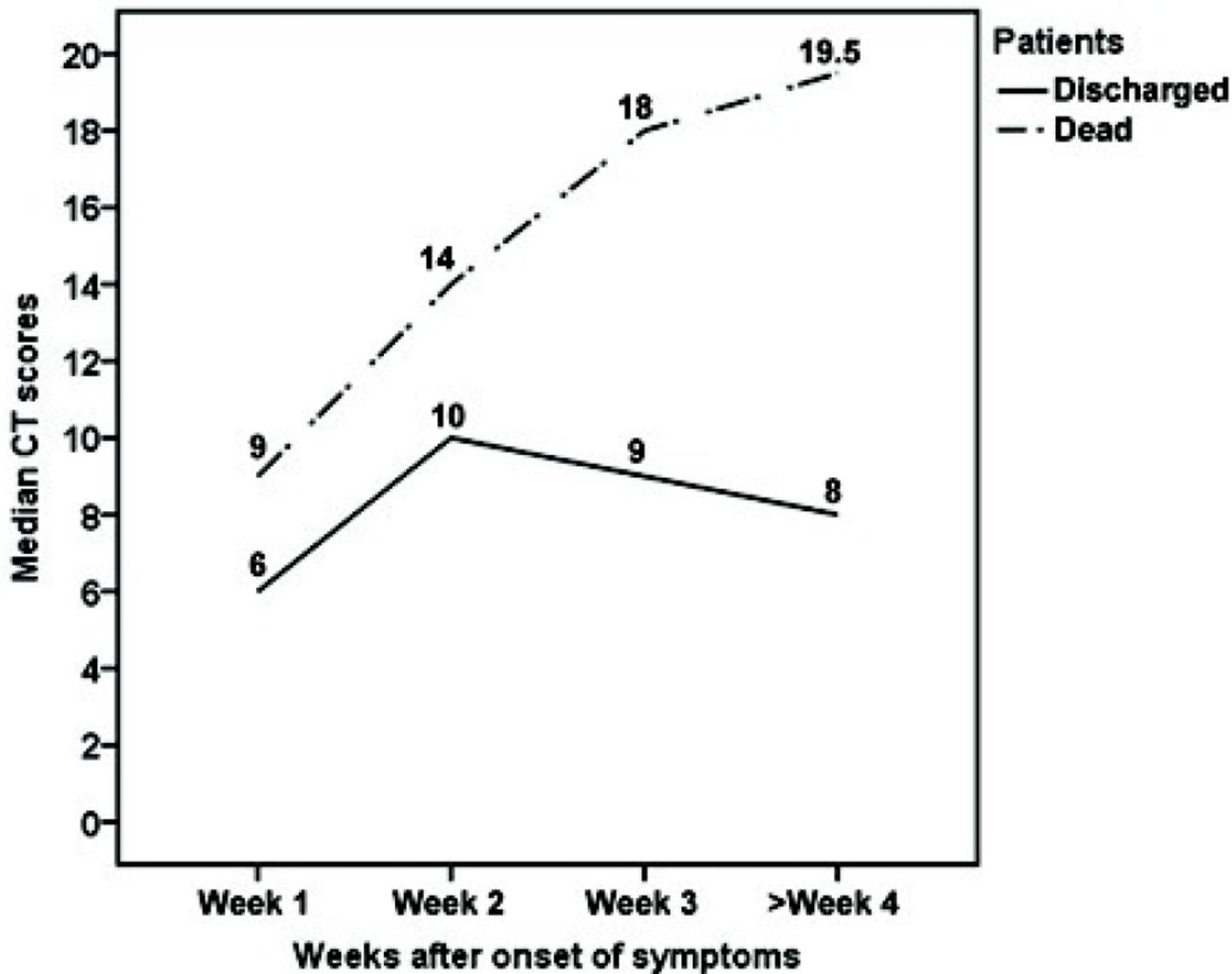


Figure 1

Line graph shows median CT scores in discharged and dead patients on CT scans at different time points after onset of symptoms.

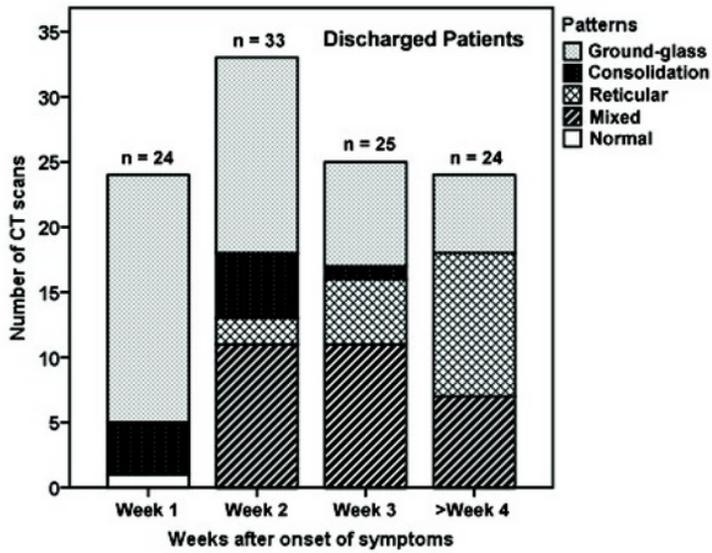


Fig. 2(a)

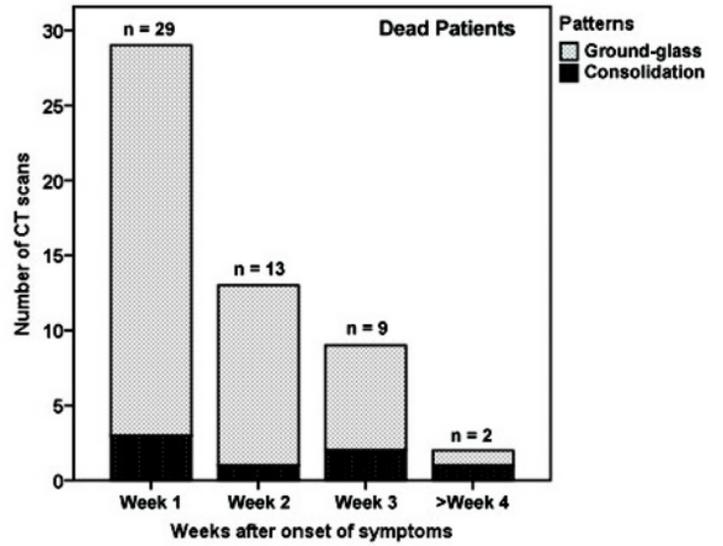


Fig. 2(b)

Figure 2

Stacked-bar graphs show distribution of various patterns of lung abnormalities in discharged (a) and dead patients (b) on CT scans at different time points after onset of symptoms.



Fig. 3(a)

Fig. 3(b)

Fig. 3(c)

Figure 3

56-year-old man with COVID-19 who was discharged after treatment. (a) Scan obtained on illness day 3 shows focal ground-glass opacities in right upper lobe, with a random distribution. (b) Scan obtained on illness day 8 shows that the ground-glass opacities were increased. (c) Scan obtained on illness day 18 shows development of a residual reticular pattern.



Figure 4

66-year-old man with COVID-19 who was discharged after treatment. (a) Scan obtained on illness day 4 shows multifocal ground-glass opacities in double lower lobes, with a subpleural distribution. (b) Scan

obtained on illness day 7 shows that the ground-glass opacities were increased, with superimposed interlobular and intralobular septal thickening and with diffuse distribution. (c) Scan obtained on illness day 12 shows that the ground-glass opacities were decreased, with superimposed irregular opacities. (d) Scan obtained on illness day 23 shows development of a mixed pattern.

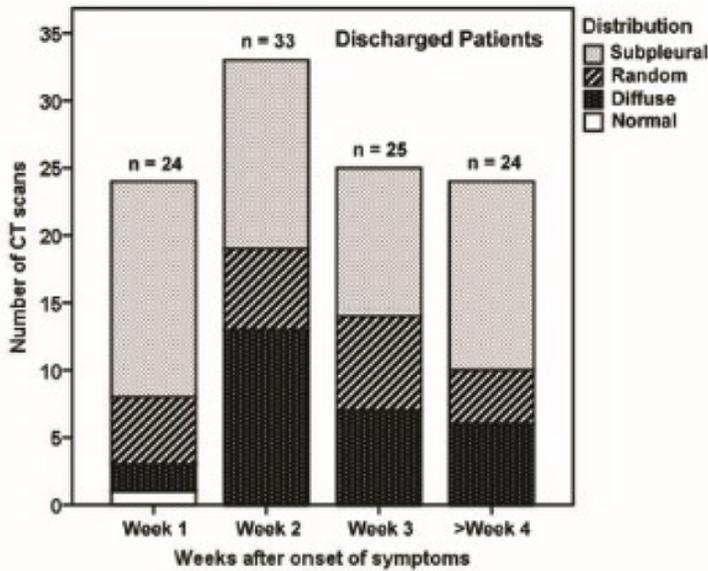


Fig. 5(a)

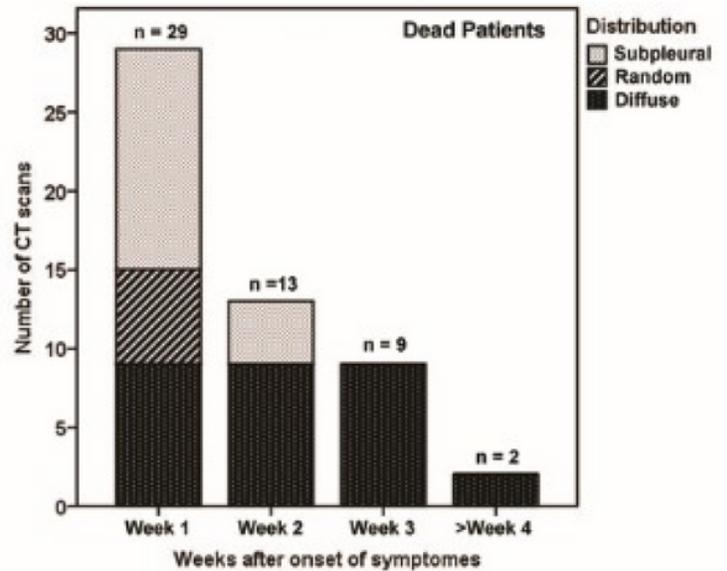


Fig. 5(b)

Figure 5

Stacked-bar graphs show distribution of various distribution of opacities in discharged (a) and dead patients (b) on CT scans at different time points after onset of symptoms.



Fig. 6(a)

Fig. 6(b)

Fig. 6(c)

Figure 6

56-year-old man with COVID-19 who died from the severe illness. (a) Scan obtained on illness day 6 shows focal ground-glass opacities in right upper lobe, with a subpleural distribution. (b) Scan obtained on illness day 14 shows that the extent of ground-glass opacities obviously increased, with involvement of multilobes. (c) Scan obtained on illness day 21 shows the transformation from ground-glass opacities to consolidation, with a pneumomediastinum.