Application of lung ultrasonography in critically ill patients with COVID-19

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Abstract

Purpose: Lung ultrasonography (LU) is useful to assess lung lesions and variations at bedside. To investigate the results of LU in severe and critical patients with coronavirus disease 2019 (COVID-19), we performed a single-institution study to evaluate the related lung lesions and variations, and prophylactic strategies, in a large referral and treatment center.

Methods: We included 91 adult patients with severe and critical COVID-19, namely 62 males and 29 females, with an average age of 59 ± 11 years, who underwent LU. We collected the following patient information: sex, age, days in hospital, and days in ICU. In the ultrasound examinations, we recorded the presence of discrete B lines, confluent B lines, consolidation, pleural thickening, pleural effusion, and pneumothorax (PTX).

Results: Among the 91 severe and critical patients, 59 cases had scattered B lines, 56 cases had confluent B lines, 58 cases had alveolar-interstitial syndrome (AIS), 48 cases had lung consolidation, six cases had pleural thickening, 39 cases had pleural effusion (average depth of the pleural effusion: 1.0 ± 1.5 cm), and 20 patients developed PTX. In the Cox multivariate analysis, there were significant differences in age, hospitalization days, ICU days, and lung consolidation.

Conclusion: Lung ultrasonography performed at the bedside can detect lung diseases, such as B lines, PTX, pulmonary edema, lung consolidation, pleural effusion, and variations of these findings. Our findings support the use of LU and measurements for estimating factors, and monitoring response to therapy in severe and critical COVID-19 patients.

KEYWORDS
lung consolidation, lung ultrasonography, severe and critical COVID-19
1 | INTRODUCTION

As of March 2, 2020, there have been 81,307 officially reported confirmed cases of COVID-19 pneumonia, and 2136 intensive care cases in China and 140,656 cases abroad. Lung ultrasonography (LU) is a useful tool to assess lung lesions and variations at bedside.\(^1\) LU for the recognition of pneumothorax (PTX), pulmonary edema, consolidation, and pleural effusion, can be performed very accurately and reliably at bedside with a hand-held device.\(^2\) LU is relatively inexpensive, easy to learn and interpret, and is not dependent on acoustic windows or having the patient in a decubitus position. Based on these features, LU is recognized as useful for evaluating intensive care unit patients (eg, hypoxemia, unstable circulation). LU provides results that are similar to CT, and LU can be used for repeated examination bedside, which is of great value for disease assessment.\(^3\)

We performed a single-institution study in 91 patients with confirmed severe and critical COVID-19 pneumonia to identify lung diseases, such as B lines, PTX, pulmonary edema, lung consolidation, pleural effusion, and variations of these conditions, in a large cohort of hospitalized patients.

2 | METHODS

2.1 | Study design and participants

In this single-center retrospective observational study, 91 adult patients with severe and critical COVID-19 pneumonia who were admitted to Wuhan Jinyintan Hospital (Wuhan, China) from January 1, 2020, to March 2, 2020, were included; 62 were male and 29 were female, with an average age of 59 ± 11 years. All patients were positive for SARS-CoV-2 RNA. We collected patients' sex, age, number of days in hospital, and days in the intensive care unit (ICU). The study was approved by the Ethics Committee of Beijing Chaoyang Hospital, Capital Medical University, China (No. KY-2020-36.01).

Severe and critical COVID-19 were diagnosed according to the diagnosis and treatment program for COVID-19 pneumonia (Trial seventh edition) issued by the National Health Commission\(^4\): (1) severe: patients had any of the following: (a) dyspnea, respiratory rate ≥30/min; (b) blood oxygen saturation (SpO2) ≤ 93% at rest; and (c) PaO2/FiO2 ratio [the ratio between the partial pressure of oxygen (PaO2) and the fraction of inspired oxygen (FiO2)] < 300 mm Hg (1 mm Hg = 0.133 kPa). (2) critical: patients had any of the following: (a) respiratory failure requiring mechanical ventilation; (b) shock; (c) multiple organ failure requiring ICU monitoring and treatment.

2.2 | Lung ultrasonography

Lung ultrasonography (LU) was performed at bedside using a Mindray M9 color Doppler ultrasound machine equipped with two linear array probes with frequencies ranging from 4 to 12 MHz (superficial pleura and sub-pleural pathology) and 1.5-5 MHz (deeper pathology and obesity). Examination position: LU can be performed in the supine, half-lying, side-lying, prone, and sitting positions. We performed LU for all 91 severe and critical patients with COVID-19 using a 12-zone method.\(^2\) The lung was divided into three areas: anterior, lateral, and posterior, and the papillary plane was used as the upper and lower boundary; that is, the left/right lung was divided into six areas, 12 areas on both sides (Figure 1). The posterior chest was...
scanned along the paravertebral line, from the scapular line to the posterior axillary line, which can be used to identify pleural effusion and determine the puncture site (Figure 2). The probe should always be perpendicular to the chest, and longitudinal and transverse scans can both be performed. We collected the following LU data: discrete B lines, confluent B lines, alveolar-interstitial syndrome (AIS), pulmonary consolidation, thickened pleural line, pleural effusion, and PTX.

To avoid cross-contamination between patients using the same probe, after applying gel to the probe surface, the probe was placed into a disposable probe cover; gel was then applied to the surface of the probe cover. After examination, the disposable probe cover was removed and discarded, then the probe was wiped with a paper towel. We recommend 3% hydrogen peroxide to clean and sanitize the surface of the ultrasound machine, and 75% alcohol or 2% glutaraldehyde is recommended to clean and sanitize the probe (Figure 3).  

2.3 | Statistical analysis

SPSS 21.0 statistical software was used for all statistical analyses with quantitative data expressed as the average ± standard deviation (mean ± SD), and these data were analyzed using the t test. P-values <.05 were considered statistically significant. Cox regression analysis 5 was used to analyze the risk factors for survival, with data presented as odds ratios (OR) and corresponding 95% CIs.

3 | RESULTS

3.1 | Clinical findings

Among the 91 intensive care COVID-19 patients, 47 died (51.6%) (37 male (78.7%) and 10 female (21.3%)), and these patients spent 20 ± 10 days in hospital and 13 ± 8 days in the ICU; 24 patients (26.4%) underwent treatment (13 male (54.2%) and 11 female (45.8%)) and spent 20 ± 9 days in hospital and 14 ± 8 days in the ICU; 20 patients were discharged (22.0%) (12 male (60%) and 8 female (40%)) after 20 ± 9 days in hospital and 14 ± 11 days in the ICU.

3.2 | Lung ultrasonography results

All 91 patients underwent at least one pulmonary ultrasonographic examination, and the results are shown in Table 1. Fifty nine patients (64.8%) had scattered B lines (starting from the pleural line and extending perpendicularly and radiating to the deep lung fields) (Figure 4A); 56 patients (61.5%) had confluent B lines involving all intercostal spaces as dense B lines, which were difficult to distinguish and count; 58 patients (63.7%) had AIS (longitudinal scans showed confluent B lines in more than two consecutive intercostal spaces) (Figure 4B); 48 patients (52.7%) had pulmonary consolidation (liver-like change in lung tissue in ultrasound images, possibly accompanied by air bronchograms) (Figure 4C); 6 patients (6.5%) had thickened pleural lines, which were rare (Figure 4D); 39 patients (42.9%) had pleural effusion (Figure 4E), with an average depth of 1.0 ± 1.5 cm; and 20 patients (22.0%) had PTX (normal M-mode lung ultrasonography showed the beach sign, and pneumothorax was associated with the stratospheric sign, in which the lung slips away from the body wall, and the particle sign below the pleural line is replaced by a series of parallel lines; Figure 4F).

3.3 | Cox regression analysis

The outcomes in this study were death, undergoing treatment, and discharge with the time period spanning from January 1, 2020, to March 2, 2020. LU findings were the main factors in the Cox regression. We adjusted for the following factors: sex, age, number of days of hospitalization, and number of days in the ICU. Univariate and multivariate Cox analysis results are shown in Table 2. In the univariate analysis, there were statistical differences for age, number of hospitalization days, number of ICU days, pulmonary consolidation, thickened pleural lines, pleural effusion, and PTX. In the multivariate analysis, there were statistical differences for age, number of hospitalization days, number of ICU days, and pulmonary consolidation, and these results are shown in a forest map in Figure 5.

3.4 | Analysis of pulmonary consolidation

Pulmonary consolidation was present in 48 of the 91 patients. Among the 48 patients, 38 had complications, and the average interval from illness onset to pulmonary consolidation was 11 ± 3 days; 10 cases had no complications, and the average number of days of pulmonary consolidation was 24 ± 9 days. The two groups were compared using the t test, and the statistical results were: t = 8.062, P < .0001, as shown in Figure 6. According to the statistical analysis of the data for the 12 lung regions, 13 cases (27.1%) of pulmonary
In this study, none of the three types of B lines were risk factors for death. It is easy to see a large area of dense B lines in COVID-19 using ultrasonography, but these lesions spread from the periphery of the lung to the center, so ultrasound cannot be used to easily judge the outcome of lung lesions. In this respect, ultrasonography cannot replace CT, MRI, and other lung examination methods.6

In this study, we found that the degree of pleural effusion (1.0 ± 1.5 cm) was low, and pleural thickening was rare (incidence: 6.5%), which is similar to other viral pneumonia infections.7 LU is sensitive for liquid detection, and transthoracic ultrasonography is

| Cases (n/%) | LU findings | Characteristics |
|------------|-------------|-----------------|
| 59 (64.8%) | Scattered B lines | Starting from the pleural line and extending perpendicularly and radiating to the deep lung fields |
| 56 (61.5%) | Confluent B lines | Involving all intercostal spaces as dense B lines, which were difficult to distinguish and count |
| 58 (63.7%) | Alveolar-interstitial syndrome (AIS) | Longitudinal scans showed confluent B lines in more than two consecutive intercostal spaces |
| 48 (52.7%) | Pulmonary consolidation | Liver-like change in lung tissue in ultrasound images, possibly accompanied by air bronchograms |
| 6 (6.5%) | Pleural thickening | |
| 39 (42.9%) | Pleural effusion | Average depth of 1.0 ± 1.5 cm |
| 20 (22.0%) | Pneumothorax (PTX) | Normal M-mode lung ultrasonography showed the beach sign, and pneumothorax was associated with the stratospheric sign, in which the lung slips away from the body wall, and the particle sign below the pleural line is replaced by a series of parallel lines (stratospheric sign) |

4 | DISCUSSION

consolidation occurred in regions 1, 2, and 3, and 35 cases (72.9%) occurred in regions 4, 5, and 6.
TABLE 2  Univariate and multivariate Cox analysis in 91 patients with severe and critical COVID-19

|                    | Univariate |                          |                       |                    | Multivariate |                          |                       |
|--------------------|------------|---------------------------|-----------------------|--------------------|--------------|---------------------------|-----------------------|
|                    | HR         | 95% CI                    |                       | P                  | HR           | 95% CI                    |                       |
| Gender             | 1.526      | 0.752-3.096               | .242                  |                    | 1.040        | 1.009-1.073               | .012                  |
| Age                | 1.045      | 1.021-1.069               | <.001                 |                    | 1.040        | 1.009-1.073               | .012                  |
| Admission (d)      | 0.751      | 0.688-0.819               | <.001                 |                    | 0.760        | 0.683-0.845               | <.001                 |
| ICU (d)            | 0.894      | 0.853-0.936               | <.001                 |                    | 0.937        | 0.879-1.000               | .049                  |
| Discrete B lines   | 1.132      | 0.597-2.147               | .703                  |                    |              |                           |                       |
| Confluent B lines  | 1.082      | 0.586-1.996               | .801                  |                    |              |                           |                       |
| AIS                | 0.718      | 0.365-1.410               | .336                  |                    |              |                           |                       |
| Consolidations     | 1.859      | 0.924-3.741               | .082                  |                    | 2.282        | 1.053-4.943               | .036                  |
| Thickened pleural  | 2.607      | 1.244-5.463               | .011                  |                    | 1.840        | 0.802-4.219               | .150                  |
| line               |            |                           |                       |                    |              |                           |                       |
| Pleural effusions  | 1.232      | 0.683-2.147               | .150                  |                    | 1.035        | 0.837-1.258               | .725                  |
| Pneumothorax       | 2.834      | 1.524-5.270               | .001                  |                    | 1.760        | 0.856-3.618               | .124                  |

Abbreviations: AIS = alveolar-interstitial syndrome; COVID-19 = coronavirus disease 2019; ICU = intensive care unit.

FIGURE 5  Forest plot of the multivariate Cox regression analysis results in our 91 severe and critical COVID-19 patients

FIGURE 6  Analysis of the number of days to developing pulmonary consolidation between patients with complications and patients without complications (with complications: 11 ± 3 days; without complications: 24 ± 9 days)

helpful to identify the puncture site. Our sonographer suggested paying special attention to observe the changes in the volume and properties of the pleural effusion, once identified.

In LU, the measurement method must be consistent. M-mode ultrasound is helpful to further diagnose pneumothorax, in which the lung slips away from the body wall, and the particle sign below the pleural line is replaced by a series of parallel lines (stratospheric sign). The incidence of PTX was high in this study, and the presence of PTX indicates decreased lung compliance and a poor prognosis. We found statistical differences in the univariate analysis, in this study, but no statistical difference in the multivariate analysis. Larger sample sizes are needed in future studies.

Currently, LU cannot diagnose the underlying etiology of lung disease; however, the advantage of LU is that it is radiation-free and can be repeated many times. In this study, LU determined the range and distribution of pulmonary consolidation, and we were able to dynamically observe changes in lung consolidation over time.
time. Pulmonary consolidation is a liver-like change in lung tissue in ultrasound images, which may be accompanied by air bronchograms.\textsuperscript{12,13} In COVID-19, the mean time to pulmonary consolidation is 20 days\textsuperscript{14,15}, early fibrosis and fleshy change may be seen 20 days after the onset of disease, and fibrous proliferation of the alveolar wall stroma is seen as fibrosis. Exudate in the alveolar cavity cannot be absorbed and organizes, which is seen as fleshy change.

According to the analysis of the pulmonary consolidation findings in patients with or without complications, in this study, the average time to pulmonary consolidation was 11 ± 3 days in patients with complications and 24 ± 9 days in patients without complications ($t = 4.715$, $P = .001$). According to the statistical analysis of the data for the 12 regions, the incidence of pulmonary consolidation in regions 4, 5, and 6 was 72.9%, which is consistent with the gravity distribution characteristics of critical patients. Our suggestion for clinical management is prone position ventilation.

In conclusion, LU is a safe, nonradioactive, reproducible, low-cost, and short-term examination method for COVID-19. LU can be used to quickly diagnose lung diseases, such as PTX, AIS, pulmonary consolidation, and pleural effusion, and for sequential examinations to evaluate evolving pathological changes. However, LU identifies only peripheral lesions in the lung, and central lesions must still be evaluated by CT.

**CONFLICT OF INTERESTS**
The authors have no conflicts of interest to declare.

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