Early fibroproliferative changes on high-resolution CT predict mortality in COVID-19 pneumonia patients with ARDS

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Abstract

Objectives: To investigate the chest high-resolution CT (HRCT) findings in coronavirus disease 2019 (COVID-19) pneumonia patients with acute respiratory distress syndrome (ARDS) and to evaluate its relationship with clinical outcome.

Materials and Methods In this retrospective study, seventy-nine COVID-19 patients with ARDS were recruited. Clinical data were extracted from electronic medical records and analyzed. HRCT scans, obtained within 3 days before clinical ARDS onset, were evaluated by three independent observers and graded into six findings according to the extent of fibroproliferation. Multivariable Cox proportional hazard regression analysis was used to assess the independent predictive value of the CT score and radiologically fibroproliferation. Patient survival was determined by Kaplan-Meier analysis.

Results: Compared with survivors, non-survivors showed higher of lung fibroproliferation, whereas there no significant differences in the area of increased attenuation without traction bronchiolectasis or bronchiectasis. A HRCT score <230 enabled prediction of survival with 73.5% sensitivity and 93.3% specificity (AUC= 0.9; 95% CI 0.831 to 0.968). Multivariate Cox proportional hazards model showed that the HRCT score is a significant independent risk factor for mortality (HR 13.007; 95% CI 3.935 to 43.001). Kaplan-Meier analysis revealed HRCT score ≥ 230 was associated with higher fatality rate. Organ injury occurred less frequently in patients with HRCT score <230 compared to those with HRCT score ≥ 230 .

Conclusion: Early pulmonary fibroproliferative changes in HRCT predicts increased mortality and susceptibility to organ injury in COVID-19 pneumonia patients with early ARDS.

Key Points

- Pulmonary fibroproliferation occurs in the early stage of ARDS due to COVID–19 pneumonia, manifested by the areas of traction bronchiolectasis or bronchiectasis within increased attenuation on HRCT scan.
- Compared with survivors, non-survivors showed higher percentage of lung fibroproliferation, whereas there no significant differences in the area of increased attenuation without traction bronchiolectasis or bronchiectasis.
- The extent of fibroproliferative changes on HRCT at diagnosis of ARDS due to COVID–19 pneumonia was an independent predictive factor for death and organ injury.

Introduction

Coronavirus disease 2019 (COVID–19) is caused by a new coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV–2), which emerged in China in December 2019[1; 2]. Until April 26, 2020, there were 209 countries and 2,804,796 confirmed COVID–19 cases globally, including over 193,710 deaths[3]. Most cases infected with SARS-CoV–2 have mild symptoms and good prognosis,

which clinical symptoms are similar to those of the regular human flu. However, similar to severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), COVID-19 could also develop to acute respiratory distress syndrome (ARDS), multiple organ failure or even death[4; 5].

Mortality from ARDS still remains above 50% despite use of low tidal volume ventilation and conservative fluid strategies[6]. ARDS is pathologically classified into three stages in which an initial inflammatory injury with protein-rich edema and hemorrhage is followed by fibroproliferation. The fibroproliferative phase of ARDS has traditionally been regarded as a late event[7]. However, previous study found fibroproliferation is initiated early in ARDS and could predict mortality in ARDS patients[8; 9]. In addition, Ichikado et al reported that fibroproliferation changes in HRCT could predict mortality in ARDS patients caused by pneumonia, aspiration, sepsis, etc[10]. Bilateral areas of ground-glass attenuation and airspace consolidation as well as involvement of multiple lung lobes were common chest CT finding in severe and critical COVID-19 pneumonia patients[11]. Recently, Zhang et al observed diffuse alveolar damage (DAD) and alveolar interstitial fibrosis in lung biopsy from a deceased COVID-19 pneumonia patient[12]. To our knowledge, no study has been performed to evaluate chest CT patterns, especially early fibroproliferative changes and their eventual prognosis value in COVID-19 pneumonia patients with ARDS. Thus, in this retrospective study, we evaluate the relation between extent of early fibroproliferative changes in HRCT and outcome in COVID-19 pneumonia with early ARDS.

Materials And Methods

Study design and participants

This study was approved by the Institutional Review Board (IRB) of Tongji Hospital, Tongji Medical College, Huazhong University of Science & Technology (IRB ID: TJ-C0200108). Patient consent in this retrospective study was waived by the Ethics Commission of the designated hospital for emerging infectious diseases. Patients were admitted from January 5 to February 16, 2020. The inclusion criteria were as follows: 1) real-time reverse transcription polymerase chain reaction (RT-PCR) assay detection of SARS-CoV-2 nucleic acid positive in throat swabs or nasopharyngeal swab; 2) diagnosis of ARDS using the Berlin definition[13] and interim guidance for clinical management of severe COVID-19 published by World Health Organization (WHO) [14]; 3) CT scan of the chest performed within 3 days before clinical ARDS onset. Exclusion criteria were as follows: pre-existing chronic pulmonary fibrosis and bronchiectasis were strictly excluded by history taking, documented from review of radiological reports and the initial CT imaging data on HRCT scans suggesting. Patients were followed up to April 17, 2020. Finally, seventy-nine patients were enrolled including 45 survivors and 34 non-survivors.

Data collection

Medical record information including demographic, clinical, laboratory, treatment and outcome data were collected and extracted by using data collection forms.

CT Examination

All patients underwent whole lung volumetric HRCT scanning of the chest within 0-3 days (median 1) before the onset of ARDS. CT was performed in the supine position during end-inspiration without intravenous contrast medium with various CT scanners using standard-dose chest CT protocols (GE Healthcare, Philips, or Toshiba Medical Systems). Imaging parameters were as follows: 80-120 kVp tube voltage, automated tube current modulation (60-300 mA), rotate time of 0.5 s, pitch of 0.984:1, slice thickness of 1.25 mm, reconstruction matrix: 512×512, with selected differences according to machine types.

HRCT assessment

All CT images were reviewed respectively by three radiologists (MX, QJH, HXG with 10, 10 and 20 years of clinical experience, respectively), who were unaware of patient outcome. Disagreements were resolved by consensus. Chest CT images assessed the presence and extent of areas for the following characteristics based on the recommendations in Fleischner Society terminologies and similar studies: ground-glass opacity (GGO)↯airspace consolidation, traction bronchiectasis, traction bronchiolectasis, and honeycombing[15; 16]. When bronchi were irregular in contour or larger than adjacent pulmonary artery, the bronchus within areas of parenchymal abnormality was recognized as traction bronchiectasis. Traction bronchiolectasis was identified by means of the presence of dilated bronchioles within areas with parenchymal abnormality. Honeycombing was defined as small, stacked 2-20 mm cysts in the subpleural lung without intervening lung parenchyma.

Scoring of HRCT Finding

The HRCT findings were graded on a scale of 1-6 based on the classification by Ichikado and colleagues[10; 16], which was correlating with previously described pathology: score of 1, normal attenuation; score of 2, ground-glass attenuation; score of 3, consolidation; score of 4, ground-glass attenuation with traction bronchiolectasis or bronchiectasis; score of 5, consolidation with traction bronchiolectasis or bronchiectasis; and score of 6, honeycombing. The extent of involvement of each abnormality was assessed independently for each of three zones of each lung: upper (above the carina), middle (below the carina and up to the inferior pulmonary vein), and lower (below the inferior pulmonary vein) zones. The extent of each abnormality was visually estimated to the nearest 10% of parenchymal involvement in each zone, and then was obtained by average the six zones extent. The abnormality score for each zone was obtained by multiplying the extent of involvement by each grading score (the score of 1-6) and then the total CT score was calculated by adding the averages for each index of the six zones.

Statistical analysis

All statistical analyses were performed using SPSS 20.0 software. The quantitative data of normal distribution were presented as mean±SD (minimum-maximum), and those of abnormal distribution were expressed as median (IQR). Normally distributed variables were compared by using the paired t-test; abnormal distributed variables were compared by using Mann-Whitney U test. The qualitative data were presented as percentage (%) and analyzed with Fisher's exact test or chi-square test. To analyze the CT

score as a predictor of survival of ARDS, receiver operator characteristic (ROC) curves and the corresponding area under the curve (AUC) was used to determine the cut-off value of the CT score yielding the highest sensitivity and specificity. Cox proportional hazards regression analysis was used to evaluate the influence of the CT score on survival and radiologically fibroproliferation while adjusting for other prognostic clinical factors, such as age, severity of illness and non-pulmonary organ dysfunctions that had been reported. Patient survival was determined by Kaplan-Meier analysis. For all statistical analyses, $p < 0.05$ was considered significant.

Results

Clinical and Laboratory Findings

Characteristics, laboratory findings, complications and treatment of patients were showed in Table 1. A total 79 COVID-19 patients with ARDS were enrolled in the research, including 45 survivors and 34 non-survivors. The average ages of the survivors and non-survivors were 64.0 and 66.5 years, respectively. The proportion of male patients in survivors was lower than in non-survivors (53% vs. 76%, $p = 0.035$). The mean $\text{SpO}_2/\text{FiO}_2$ ratio of survivors and non-survivors were 222.0 and 146.7. There were significant differences in ratio of $\text{qSOFA} \geq 1$ between two groups (67% vs. 91%, $p = 0.010$). No significant differences were observed between two groups in any comorbidity including chronic respiratory diseases, hypertension, coronary artery disease, diabetes mellitus, chronic kidney disease, chronic liver disease, cerebrovascular disease and tumor. At onset of ARDS, the deceased cases were more likely to have leukocytosis, lymphopenia and thrombocytopenia. In addition, non-survivors displayed elevated levels of blood urea nitrogen, blood creatinine, prothrombin time, D-dimer, cardiac troponin I, procalcitonin compared with survivor. All complications (respiratory failure, heart injury, liver injury and renal dysfunction) significantly differed between survivors and non-survivors. Most patients received antiviral (95%), antibacterial (97%) and glucocorticoid therapy (90%). With regard to respiratory support, higher percentages of non-survivors received high oxygen flow, noninvasive ventilation and invasive mechanical ventilation (Table1).

Table1. Characteristics, laboratory findings, complications and treatment in non-survivors and survivors

	Total (n=79)	Survivors (n=45)	Non-survivors (n=34)	<i>P</i> Value
Characteristics				
Age, yrs	65.0(57.0-71.0)	64.0(56.5-71.0)	66.5(57.0-73.0)	0.415
Males, n (%)	50(63%)	24(53%)	26(76%)	
SPO2/FiO2 ratio	177.4(134.4-231.7)	222.0(154.1-231.7)	146.7(90.0-225.6)	0.035
qSOFA $\geq$ 1	61	30	31	0.004
Any comorbidity				0.010
Chronic respiratory diseases, n (%)	10(13%)	5(11%)	5(15%)	0.738
Hypertension, n (%)	39(49%)	26(58%)	13(38%)	
Coronary artery disease, n (%)	7(9%)	2(4%)	5(14%)	0.085
Diabetes mellitus, n (%)	13(16%)	10(22%)	3(9%)	0.133
Chronic kidney disease, n (%)	3(4%)	0(0)	3(8%)	0.112
Chronic liver disease, n (%)	3(4%)	0(0)	3(9%)	0.076
Cerebrovascular disease	3(4%)	1(2%)	2(6%)	0.076
Tumor, n (%)	2(3%)	0(0)	2(6%)	0.574
				0.182
Laboratory findings				
White blood cell count, $\times 10^9/L$	7.7(5.4-12.1)	6.5(4.8-10.5)	8.9(5.5-13.7)	0.040
Lymphocyte count, $\times 10^9/L$	0.7(0.4-0.9)	0.7(0.5-1.0)	0.5(0.3-0.9)	0.033
Platelet count, $\times 10^9/L$	169.0(127.0-237.0)	194.0(146.0-290.0)	157.0(116.3-196.5)	0.010
Alanine aminotransferase, U/L	27.5(17.0-39.3)	29.0(17.5-39.0)	27.0(17.0-45.0)	0.708
Aspartate aminotransferase, U/L	36.0(25.0-50.5)	34.0(24.5-46.5)	41.0(29.5-67.0)	0.098
Total bilirubin, mmol/L	9.0(6.9-12.9)	9.2(7.1-12.6)	8.4(5.9-14.5)	0.840
Blood urea nitrogen, mmol/L	6.4(5.0-10.0)	5.3(4.1-6.7)	9.0(6.8-13.2)	<0.001
Blood creatinine, $\mu\text{mol/L}$	76.0(64.0-93.3)	68(60.5-86.5)	80.0(72.0-122.0)	0.015
Prothrombin time, s	14.6(13.9-16.1)	14.3(13.7-15.0)	15.5(14.1-17.9)	0.002
D-dimer, $\mu\text{g/mL}$	2.2(0.9-10.2)	2.0(0.7-2.8)	4.9(1.3-21.0)	0.010
Cardiac troponin I, pg/mL	11.2(6.2-32.0)	8.5(4.1-20.4)	23.1(8.4-146.7)	0.002
Procalcitonin, ng/mL	0.2(0.1-0.4)	0.1(0.1-0.2)	0.2(0.2-1.0)	<0.001
C-reactive protein, mg/L	82.5(47.5-130.3)	78.6(36.8-117.1)	89.4(55.4-143.0)	0.246

Complications				
Respiratory failure, n (%)	33(42%)	1(2%)	32(94%)	<0.001
Heart injury, n (%)	18(23%)	5(11%)	13(38%)	
Liver injury, n (%)	11(14%)	2(4%)	9(26%)	0.004
Renal dysfunction, n (%)	13(16%)	3(7%)	10(29%)	0.008
				0.007
Treatment				
Antibiotics, n (%)	77(97%)	43(96%)	34(100%)	0.503
Antivirus, n (%)	75(95%)	44(98%)	31(91%)	
Glucocorticoid therapy, n (%)	71(90%)	40(89%)	31(91%)	0.309
Intravenous immunoglobulin, n (%)	27(34%)	12(27%)	15(44%)	1.000
High oxygen flow, n (%)	15(19%)	4(9%)	11(32%)	0.105
Noninvasive ventilation, n (%)	36(46%)	8(18%)	28(82%)	0.008
Invasive mechanical ventilation, n (%)	13(16%)	2(4%)	11(32%)	<0.001
				0.001

Data are expressed as median (IQR) or n (%). Laboratory findings were collected at time of CT examination. *P* values comparing survivors and Non-survivors are from student t test, Mann-Whitney U test, χ^2 or Fisher's exact test appropriately.

HRCT findings for survivors and non-survivors

The extent of CT finding in survivors and non-survivors is summarized in Table 2. The average percent lung affected was 75.93% in non-survivors compared with 59.22% in survivors ($p < 0.001$). The area of traction bronchiolectasis or bronchiectasis and honeycombing, was indicative of radiologically fibroproliferation. Similarly, the area of traction bronchiolectasis or bronchiectasis significantly smaller in survivors than in non-survivors (Figure 1 and Figure 2), whereas the extent of increased attenuation without traction bronchiolectasis or bronchiectasis did not differ significantly between survivors and non-survivors (Table 2). Multivariate Cox proportional hazards model with adjustment for demographic characteristics, severity of illness, non-pulmonary organ dysfunctions and traction bronchiolectasis or bronchiectasis at diagnosis, the total area of the traction bronchiolectasis or bronchiectasis remained an independent risk factor for mortality (HR 5.426; 95% CI 1.307 to 22.526; $p = 0.020$) (Table 3).

Table 2 Extent of each high-resolution CT finding in survivors and non-survivors of ARDS with COVID-19

CT finding	Survivors (n=45)	Non-survivors (n=34)	p Value
GGO without traction bronchiolectasis or bronchiectasis	34.29(14.28)	32.89 (17.69)	0.697
Consolidation without traction bronchiolectasis or bronchiectasis	20(12.5-17.08)	16.67(7.92-25.42)	0.168
Total area without traction bronchiolectasis or bronchiectasis	54.48(13.2)	50.74(19.52)	0.312
GGO with traction bronchiectasis or traction bronchiolectasis	0(0-2.5)	12.5(2.92-17.08)	<0.001
Consolidation with traction bronchiolectasis or bronchiectasis	0(0-.4.17)	10.83[4.12-18.75]	<0.001
Total area with traction bronchiolectasis or bronchiectasis	1.67(0-6.67)	21.67 [13.33-36.67]	<0.001

Data are expressed as median (IQR). *P* values comparing survivors and non-survivors are by student t test or Mann-Whitney U test appropriately.

Table 3. Multivariate Cox regression analysis of HRCT findings, HRCT score and clinical characteristics associated with mortality in ARDS patients with COVID-19			
NO	Variable	<i>P</i> Value	HR (95% CI)
1	HRCT score $\geq$ 230	<0.001	13.01 (3.94-43.00)
	Prothrombin time $\geq$ 16s	0.028	4.76(1.18-19.12)
2	Existence of GGO with traction bronchiectasis or traction bronchiolectasis	0.032	3.36(1.11-10.20)
	Existence of consolidation with traction bronchiectasis or traction bronchiolectasis	0.006	4.91(1.58-15.32)
	Prothrombin time $\geq$ 16s	0.021	4.40(1.25-15.52)
3	Total existence of traction bronchiolectasis or bronchiectasis	0.02	5.43(1.31-22.53)
	Prothrombin time $\geq$ 16s	0.037	3.40(1.07-10.76)

Cox proportional hazard regression models were applied to determine the potential risk factors associated with mortality, with the hazards ratio (HR) and 95% confidence interval(95%CI) being reported.

Prognostic value of the HRCT score

The overall HRCT score of survivors (mean, 191.93 $\pm$ 29.47; range, 146.67-273.33) was significantly lower than that of non-survivors (mean, 255.78 $\pm$ 40.13; range, 171.67-331.67, *p* <0.001). Construction of a ROC curve yielded an optimal cut-off value of a HRCT score of 230 for prediction of survival, with 73.5% sensitivity and 93.3% specificity (AUC, 0.9; 95% CI 0.831 to 0.968) (Figure 3). Multivariate Cox proportional hazards model analysis, with adjustment for demographic characteristics, general severity,

underlying disease condition, and non-pulmonary organ dysfunctions, revealed that the HRCT score remained an independent risk factor for mortality (HR 13.007; 95% CI 3.935 to 43.001; $p < 0.0001$) (Table 3). Kaplan-Meier analysis revealed higher CT score was associated with higher fatality rate (Figure 4). However, the overall HRCT scores in 9 non-survivors are less than 230. The non-survivors divided into two groups according to the HRCT score of 230. The clinical and laboratory findings are compared between the two non-survivor groups. The non-survivors with a lower CT score had the decreased lymphocyte count compared with the non-survivors with a higher CT score ($0.9 \times 10^9/L$ vs $0.4 \times 10^9/L$, $p = 0.008$, supplement Table).

Relation between the HRCT score and the number of organ failure

Organ injury occurred less frequently in patients with HRCT score < 230 compared to those with HRCT score ≥ 230 (Table4).

Table 4 Comparison of organ injury between the between higher and lower CT score patients

	Total (n=79)	CT score ≥ 230 (n=31)	CT score < 230 (n=48)	<i>P</i> value
Respiratory failure	33(42%)	23(74%)	10(21%)	< 0.001
Heart injury	18(23%)	10(32%)	8(17%)	0.107
Liver injury	11(14%)	8(26%)	3(6%)	0.014
Renal dysfunction	13(16%)	7(23%)	6(13%)	0.238

Data are expressed as n (%). *P* values comparing higher and lower CT score are from χ^2 or Fisher’s exact test appropriately.

Discussion

In this retrospective cohort study, we comprehensively evaluated and analyzed the HRCT imaging characteristics of 79 COVID-19 pneumonia patients with ARDS. We found that pulmonary fibroproliferation occurs in the early stage of ARDS due to COVID-19 pneumonia, manifested by the areas of traction bronchiolectasis or bronchiectasis within increased attenuation on HRCT scan. Furthermore, we demonstrated the extent of fibroproliferative changes on HRCT and a higher CT score at diagnosis of ARDS due to COVID-19 pneumonia was an independent predictive factor for death. Our observation suggested pulmonary fibroproliferation at the early stage of COVID-19 ARDS is an important determinant of outcome. To our knowledge, it is the first study in which complementary fibroproliferative changes on HRCT as higher HRCT score and to evaluate whether fibroproliferation on HRCT in COVID-19 pneumonia patients with ARDS predict mortality.

Traditionally, ARDS is divided into three stages in which an initial inflammatory phase is followed by fibroproliferation[7]. Interesting, fibroproliferative pathways are activated early in ARDS, demonstrated by increased fibrotic marker in bronchoalveolar lavage fluid (BALF) [9]. HRCT scans of acute interstitial

pneumonia showed more extensive areas of increased attenuation associated with traction bronchiectasis, which corresponded to fibroproliferative phases of DAD[17]. In the present study, traction bronchiolectasis or bronchiectasis within areas of increased attenuation, suggesting radiologically fibroproliferation, was already detectable on HRCT scans obtained within three days (median 1 day) before the ARDS diagnosis in 49 patients (62.03%). Some investigations have shown that the typical findings of chest CT images in COVID pneumonia patients are bilateral multiple lobular and subsegmental areas of consolidation and ground-glass opacity, most commonly in the peripheral, subpleural area, or distributed diffusively[18-20]. In addition, Li et al reported that HRCT findings associated with severe and critical COVID-19 pneumonia were bilateral areas of ground-glass attenuation and consolidation in multiple lung lobes. However, this new radiological evidence provided an innovative new method compared with previous investigations. Nevertheless, our study together with previous observations, suggests an alternative to traditional models of the lung injury response, whereby inflammatory and repair mechanisms occur in parallel rather than in series.

Several retrospective cohort studies have clarified clinical risk factors for death in patients with COVID-19 pneumonia[21-24]. However, as we known, few studies have focused on the chest CT imaging appearance and COVID-19 pneumonia mortality. Our data suggested extensive fibroproliferative changes on HRCT in the early stage were associated with ARDS mortality in patients with COVID-19 pneumonia. Similarly, Ichikado et al. showed higher mortality in patients with areas of increased lung attenuation and varicoid bronchiectasis in the setting of clinically diagnosed ARDS caused by diverse diseases[10; 16]. These findings suggest that fibroproliferative changes on HRCT could be used for the assessment of direct and indirect ARDS severity.

The potential mechanisms by which fibroproliferative changes on HRCT might lead to poorer outcome are unclear and are related to pathological process. ARDS patients, who were in the acute exudative phase histologically had a better prognosis than did those who were in the fibroproliferative phase which confirmed by lung biopsy[9]. On the basis of our evaluation of 79 COVID-19 pneumonia ARDS patients, some patients with fibroproliferative changes would be diagnosed with early ARDS if only the parameter of time elapsed since onset of ARDS. Our present data suggest the discrepancy between “clinically” early phase of ARDS and “pathologically” early phase of ARDS. However, it is difficult to distinguish the transition from exudative to fibroproliferative these pathological phases without a lung biopsy in ARDS patients. Chest CT scan could be useful to distinguish these pathological phases and for the early diagnosis of lung injury.

A definitive role of corticosteroids in the treatment of ARDS is not established, however, corticosteroids treatment started after the onset of ARDS was suggested[25]. A recent study showed corticosteroid treatment may be beneficial for COVID-19 pneumonia who have developed ARDS on disease progression[26]. In our study, COVID-19 ARDS patients with limited lung fibroproliferation benefited from corticosteroid treatment. Our results confirmed the hypothesis that the early use of corticosteroid in ARDS patients may improve mortality. Prospective evaluation of HRCT findings in ARDS patients not only has

its prognostic implications, but also helps therapeutic implications based on the extent of fibroproliferative changes.

In the present study, patients with extensive fibroproliferation shown as higher HRCT score predicts increased mortality with 93.3% specificity and 73.5% sensitivity. However, we found that the overall HRCT score in 9 non-survivors was less than 230. We further compared the clinical and laboratory findings between the two non-survivor groups according to the HRCT score of 230. The non-survivors with a lower CT score had the increased lymphocyte count compared with the non-survivors with a higher CT score. Our findings support that suggesting there are subphenotypes of COVID-19 ARDS that affect clinical outcomes.

Abbreviations

HRCT: high resolution computed tomograph

ARDS: acute respiratory distress syndrome

COVID-19: Corona Virus disease 2019

SARS-Cov-2: Severe acute respiratory syndrome coronavirus 2

ROC: receiver operator characteristic curves

AUC: area under the curve

Declarations

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Author contributions

ZLZ and MX contributed equally to this paper. JZ and QJH designed the study, had full access to all data in the study, and take responsibility for the integrity and accuracy of the data analysis. JMZ, YWL, HXG and LMX contributed to patient recruitment, data collection, data analysis, data interpretation and literature search. ZLZ and MX drafted the manuscript. JZ and QJH final revised the manuscript. All authors contributed to data acquisition, data analysis, or data interpretation, and all reviewed and approved the final version of the manuscript.

Competing interests

The authors declare no competing interests.

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Figures

Figure 1

HRCT findings in a 55-year-old man with ARDS due to COVID-19 pneumonia who did not survive. HRCT scan shows bilateral areas of extensive ground-glass opacities associated with traction bronchiolectasis and bronchiectasis (arrows) and small consolidation in most lobes. (A) (B) axial images, (C) (D) coronal images.

Figure 2

HRCT findings in 40-year-old man with ARDS due to COVID-19 pneumonia who survived. HRCT scan shows extensive ground-glass opacity predominantly and patchy consolidation without traction bronchiolectasis or bronchiectasis (arrows) involved multiple lung lobes. (A) (B) axial images, (C) (D) coronal images.

Figure 3

ROC curve of the CT score identified the optimal cut-off value of 230 for prediction of survival.

Figure 4

Kaplan-Meier analysis showed a significant difference for the survival ratio for a CT score cut-off of 230.

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