Original Article

Ultrasound and clinical characteristics of patients with COVID-19 pneumonia: a cross-sectional study

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Background: This study aimed to demonstrate the clinical and lung ultrasound (LUS) characteristics at hospital admission related to the severity and survival in patients with coronavirus disease 2019 (COVID-19) pneumonia.

Methods: This was a retrospective cross-sectional, single-center study. The data on 36 COVID-19 pneumonia cases between 22 January 2020 and 3 March 2020, were retrospectively collected. According to the moderate or severe clinical status, the baseline clinical and detailed LUS characteristics at admission were evaluated and compared. Analyses of demographic, laboratory, LUS, and prognostic data of the two groups were performed to determine the risk of severe illness.

Results: Among 36 patients, 29 were severe cases, and 7 were moderate cases. The mortality was 13.9%, and 31 patients were discharged. Compared with moderate patients, severe patients showed higher level of blood urea nitrogen (BUN) (5.3 *vs.* 3.8 mmol/L, P=0.036), albumin (43.1 *vs.* 36.4 U/L, P=0.001), creatine kinase-MB (CK-MB) (9.0 *vs.* 7.0 U/L, P=0.011), N-terminal pro-brain natriuretic peptide (NT-proBNP) (68.7 *vs.* 8.2 pg/mL, P=0.006), C-reactive protein (CRP) (17.6 *vs.* 1.7 mg/L, P=0.008), lactate dehydrogenase (LDH) (198.0 *vs.* 139.0 U/L, P=0.026). Compared to the survivors, the non-survivors had lower lymphocyte counts (0.8×10^9/L *vs.* 1.5×10^9/L, P=0.020), lower albumin (31.1 *vs.* 38.9 g/L, P=0.007), and higher levels of BUN (9.4 *vs.* 5.0 mmol/L, P=0.020), total bilirubin (TBIL) (28.0 *vs.* 10.2 μmol/L, P=0.019), direct bilirubin (DBIL) (14.0 *vs.* 3.2 μmol/L, P=0.012), CRP (86.2 *vs.* 4.6 mg/L, P<0.001), white blood cell (WBC) count (10.6×10^9/L *vs.* 6.0×10^9/L, P=0.030). Regarding ultrasound characteristics, the LUS score on admission was significantly higher in severe/critical patients (9 *vs.* 2 scores, P<0.001), while the collapsibility index of IVC (0.4 *vs.* 0.6%, P<0.001) were lower in severe/critical cases.

Conclusions: Severe/critical COVID-19 pneumonia demonstrated higher BUN, albumin, CK-MB, NT-proBNP, CRP, and LDH level than moderate cases. LUS score, which is simple and handily accessible, could help in the evaluation of the severity and prognosis of COVID-19 pneumonia. LUS imaging features require attentive inspection and timely intervention to prevent the deterioration of COVID-19 pneumonia.

Keywords: Coronavirus disease 2019 (COVID-19); lung ultrasound (LUS); prognosis; pneumonia

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Introduction

Coronavirus disease 2019 (COVID-19) is caused by infection of severe acute respiratory syndrome coronavirus 2 (1,2). Early diagnosis and timely intervention can prevent the disease from developing into a severe/critical state (1). The diagnosis of COVID-19 relied on real-time fluorescence quantitative reverse transcription polymerase chain reaction (RT-PCR) to detect viral nucleic acid and chest computed tomography (CT) scan (3,4). However, disinfection after using the CT machine will delay the care of other patients who require CT examination (5). Lung ultrasound (LUS) examination is significant in the early screening of suspected cases because it can be performed without conveying the patient from the intensive care unit (ICU) or ward (6,7). LUS reduces the risk of viral disease among medical staff and gets an immediate result (6,7). At the same time, LUS, as a useful tool to assess lung pathophysiology, also has practical value in evaluating changes in lung ventilation (8,9). However, there is little research reported on the impact of the detailed characteristics of LUS on the severity of COVID-19.

Highlight box

Key findings

- Severe/critical COVID-19 pneumonia demonstrated higher BUN, albumin, CK-MB, NT-proBNP, CRP, and LDH level than moderate cases. LUS score, which is simple and handily accessible, could help in the evaluation of the severity and prognosis of COVID-19 pneumonia.

What is known and what is new?

- LUS was effectively used to diagnose acute respiratory distress syndrome, monitor the response to treatment, and detect bacterial superinfection, as well as COVID-19 pneumonia.
- There is a paucity of evidence on assessing the association between LUS characteristics and the severity of COVID-19.

What is the implication, and what should change now?

- Studying the clinical and ultrasound characteristics of COVID-19 help understand the features of critical conditions and promote evaluation and therapeutical decisions.

This study aimed to demonstrate the clinical and bedside LUS features at hospital admission related to the severity and survival of patients with COVID-19 pneumonia. We present the following article in accordance with the STROBE reporting checklist (available at https://aoi.amegroups.com/article/view/10.21037/aoi-22-4/rc).

Methods

Data collection

It was a single-center, retrospective, cross-sectional study. Between 22 January 2020 and 3 March 2020, consecutive patients confirmed COVID-19 pneumonia established by the World Health Organization interim guidance (10) were included in the First People's Hospital of Jingzhou, China. COVID-19 infection was diagnosed via RT-PCR using the throat-swab specimens. Patients with missing data of LUS data or major laboratory tests were excluded. The major laboratory test consisted of a complete blood count, blood urea nitrogen (BUN), albumin, serum creatinine, prothrombin time, activated partial thromboplastin time (APTT), D-dimer, lactate dehydrogenase (LDH), immunoglobulin M (IgM) antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), immunoglobulin G (IgG) antibodies against SARS-CoV-2, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), direct bilirubin (DBIL). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of the First People's Hospital of Jingzhou and Guangdong Provincial People's Hospital (No. 2020-056), and written informed consent was waived.

Clinical and ultrasonic evaluation

According to the guideline on the management of COVID-19 (6th edition) issued by the National Health Commission (11) and the Proposal for use of LUS (12,13), the severity was classified (*Table 1*), and point of care LUS was scanned systematically from the front to the

Table 1 Classification of the severity of COVID-19

Classification	Condition
Severe case	Dyspnea with a respiratory rate of ≥30 times/minute
	Saturation ≤93%
	PaO_2/FiO_2 ≤300 mmHg
Critical case	Respiratory failure requiring mechanical ventilation
	Shock
	Co-existing multiple organ failure requiring close monitoring in the ICU

Severe/critical case was diagnosed if one of the corresponding conditions was present; COVID-19, coronavirus disease 2019; PaO_2, arterial partial pressure of oxygen; FiO_2, fractional inspiratory oxygen concentration; ICU, intensive care unit.

backside of each hemithorax with the patient in the sitting position (14). Patients were admitted to ICU or isolated wards at the discretion of the physicians according to the severity of the disease. Baseline demographic and clinical information, ultrasound features, and survival status were recorded. Disease scoring systems were calculated by the physicians or nurses, including acute physiology and chronic health evaluation II (APACHE II) score (13), the sequential organ failure assessment (SOFA) score (15), and the Glasgow Coma Scale (GCS). The scores represent the worst scores during the first 24 hours after ICU admission or hospitalization.

LUS was performed using a 2- to 4-MHz convex probe by trained physicians. Five regions of interest on each side were investigated according to the BLUE-Protocol (16), including the upper and lower BLUE-point in the anterior/posterior zone and posterolateral alveolar and/or pleural syndrome (PLAPS) point. Points were allocated according to the worst ultrasound pattern observed: (I) normal aeration (0 points): horizontal A-lines (or no more than two B-lines); (II) moderate loss of aeration (1 point): multiple B lines (either regularly spaced, or irregularly and even coalescent, but only visible in a limited area of the intercostal space); (III) severe loss of aeration (2 points): multiple coalescent B lines in prevalent areas of the intercostal spaces and observed in one or several intercostal spaces; and (IV) complete loss of aeration (3 points): lung consolidation with or without air bronchograms (*Figure 1*). The abnormal findings in each LUS scan were summed up with a minimum score of zero and a maximum score of 30 (17,18).

Statistical analysis

Data were analyzed using SPSS 21.0 for Windows (IBM Corp. Armonk, NY, USA). The continuous values were presented as the means ± standard deviation or median (quartiles) and were compared using independent *t*-tests or the Mann-Whitney test, according to their distribution. The categorical variables were presented as counts (percentages) and were compared using the chi-square test or Fisher exact test. A two-sided P value <0.05 was considered statistically significant.

Results

Baseline characteristics

Among 146 patients, a total of 36 patients with ultrasound data were finally analyzed. Demographics, clinical, and laboratory findings were reported in *Table 2*. Twenty-nine (80.6%) patients were severe/critical cases, and 7 (19.4%) were moderate cases. The median age was 65.1 years, ranging from 21 to 89 years. Compared with moderate patients, severe patients showed lower levels of creatine kinase (CK) (22.0 *vs.* 60.0 U/L, P=0.018), but a higher level of BUN (5.3 *vs.* 3.8 mmol/L, P=0.036), albumin (43.1 *vs.* 36.4 U/L, P=0.001), creatine kinase-MB (CK-MB) (9.0 *vs.* 7.0 U/L, P=0.011), N-terminal pro-brain natriuretic peptide (NT-proBNP) (68.7 *vs.* 8.2 pg/mL, P=0.006), C-reactive protein (CRP) (17.6 *vs.* 1.7 mg/L, P=0.008), LDH (198.0 *vs.* 139.0 U/L, P=0.026), and higher SOFA scores (2.0 *vs.* 0.0 points, P=0.001). There was no significant difference in age, gender, low IgM, IgG, ALT, AST, TBIL, DBIL, white blood cell (WBC), procalcitonin (PCT), and monocyte count between severe and moderate patients (P>0.05).

Ultrasound findings in the severe/critical group and moderate group

Ultrasound characteristics were described in *Table 3*. Echocardiography and LUS examination for 36 patients were performed after admission. No significant difference was found between the severe group and the moderate group, including the left ventricular ejection fraction (LVEF), tricuspid annular plane systolic excursion (TAPSE), and mitral annular plane systolic excursion (MAPSE) (P>0.05). The inferior vena cava (IVC) value on inhalation (10.6 *vs.* 5.1 mm, P<0.001) in severe/critical patients was higher than those of the moderate group. The LUS score in the severe/critical group was also higher than those in

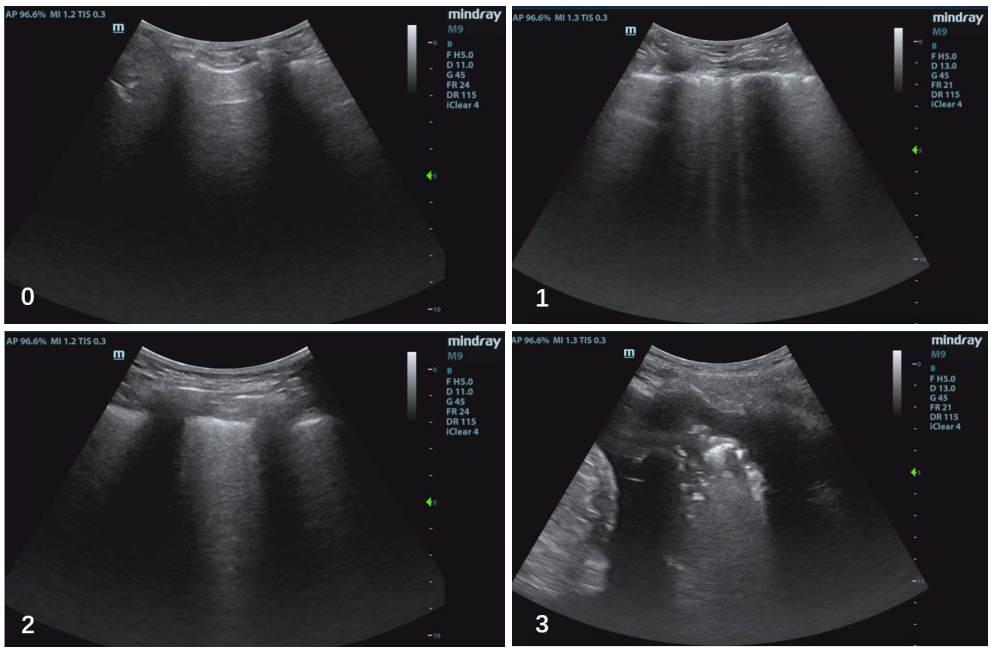

Figure 1 Examples of ultrasonic images with the corresponding pattern of lung aeration and lung ultrasound score (0, 1, 2, and 3 points). AP, acoustical power; MI, mechanical index; TIS, thermal index of soft tissue; m, marker; B, B-mode; F H 5.0, harmonic wave with a frequency of 5 MHz; D, penetration depth (cm); G, gain; FR, frame rate (frames per second); DR, dynamic range; iClear, Mindray's unique image enhancement feature, where 4 represents the 4th gear.

the moderate group (9.0 *vs.* 2.0 points, P<0.001). Each acquisition point of LUS was scored. The LUS score of severe/critical group patients in the posterior blue point (3.0 *vs.* 1.0 points, P=0.040) and diaphragmatic point (4.0 *vs.* 0.0 points, P=0.001) were significantly higher than those of the moderate group. The incidences of the alveolar-interstitial syndrome (48.3% *vs.* 0.0%, P=0.029), lung consolidations (96.6% *vs.* 57.1%, P=0.003), and lung shred signs (89.7% *vs.* 42.9%, P=0.009) in severe/critical patients were higher than those of the moderate patients. The consolidated locations were different between the two groups.

Clinical characteristics of survivor and non-survivor group

As shown in *Table 4*, 31 patients recovered and were discharged, while 5 patients died in the hospital. The lethal cases were all diagnosed with severe (2 cases) and critical (3 cases) illnesses. The survivors and non-survivors had no significant differences in gender or age (P>0.05). The APACHE II (25.0 *vs.* 6.0 points, P<0.001) and SOFA scores (11.0 *vs.* 1.0 points, P<0.001) of non-survivors were significantly higher than survivors. WBC (10.6×10^9/L *vs.* 6.0×10^9/L, P=0.030), BUN (9.4 *vs.* 5.0 mmol/L, P=0.020), TBIL (28.0 *vs.* 10.2 μmol/L, P=0.019), DBIL (14.0 *vs.* 3.2 μmol/L, P=0.012), and CRP levels (86.2 *vs.* 4.6 mg/L, P<0.001) in the non-survivors' group were higher than those in the survivors' group. Compared with the survivors, the non-survivors had a lower lymphocyte count (0.8 *vs.* 1.5×10^9/L, P=0.020) and albumin (31.1 *vs.* 38.9 g/L, P=0.007) on admission. No significant differences in IgM, IgG, AST, PCT, APTT, and monocyte count were found between the two groups (P>0.05).

Ultrasound findings are summarized in *Table 5*. The LUS score of the mortality was significantly higher than that of the survival group (17.0 *vs.* 7.0 points, P=0.003). We scored each acquisition point of LUS. The results showed that the scores of the upper blue point (3.0 *vs.* 0.0 points, P=0.004), lower blue point (4.0 *vs.* 0.0 points, P=0.019), and diaphragmatic point (3.0 *vs.* 0.0 points, P=0.032) of the non-survivors were significantly higher than those of the survival group. The incidences of the alveolar-interstitial syndrome (100.0% *vs.* 29.0%, P=0.005) and pleural effusion (80.0% *vs.* 19.4%, P=0.015) in non-survivors were significantly higher than those of the survivors. The diameter of the IVC value on inhalation in non-survivors was higher than that in surviving patients (10.6 *vs.* 6.4 mm, P=0.001). However,

Table 2 Demographics, clinical presentations in severe/critical group and moderate group

Parameters	Total (n=36)	Severe/critical group (n=29)	Moderate group (n=7)	P value
Age (years)	64.3±15.2	67.0±14.0	54.0±19.0	0.138
Gender				
Male	20 (55.6)	16 (55.2)	4 (57.1)	0.631
Female	16 (44.4)	13 (44.8)	3 (42.9)	
Oxygen device				0.011
Without oxygenation therapy	3 (8.3)	0 (0.0)	3 (42.9)	
Nasal oxygen	27 (75.0)	23 (79.3)	4 (57.1)	
Mask oxygen	1 (2.8)	1 (3.4)	0 (0.0)	
Mechanical ventilation	5 (13.9)	5 (17.2)	0 (0.0)	
APACHE II score	6.0 (4.3–8.0)	6.0 (5.0–8.0)	4.0 (0.0–6.0)	0.440
SOFA score	1.0 (0.0–2.8)	2.0 (1.0–4.0)	0.0 (0.0–0.0)	0.001
GCS	15.0 (0.0–2.8)	15.0 (15.0–15.0)	15.0 (15.0–15.0)	0.345
WBC ($\times10^9$/L)	6.1 (5.0–8.0)	6.1 (5.0–9.6)	6.0 (4.4–7.1)	0.584
Lymphocytes ($\times10^9$/L)	1.4±0.6	1.3±0.6	1.8±0.4	0.050
Monocyte count ($\times10^9$/L)	0.4 (0.3–0.5)	0.4 (0.3±0.5)	0.3 (0.2±0.9)	0.531
PCT (ng/mL)	1.0 (0.3–5.2)	1.2 (0.3–6.4)	0.59 (0.3–3.4)	0.584
CRP (mg/L)	6.4 (2.1–4.3)	17.6 (2.6–72.8)	1.7 (0.5–3.8)	0.008
BUN (mmol/L)	5.1 (3.9–6.2)	5.3 (4.2–6.5)	3.8 (3.0–5.0)	0.036
Creatinine clearance (μmol/L)	58.0 (45.7–74.8)	61.1±22.5	65.8±17.3	0.606
ALT (U/L)	27.0 (14.0–36.8)	27.0 (14.0–36.5)	23.0 (12.0–37.0)	0.938
AST (U/L)	26.0 (22.0–33.0)	25.0 (22.0–33.0)	27.0 (18.0–29.0)	0.696
TBIL (μmol/L)	10.5 (8.9–17.4)	10.6 (8.2–18.3)	9.6 (9.4–13.9)	0.584
DBIL (μmol/L)	3.7 (2.4–6.7)	3.8 (2.5–8.0)	2.8 (2.3–5.5)	0.505
Albumin (g/L)	37.0 (33.0–40.9)	43.1 (42.1–43.7)	36.4 (32.4–39.5)	0.001
Prothrombin time (s)	10.5 (10.0–11.5)	10.5 (9.6–11.6)	10.3 (10.0–11.5)	0.845
APTT (s)	25.5 (22.8–31.1)	27.2±6.6	25.6±4.4	0.543
D-dimer (mg/L)	3.7 (0.5–6.0)	3.4 (0.7–6.1)	2.1 (0.2–6.0)	0.131
Troponin T (U/L)	18.7 (7.4–37.2)	13.3 (6.0–34.1)	29.0 (24.7–104.5)	0.086
CK (U/L)	39.0 (18.3–59.8)	22.0 (15.0–53.0)	60.0 (48.0–76.0)	0.018
CK-MB (U/L)	9.0 (7.0–11.8)	9.0 (7.5–12.0)	7.0 (6.0–8.0)	0.011
NT-proBNP (pg/mL)	60.1 (11.4–123.3)	68.7 (27.9–128.8)	8.2 (6.8–11.2)	0.006
LDH (U/L)	189.0 (162.3–238.0)	198.0 (171.5–250.0)	139.0 (124.0–189.0)	0.026
IgM* (g/L)	25.9 (14.2–105.7)	25.6 (12.4–107.9)	49.4 (21.3–108.9)	0.554
IgG* (g/L)	174.4 (137.5–207.5)	174.3 (139.9–204.3)	57.9 (116.6–229.0)	0.738

The continuous values were presented as the means ± standard deviation or median (quartiles) according to their distribution; the categorical variables were presented as counts (percentages). *, antibodies against SARS-CoV-2. APACHE II, acute physiology and chronic health evaluation II; SOFA, sequential organ failure assessment; GCS, Glasgow Coma Scale; WBC, white blood cell; PCT, procalcitonin; CRP, C-reactive protein; BUN, blood urea nitrogen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; DBIL, direct bilirubin; APTT, activated partial thromboplastin time; CK, creatine kinase; CK-MB, creatine kinase-MB; NT-proBNP, N-terminal pro-brain natriuretic peptide; LDH, lactate dehydrogenase; IgM, immunoglobulin M; IgG, immunoglobulin G; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 3 Ultrasound characteristics of patients with COVID-19

Parameters	Total (n=36)	Severe/critical group (n=29)	Moderate group (n=7)	P value
LUS findings				
LUS score	8.0 (4.0–13.0)	9.0 (6.0–15.0)	2.0 (0.0–4.0)	<0.001
Upper blue point score	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.410
Lower blue point score	0.0 (0.0–1.0)	0.0 (0.0–3.0)	0.0 (0.0–0.0)	0.178
Diaphragmatic point score	3.0 (1.0–6.0)	4.0 (3.0–6.0)	0.0 (0.0–3.0)	0.001
Posterior blue points score	3.0 (1.0–6.0)	3.0 (1.0–6.0)	1.0 (0.0–3.0)	0.04
Alveolar-interstitial syndrome	14 (38.9)	14 (48.3)	0 (0.0)	0.029
Pleural effusion	10 (27.8)	10 (34.5)	0 (0.0)	0.079
Lung consolidations	32 (88.9)	28 (96.6)	3 (42.9)	0.003
Shred signs	29 (80.6)	26 (89.7)	3 (42.9)	0.009
Tissue-like sign	4 (11.1)	4 (13.8)	0 (0.0)	0.566
Where the lung consolidations appeared				0.003
No lung consolidations	5 (13.9)	1 (3.4)	4 (57.1)	
Upper blue point	2 (5.6)	2 (6.9)	0 (0.0)	
Lower blue point	5 (13.9)	5 (17.2)	0 (0.0)	
Diaphragmatic point	2 (5.6)	2 (6.9)	0 (0.0)	
Posterior blue points	16 (44.4)	14 (48.3)	2 (28.6)	
PLAPS points	9 (25.0)	8 (27.6)	1 (14.3)	
Echocardiography findings				
LVEF (%)	55.0±8.0	54.0±8.0	56.0±3.0	0.492
IVCe (mm)	16.2±3.8	16.8±3.6	13.8±4.2	0.064
IVCi (mm)	9.4±5.0	10.6±5.0	5.1±1.0	<0.001
cIVC	0.4±0.2	0.4±0.20	0.6±0.1	<0.001
TAPSE (mm)	20.7±4.3	20.9±4.2	19.6±4.9	0.496
MAPSE (mm)	13.0±3.5	12.9±3.7	13.8±3.0	0.504

The continuous values were presented as the means ± standard deviation or median (quartiles) according to their distribution; the categorical variables were presented as counts (percentages). COVID-19, coronavirus disease 2019; LUS, lung ultrasound; PLAPS, posterolateral alveolar and/or pleural syndrome; LVEF, left ventricular ejection fraction; IVCe, inferior vena cava maximal diameter during expiration; IVCi, inferior vena cava maximal diameter during inhalation; cIVC, collapsibility index of inferior vena cava; TAPSE, tricuspid annular plane systolic excursion; MAPSE, mitral annular plane systolic excursion.

non-survivors have a lower IVC collapsibility index (0.3 *vs.* 0.5, P=0.048) than the survivors. No significant differences in LVEF, TAPSE, or MAPSE were found between the two groups (P>0.05).

Discussion

Although most COVID-19 cases remain moderate symptoms, severe cases can progress to pneumonia, acute respiratory distress syndrome, and death (19). At present, there is no specific treatment for COVID-19, mainly isolation and symptomatic supportive treatment (20). CT is the most effective way to screen and clinically diagnose COVID-19 pneumonia (11). However, the high risk of transporting ventilated patients limits CT availability (21). LUS was effectively used to diagnose acute respiratory

Table 4 The demographics, comorbidities, and clinical characteristics of survivors and non-survivors infected with COVID-19

Parameters	Survivor (n=31)	Non-survivor (n=5)	P value
Age (years)	64.0±16.0	63.0±11.0	0.890
Gender			
Male	17 (54.8)	3 (60.0)	0.610
Female	14 (45.2)	2 (40.0)	
Oxygen device			0.030
Without oxygenation therapy	3 (9.7)	0 (0.0)	
Nasal cannula	25 (80.6)	2 (40.0)	
Mask oxygen	1 (3.2)	0 (0.0)	
Mechanical ventilation	2 (6.5)	3 (60.0)	
APACHE II score	6.0±3.0	25.0±16.0	<0.001
SOFA score	1.0 (0.0–2.0)	11.0 (5.0–12.5)	<0.001
GCS	15.0 (15.0–15.0)	3.0 (3.0–15.0)	0.059
WBC ($\times10^9$/L)	6.0 (4.4–7.1)	10.6 (6.6–21.0)	0.030
Lymphocytes ($\times10^9$/L)	1.5±0.6	0.8±0.5	0.020
Monocyte count ($\times10^9$/L)	0.4 (0.3–0.5)	0.28 (0.16–0.88)	0.450
PCT (ng/mL)	0.7 (0.3–6.3)	1.2 (0.8–2.4)	0.690
CRP (mg/L)	4.6 (1.7–20.0)	86.2 (72.8–183.9)	<0.001
BUN (mmol/L)	5.0 (3.7–5.7)	9.4 (5.4–10.2)	0.020
Creatinine clearance (μmol/L)	60.5 (46.7–74.8)	53.0 (27.1–69.0)	0.496
Albumin (g/L)	38.9±4.8	31.1±6.8	0.007
ALT (U/L)	27.0 (14.0–37.0)	22.0 (12.0–34.0)	0.861
AST (U/L)	25.0 (21.0–33.0)	34.0 (22.5–48.5)	0.295
TBIL (μmol/L)	10.2 (8.8–13.9)	28.0 (14.5–37.2)	0.019
DBIL (μmol/L)	3.2 (2.1–5.5)	14.0 (8.0–30.2)	0.012
Prothrombin time (s)	10.4 (10.0–11.5)	11.2 (9.7–11.9)	0.825
APTT (s)	26.7±6.5	28.2±4.3	0.629
D-dimer (mg/L)	2.0 (0.45–6.01)	3.6 (0.4–7.2)	0.967
CK (U/L)	36.0 (19.0–60.0)	42.0 (12.0–242.0)	0.910
CK-MB (U/L)	8.9 (7.0–11.0)	17.0 (8.0–26.0)	0.066
Troponin T (U/L)	17.3 (7.5–34.6)	24.0 (1.8–92.5)	0.760
NT-proBNP (pg/mL)	55.0 (10.6–105.4)	131.5 (83.7–1,699.9)	0.056
LDH (U/L)	186.0 (160.2–208.0)	267.0 (183.5–531.1)	0.226
IgM* (g/L)	30.2 (16.8–120.0)	21.7 (4.4–59.9)	0.361
IgG* (g/L)	175.1 (144.6–219.8)	156.6 (80.9–206.7)	0.718

The continuous values were presented as the means ± standard deviation or median (quartiles) according to their distribution; the categorical variables were presented as counts (percentages). *, antibodies against SARS-CoV-2. COVID-19, coronavirus disease 2019; APACHE II, acute physiology and chronic health evaluation II; SOFA, sequential organ failure assessment; GCS, Glasgow Coma Scale; WBC, white blood cell; PCT, procalcitonin; CRP, C-reactive protein; BUN, blood urea nitrogen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; DBIL, direct bilirubin; APTT, activated partial thromboplastin time; CK, creatine kinase; CK-MB, creatine kinase-MB; NT-proBNP, N-terminal pro-brain natriuretic peptide; LDH, lactate dehydrogenase; IgM, immunoglobulin M; IgG, immunoglobulin G; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 5 Ultrasound characteristics of survivors and non-survivors infected with COVID-19

Parameters	Survivor (n=31)	Non-survivor (n=5)	P value
LUS findings			
LUS score	7.0 (3.0–10.0)	17.0 (10.0–24.0)	0.003
Upper blue point score	0.0 (0.0–0.0)	3.0 (1.0–5.0)	0.004
Lower blue point	0.0 (0.0–1.0)	4.0 (2.0–4.0)	0.019
Diaphragmatic point score	0.0 (0.0–1.0)	3.0 (1.0–5.0)	0.032
Posterior blue points score	3.0 (1.0–6.0)	6.0 (2.0–6.0)	0.396
PLAPS points score	3.0 (1.0–6.0)	6.0 (2.0–6.0)	0.282
Alveolar-interstitial syndrome	9 (29.0)	5 (100.0)	0.005
Pleural effusion	6 (19.4)	4 (80.0)	0.015
Lung consolidations	26 (83.9)	5 (100.0)	1.000
Shred signs	25 (80.6)	4 (80.0)	1.000
Tissue-like sign	2 (6.5)	2 (40.0)	0.084
Where the lung consolidations appeared			0.011
No B lines	5 (16.1)	0 (0.0)	
Upper blue point	0 (0.0)	2 (40.0)	
Lower blue point	4 (12.9)	1 (20.0)	
Diaphragmatic point	1 (3.2)	1 (20.0)	
Posterior blue points	13 (41.9)	1 (20.0)	
PLAPS points	8 (25.8)	0 (0.0)	
Echocardiography findings			
LVEF	55.0 (50.0–60.0)	55.0 (48.0–63.0)	0.379
IVCe (mm)	15.8±3.5	18.1±5.6	0.224
IVCi (mm)	6.4 (5.5–12.6)	10.6 (9.0–18.7)	0.001
cIVC	0.5±0.2	0.3±0.2	0.048
TAPSE (mm)	21.1±3.9	18.2±6.1	0.174
MAPSE (mm)	13.2±3.7	12.0±2.3	0.500

The continuous values were presented as the means ± standard deviation or median (quartiles) according to their distribution; the categorical variables were presented as counts (percentages). COVID-19, coronavirus disease 2019; LUS, lung ultrasound; PLAPS, posterolateral alveolar and/or pleural syndrome; LVEF, left ventricular ejection fraction; IVCe, inferior vena cava maximal diameter during expiration; IVCi, inferior vena cava maximal diameter during inhalation; cIVC, collapsibility index of inferior vena cava; TAPSE, tricuspid annular plane systolic excursion; MAPSE, mitral annular plane systolic excursion.

distress syndrome, monitor the response to treatment, and detect bacterial superinfection (22,23), as well as COVID-19 pneumonia (24,25). There is a paucity of evidence on assessing the association between LUS characteristics and the severity of COVID-19. Studying the clinical and ultrasound characteristics of COVID-19 help understand the features of critical conditions and promote evaluation and therapeutical decisions.

The LUS score of the lethal cases was higher than that of the survivors in the present study. Our findings are consistent with previous reports on diffuse B lines and subpleural consolidation in critically ill patients (26,27),

indicating the more severe pulmonary inflammatory exudation and more abundant mucus in severe/critical cases. On the contrary, the reduced B lines suggested the recovery of gas exchange, underlying the amelioration of consolidations or air-bronchogram reappearance (28,29). Therefore, the features on each part of the lung are conducive for the treatment such as diuresis, mechanical ventilatory support, pleural effusion drainage, and sputum drainage (26).

The incidences of alveolar-interstitial syndrome and lung consolidations in severe/critical patients were higher than those of moderate patients. "Alveolar-interstitial syndrome" showed up in the context of worsened alveolar edema, exudates, and lymphocyte infiltration filling the interstitial space (26,30). Monitoring LUS characteristics could guide continuous positive airway pressure therapy by adjusting the weaning time. In the present study, the proportion of pleural effusion was higher in the lethal cases, indicating that pleural effusions might be related to refractory respiratory failure. It was proven that pleural effusion predicted poor prognosis in H5N1 infection (31), which was similar to the CT distribution of COVID-19 lung lesions reported by Chung *et al.* (32). It suggested that more attention be paid to combining LUS with clinical values including arterial blood gas to detect the deterioration into severe/critical cases in early stage (11,19,21,22,24,33).

The present study found that the index of the IVC of the severe/critical patients was higher than that of the moderate group because the severe/critical patients had higher blood volume and intrathoracic pressure. It is suggested that attention should be paid to the management of patient's blood volume, and comprehensive measures should be taken to treat patients to reduce mortality (34). Although the confirmation of COVID-19 pneumonia cannot be achieved via ultrasound, the abovementioned ultrasound characteristics might avail the identification of diverse pathogens and the triage of patients.

Lymphocyte counts in severe/critical cases usually decrease, while WBCs increase. The decrease of lymphocytes indicates the large consumption of immune cells and suppressed immune function. The increased values of the neutrophil ratio and CRP may be associated with the cytokine storm caused by virus invasion and other infectious comorbidities (35). Severe viral infections may cause systemic loss by affecting the balance of pro-inflammatory and anti-inflammatory and inducing the secretion of inflammatory cytokines (36). The worsening lung patterns could be exposed to LUS score, prompting the administration of immunomodulatory therapy. Timely intervention may help reduce complications and mortality. In the present study, LDH, AST, BUN, APTT, and CK-MB generally increased. The changes were more obvious in the severe/critical than in the moderate patients, indicating that severe/critical cases had more severe cardiac, hepatic, renal, and coagulation impairment, which was consistent with previous studies (37,38).

There were still limitations in our study. First, the small size of the study population hindered the exploration of whether the severity of abnormal LUS findings could predict the prognosis for COVID-19 pneumonia. Due to the lack of research, we were unable to analyze the relationship between ultrasound findings and the course of the disease. Second, LUS was performed either in ICU or an isolated ward, resulting in a poor-quality imaging system and incomplete ultrasound data. Third, the demographics were rather simple and lacked relevant characteristics such as cigarette smoking and comorbidities. Also, data on the length of hospital stays and length of ICU stays were missing. Intravenous albumin infusion was given to patients who were prone to turn severe/critical cases, which might result in a higher level in the severe/critical group than in the moderated group in the baseline. More evidence is needed to provide more ultrasound information related to clinical manifestations.

Conclusions

Severe/critical COVID-19 pneumonia demonstrated higher BUN, albumin, CK-MB, NT-proBNP, CRP, and LDH level, as well as higher SOFA scores than moderate cases. The study demonstrated that IVC and LUS score in admission was significantly different in severe patients compared with moderate patients. Patients in severe/critical cases had more alveolar-interstitial syndrome and lung consolidations. The abovementioned features help quantify the severity of COVID-19.

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Footnote

Reporting Checklist: The authors have completed the

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://aoi.amegroups.com/article/view/10.21037/aoi-22-4/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of the First People's Hospital of Jingzhou and Guangdong Provincial People's Hospital (No. 2020-056), and written informed consent was waived.

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