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UTILITY OF POINT-OF-CARE LUNG ULTRASOUND FOR CLINICAL CLASSIFICATION OF COVID-19

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Abstract—In this study, the utility of point-of-care lung ultrasound for clinical classification of coronavirus disease (COVID-19) was prospectively assessed. Twenty-seven adult patients with COVID-19 underwent bedside lung ultrasonography (LUS) examinations three times each within the first 2 wk of admission to the isolation ward. We divided the 81 exams into three groups (moderate, severe and critically ill). Lung scores were calculated as the sum of points. A rank sum test and bivariate correlation analysis were carried out to determine the correlation between LUS on admission and clinical classification of COVID-19. There were dramatic differences in LUS (p < 0.001) among the three groups, and LUS scores (r = 0.754) correlated positively with clinical severity (p < 0.01). In addition, moderate, severe and critically ill patients were more likely to have low (≤9), medium (9–15) and high scores (>15), respectively. This study provides stratification criteria of LUS scores to assist in quantitatively evaluating COVID-19 patients. (E-mail: liqiao214@126.com) © 2020 World Federation for Ultrasound in Medicine & Biology. All rights reserved.

Key Words: COVID-19, Point-of-care ultrasound, Pneumonia severity.

INTRODUCTION

Coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a new public health crisis threatening the world. The disease is transmitted primarily via direct contact or through droplets generated by an infected individual when coughing or sneezing (Rothe et al. 2020). SARS-CoV-2 binds to angiotensin receptor 2 expressed by cells of the lung, making the lung the primary site of damage (Singhal 2020). The most frequent symptoms of COVID-19 pneumonia are fever, cough and fatigue; other symptoms include sore throat, myalgia, hemoptysis and dyspnea. These symptoms are similar to those of other respiratory infections. Interestingly, the severity of COVID-19 varies, ranging from an asymptomatic state to acute respiratory distress syndrome and multiorgan dysfunction (Huang et al. 2020; Ren et al. 2020; Wang et al. 2020). Therefore, effective therapies warrant specific identification of disease severity.

LUS has been rapidly developed in the last few years. Although it was originally proposed for a range of clinical applications in the 1990s, the technique has spread mainly in the last decade. Currently, acute respiratory failure, circulatory failure, and cardiac arrest can be assessed by LUS. It can also be used for quantitative assessment of lung aeration and may be a useful tool to guide mechanical ventilation (Mojoli et al. 2019). Moreover, prior research has shown that LUS can affect clinical decisions for up to 50% of patients in the intensive care unit (Xirouchaki et al. 2014). The unique benefits of LUS in the current context include bedside feasibility, lack of radiation, low cost and easy application (See et al. 2018). Indeed, due to its ready availability at the bedside, LUS may play a pivotal role in monitoring serial changes in COVID-19 pneumonia.

The current clinical evidence strongly suggests the potential diagnostic accuracy of LUS for COVID-19 (Volpicelli and Gargani 2020). Previous studies have reported that bedside LUS correlates with computed tomography findings in adults with COVID-19 pneumonia (Poggiali et al. 2020). Although the latter technique
is considered one of the primary imaging criteria for diagnosis of COVID-19, the disadvantages of radiographic examinations make LUS a complementary method for COVID-19 patients. Some investigators suggest that lung abnormalities in the pediatric population and pregnant women with COVID-19 can be effectively detected by radiation-free LUS (Buonsenso et al. 2020c; Denina et al. 2020). In addition, ultrasound, especially using pocket devices, is considered relatively safer because it reduces the exposure of health care workers to infected patients (Buonsenso et al. 2020a). Early studies have suggested that an irregular pleural line with small subpleural consolidations, white lung, confluent and irregular vertical artifacts (B-lines) are ultrasonic manifestations of COVID-19 pneumonia (Buonsenso et al. 2020b), and LUS scores have been used to identify patients with lung involvement and disease severity (Vetrugno et al. 2020). However, such studies are mostly case reports, and further research is lacking. Thus, the present study was undertaken to investigate correlations between LUS and the severity of COVID-19, aiming to clarify the diagnostic and monitoring role of LUS in COVID-19 pneumonia.

MATERIALS AND METHODS

Participants

The prospective observational study included 27 patients with imaging signs of COVID-19 pneumonia (moderate and above) in the isolation ward of the First Affiliated Hospital of Wenzhou Medical University from February 1 to March 1, 2020. All patients underwent three bedside LUS scans within the first 2 wk of admission. We ensured that all patients were admitted in the early stages of COVID-19 because patients with confirmed COVID-19 are immediately admitted to the isolation ward in China. The interval between ultrasound examinations was 3 to 5 d. The study protocol was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University. Informed consent was provided by the next of kin for all patients to participate in this study.

Exclusion criteria were mild disease with no imaging signs of pneumonia; any conditions that interfered with LUS assessment, such as obstruction of the scan area or chest deformity; receiving fewer than three examinations due to a short duration of hospitalization; and lack of clinical data.

LUS assessment

A bedside LUS was performed by a trained sonographer using a C1-5-RS transducer (1.5–5 MHz) and GE Vivid IQ set (GE Healthcare, Wuxi, Jiangsu, China). The study depth was set to approximately 10–15 cm (depending on the body habitus). The sonographer wore the standard personal protections as per World Health Organization indications and disinfected the probe with 3% hydrogen peroxide after the examination.

Ten lung zones (two anterior, two lateral and one posterior) were scanned in sequence (Fig. 1). The

Fig. 1. Detailed illustration of scanning zones at the right thorax: RA1 (up to the clavicle, down to the fourth rib; medial to the margin of the sternum, lateral to the anterior axillary line); RA2 (up to the fourth rib, down to the superior border of the liver; medial to the margin of the sternum, lateral to the anterior axillary line); RL1 (up to axilla, down to the axis of the fourth rib; anterior: from the front to the axillary line, then to the posterior axillary line); RL2 (up to the axis of the fourth rib, down to the liver; front side to the anterior axillary line, back side to the posterior axillary line); RP (up to the upper bound of the lung, down to the appearance of abdominal contents; medial to the thoracic spine, lateral to the medial border of the scapula).
anterior, lateral and posterior zones were divided by the anterior and posterior axillary lines. The anterior and lateral regions were divided into upper and lower parts by the fourth rib. Scanning started in the anterior zone, descending from the clavicle to the fourth rib (zone A1) and then downward to the upper surface of the abdominal organs (zone A2). After that, it proceeded down from the axilla to the fourth rib (zone L1) and then to the upper margin of the abdominal organs (zone L2). We examined the posterior (zone P) and scanned the abdominal contents from the upper lung boundary. The contralateral thoracic cavity was then examined. The anterolateral parts of the chest wall were examined in a supine position and the posterior parts in either a lateral or a seated position. This study had no impact on the treatment of the patients.

Sonographic signs of lung aeration were classified into four scoring patterns (Fig. 2; Soldati et al. 2020a)—score 0: the presence of lung sliding, with A-lines or isolated B-lines ($\leq 2$), and the pleural line continuous and regular; score 1: indented pleural, with multiple spaced B-lines at an interval of approximately 7 mm; score 2: broken pleural line, with coalescent B-lines at an interval of $\leq 3$ mm; score 3: dense and largely extended white lung with or without larger consolidations. For a given region of interest, points were allocated according to the worst ultrasound score pattern observed. The lung scores were calculated as the sum of points (the highest score was 30).

Fig. 2. Four ultrasound patterns according to lung aeration. (a) Score 0: the presence of lung sliding with A-lines; continuous and regular pleural lines. (b) Score 1: multiple spaced B-lines; indented pleural line. (c) Score 2: multiple coalescent B-lines; broken pleural line. (d) Score 3: consolidation of the lung.
Statistical analysis was performed with SPSS 26.0 software (SPSS, Chicago, IL, USA). We divided the 81 exams into three groups (moderate, severe and critically ill) according to Guidelines on Diagnosis and Treatment of Novel Coronavirus Pneumonia (Trial, seventh edition, 2020) at each examination (Table 1). Clinical data, including the LUS score, blood biochemistry (alanine aminotransferase, aspartate aminotransferase [AST], \( \gamma \)-glutamyltransferase [GGT], creatinine and blood urea nitrogen [BUN]), routine blood examinations (leukocyte and lymphocyte counts) and blood coagulation function (D dimer) were monitored synchronously. The distribution of LUS scores among the three groups is provided (Figure 3). In addition, categorical variables with \( p < 0.05 \) according to the Spearman test were analyzed. Such categorical variables are expressed as percentages, and results were compared with those of the Kruskal–Wallis test or Wilcoxon test, as appropriate. A \( p \) value less than 0.05 was considered statistically significant.

RESULTS

Of the 27 patients with COVID-19 enrolled in our study, 16 (59%) were male and 11 (41%) female, with an average age of 63.0 ± 14.2 y (range, 35–93 y). The distribution of LUS scores for the three COVID-19 groups is summarized in Figure 3. Thirty-five exams (43%) were classified into the moderate group, 20 (25%) into the severe group and 26 (32%) into the critically ill group. The mean LUS scores of the critically ill, severe and moderate groups were 16.2 ± 2.4 (range, 11–20), 12.9 ± 3.7 (range, 7–20) and 7.8 ± 3.7 (range, 11–20), respectively. According to Spearman correlation test results (Table 2),...
LUS score ($r = 0.754$), leukocyte count ($r = 0.304$), D dimer ($r = 0.576$), AST ($r = 0.343$), $\gamma$-glutamyltransferase ($r = 0.306$) and BUN ($r = 0.461$) correlated positively with clinical severity ($p < 0.01$). In contrast, lymphocyte count ($r = -0.588$) correlated negatively with COVID-19 clinical severity.

Then we divided the LUS scores into three bins (low $\leq 9$; $9 <$ medium $< 15$; high $\geq 15$) and compared them with the severity of COVID-19 disease (Table 3).

Wilcoxon test results ($p < 0.001$) showed that the distribution of severity among the low-, medium- and high-LUS groups differed. In addition, critically ill patients had a high proportion in the high-LUS group (72%), with lower proportion in the medium- and low-LUS groups (27.6% and 0.0%, respectively). Moderately, severely and critically ill patients are more likely to be present in the low-, medium- and high-LUS groups, respectively.

### Table 1. Clinical classification for novel coronavirus pneumonia

| Mild | Moderate | Severe* | Critically ill* |
|------|----------|---------|-----------------|
| Clinical symptoms were mild; no manifestations of pneumonia were found on imaging. | Fever and/or respiratory symptoms or/and other symptoms; pneumonia sign found in chest imaging. | RR $\geq 30$ times/min Oxygen saturation $\leq 93\%$ in the resting state PaO$_2$/FiO$_2$ $\leq 300$ mm Hg; (1 mmHg $= 0.133$ kPa) More than 50% of lesions progressed on chest imaging within 24 to 48 h | Respiratory failure, requiring mechanical ventilation Shock Patients with other organ failure should be treated in the ICU |

FiO$_2$ = fractional inspired oxygen; PaO$_2$ = arterial oxygen partial pressure; RR = respiratory rate.

* Only one criterion need be met.

### Table 2. Comparison of data correlations

| Spearman test | Severity | Lymphocyte count | Leukocyte count | D dimer | AST | ALT | GGT | CRcrit | BUN | LUS score |
|---------------|----------|------------------|-----------------|---------|-----|-----|-----|--------|------|-----------|
| $r$           | 1        | -0.588           | 0.304           | 0.576   | 0.343 | 0.187 | 0.306 | 0.02   | 0.461 | 0.754     |
| $p$           | 0.001    | 0.006            | 0.001           | 0.002   | 0.094 | 0.005 | 0.861 | 0.001  | 0.001 |           |

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CRcrit = creatinine; LUS = lung ultrasound; GGT = $\gamma$-glutamyltransferase.
According to Kruskal–Wallis test results, lymphocytopenia ($p < 0.001$), leukocytosis ($p = 0.004$), increased AST ($p = 0.014$), increased GGT ($p = 0.016$) and increased BUN ($p = 0.001$) were more commonly observed in the critically ill group (Table 4). However, no significant difference in D-dimer levels was observed among the three groups.

**DISCUSSION**

The spread of COVID-19 around the world is posing a tremendous danger to human health in 2020 and putting unprecedented pressure on health care workers. The number of cases continues to rise, and more than six million people have been infected thus far. Therefore, effective therapies warrant specific identification of disease severity, as the severity of the disease varies according to patients’ symptoms and imaging characteristics. However, limitations of radiologic imaging are obvious: it is dangerous and time-consuming because of transport of critically ill patients followed by the necessary decontamination procedures (Peng et al. 2020); it is not suitable for pregnant women or children to receive repeated examinations owing to the radioactivity involved (Yoon et al. 2020); and the depiction based on a portable device does not always correlate with the clinical picture. Conversely, LUS examinations do not have these limitations, and changes in pulmonary and cardiac signs can be observed by bedside ultrasound in real time. In a previous observational study, LUS was considered a useful tool to assess and monitor lung involvement in pregnant women with COVID-19 and even played a significant role in treatment decisions (Buonsenso et al. 2020c). As a result, LUS is probably regarded as the best complement to radiography of the chest (See et al. 2018; Pierce 2020).

Ultrasound is an appropriate tool for the management of respiratory failure and lung injury caused by COVID-19 because histopathologic progression of COVID-19 pneumonia occurs in the distal region of the lung and is characterized by alveolar injury and edema, interstitial thickening and gravitational enhancement (Soldati et al. 2020b). LUS patterns of COVID-19 pneumonia described in the literature include separate and

### Table 3. Comparison of LUS scores between categories with different COVID-19 severities

| LUS score | Number | Severity | Kruskal–Wallis | $p$ |
|-----------|--------|----------|---------------|-----|
| Low       | 27     | Moderate | 22 (81.5%)    | 20 (74.1%) | 0 (0.0%) |
|           |        | Severe   | 5 (18.5%)     | 7 (25.9%) |
| Medium    | 29     | Moderate | 12 (41.4%)    | 14 (48.3%) | 1 (3.4%) |
|           |        | Severe   | 9 (31.0%)     | 9 (31.0%) |
| High      | 25     | Moderate | 4 (14.0%)     | 4 (14.0%) |
|           |        | Severe   | 6 (24.0%)     | 13 (45.8%) |

LUS = lung ultrasound.

Low: LUS $< 9$; medium: LUS $> 9$ and $< 15$; high: LUS $> 15$.

### Table 4. Comparison of routine blood tests, blood coagulation function and blood biochemistry in different COVID-19 severity levels

| Variable     | Number | Severity | Wilcoxon test | $p$   |
|--------------|--------|----------|---------------|-------|
| Lymphocytes  |        | Moderate | 2030          | 0     |
| Reduced      | 22     | Severe   |               |       |
| Normal       | 59     |          |               |       |
| Leukocytes   |        | Critically ill |       |       |
| Increased    | 39     |          |               |       |
| Normal       | 42     |          |               |       |
| D dimer      |        | Moderate | 1435          | 0.004 |
| Increased    | 77     | Severe   |               |       |
| Normal       | 4      |          |               |       |
| AST          |        | Critically ill |       |       |
| Increased    | 31     |          |               |       |
| Normal       | 50     |          |               |       |
| GGT          |        | Moderate | 921.5         | 0.016 |
| Increased    | 53     | Severe   |               |       |
| Normal       | 28     |          |               |       |
| BUN          |        | Critically ill |       | 0.001 |
| Increased    | 30     |          |               |       |
| Normal       | 51     |          |               |       |

$AST =$ aspartate aminotransferase; $BUN =$ blood urea nitrogen; $GGT =$ γ-glutamyltransferase.
coalescent B-lines, irregular and fragmented pleural lines and small peripheral consolidations. These LUS patterns were confirmed in this study as well. Some previous articles strongly emphasize the importance of bedside LUS for the diagnosis and clinical management of COVID-19 in the novel COVID-19 era. However, there is little further research on whether LUS can quantitatively assess the severity of this disease. In this study, we used LUS scores of 10 points to explore the applicability of the technique for COVID-19, rather than the 14 points suggested by Soldati et al. (2020a). The two evaluation methods are essentially the same, with the 14-point LUS score dividing the posterior (zone P) into three sections. However, because a 10-point scan can be completed in a shorter time, it would be extremely useful for patients in the intensive care unit.

The results showed that the LUS score correlated highly positively with clinical severity, demonstrating the potential of LUS for quantitative management of COVID-19. We first found that moderately, severely and critically ill patients were more likely to have low, medium and high LUS scores, respectively. This kind of classification of LUS scores can effectively stratify COVID-19 pneumonia severity and helpfully guide clinical monitoring. In addition, lymphocytopenia ($p < 0.001$) and leukocytosis have been reported to occur as the disease progresses (Cheng et al. 2020), as verified in the present research. AST, GGT and BUN levels correlated weakly with COVID-19 severity, and their distributions were different in the three COVID-19 groups.

**Limitations**

Our study has certain limitations. First, our sample size was small. To better evaluate the utility of LUS in the management of COVID-19, future studies with larger numbers of patients are needed. Second, multiple LUS exams were performed for the same patients, resulting in the inclusion of independent exams; this is because the total number of cases in this study was very small in the early stages of the epidemic. This situation may have caused statistical error but did not change the final conclusion. Third, the lack of clinical outcomes (death, intensive care admission, ventilation) was also a limitation. As a result, using LUS to predict the risk for intensive care unit admission and death, as in the research of Bonadina et al. (2020), was not involved. Finally, our study was a cross-sectional study, which can only indicate whether LUS scores are highly related to the severity of COVID-19; it cannot provide prognostic information.

**CONCLUSION**

In this study, a significant correlation was found between LUS scores, leukocyte and lymphocyte counts and clinical classification of COVID-19. We also obtained stratification criteria of LUS scores for COVID-19. Although further research is needed, the findings expand the applications of ultrasound in COVID-19 from complementary point of care to severity stratification, which will be helpful for guiding clinicians in accurate diagnosis and treatment outcome follow-up for patients with COVID-19.

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**Conflict of interest disclosure**—The authors declare that they have no conflicts of interest.

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