Lung Ultrasound Score: A Potential Prediction Tool In Covid-19

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Research
Abstract

1. Background:

During the COVID-19 pandemic, adequate management of available resources may be key to overcoming the excess of seriously ill patients and saving lives. Creating tools to assess disease severity is one of the most important aspects for reducing the burden on emergency departments. Lung ultrasound has high accuracy for diagnosis of pulmonary diseases; however, there are no prospective studies demonstrating that lung ultrasound can predict outcomes in COVID-19. We hypothesized that Lung Ultrasound Score (LUSS) at hospital admission would be able to predict the outcomes of patients with COVID-19.

2. Methods:

Prospective cohort study conducted from 14 March through 6 May 2020 in the Emergency Department (ED) of an urban, academic, level I trauma center. This 2,200-bed hospital has been designated exclusive for COVID-19 patients for the duration of the pandemic. Patients aged 18 years and older and admitted to the ED with confirmed COVID-19 were considered eligible. Emergency physicians performed lung ultrasounds and calculated LUSS, which was tested for correlation with outcomes.

3. Results:

Primary endpoint was death from any cause. Secondary endpoints were ICU admission and endotracheal intubation for respiratory failure. Among 180 patients with confirmed COVID-19 who were enrolled (mean age, 60 years; 105 male), the average LUSS was 18.7 ± 6.8. LUSS correlated with findings on chest CT and was able to predict the estimated extent of parenchymal involvement (mean LUSS with < 50% involvement on chest CT, 15±6.7 vs. 21±6.0 with >50% involvement, p<0.001), death (AUC 0.71, OR 1.13, 95%CI 1.07 to 1.21; p < 0.001), endotracheal intubation (AUC 0.75, OR 1.17, 95%CI 1.09 to 1.26; p < 0.001), and ICU admission (AUC: 0.71, OR 1.14, 95%CI 1.07 to 1.21; p < 0.001).

4. Conclusion:

LUSS was a good predictor of death, ICU admission, and endotracheal intubation in COVID-19 patients.

5. Trial Registration

This protocol was approved by the local Ethics Committee number 3.990.817 (CAAE: 30417520.0.0000.0068).

Background

The novel coronavirus disease 2019 (COVID-19) poses an immense, urgent threat to global health (1). The whole world is witnessing as health care systems, and Emergency Departments in particular, are overwhelmed by the COVID-19 pandemic (2). Adequately managing available resources may be the key...
point to overcoming the surge of patients and saving lives (3). In this context, tools to assess disease severity and prognosis in COVID-19 patients are one of the most important assets in reducing the burden on Emergency Departments.

Prediction models that combine several variables or features to estimate the risk of poor outcome from COVID-19 infection could assist medical staff in triaging patients and allocating limited healthcare resources (1). Most models developed to date combine clinical, laboratory, and imaging parameters and are indeed helpful (4). However, all carry a high risk of bias, and none has been extensively tested under routine circumstances (1).

Moreover, the symptoms of COVID-19 vary widely, from asymptomatic disease to severe pneumonia with life-threatening complications (5). Severe illness usually begins approximately one week after the onset of symptoms, and a striking feature of COVID-19 is the rapid progression to respiratory failure (6). Patients with severe COVID-19 commonly meet the criteria for the acute respiratory distress syndrome (ARDS), which is defined as the acute onset of bilateral infiltrates, severe hypoxemia, and lung edema that is not fully explained by cardiac failure or fluid overload (7, 8).

Since most patients with severe COVID-19 have pneumonia, imaging is particularly useful for diagnosis and possibly able to predict adverse outcomes (9). Unfortunately, there are downsides. Chest radiography is not sensitive for COVID-19, and usually shows no abnormal findings in the early stages of infection (10). Chest computed tomography (CT) detects early COVID-19 pneumonia with high sensitivity, and small studies suggest that it can be used to assess disease severity and guide clinical management (9–12). However, obtaining a CT scan requires transporting critically ill patients (13), exposes the patient to radiation (14), and demands that rigorous infection control procedures be followed before scanning subsequent patients (15). Moreover, CT equipment is not widely available, especially in developing countries (16).

Lung ultrasound is widely used in Emergency Departments because it is user-friendly, broadly available, low-cost, and has high accuracy for diagnosing pulmonary diseases (17). Recent reports suggest that, in COVID-19 patients, lung ultrasound could be useful in several scenarios: to quantify severity of lung involvement in periodic assessments; to look for findings suggestive of pneumonia; and to monitor the dynamic effects of mechanical ventilation and recruitment maneuvers on lung aeration (3, 18). However, there are no prospective studies demonstrating that lung ultrasound can change management or predict outcomes in COVID-19.

The lung ultrasound score (LUSS) is a semiquantitative score that measures lung aeration loss caused by different pathological conditions (19, 20). Several studies have demonstrated that LUSS is accurate for assessing lung reaeration following antimicrobial therapy in ventilator-associated and community-acquired pneumonia (19).

Within this context, we hypothesized that LUSS at hospital admission would be able to predict outcomes in patients with COVID-19.
Methods

STUDY DESIGN AND SETTING:

This prospective cohort study was conducted from 14 March through 6 May 2020 in the Emergency Department (ED) of Hospital das Clínicas da Universidade de São Paulo (HC-FMUSP), a 2,200-bed urban, academic medical center comprising five institutes and two auxiliary hospitals. During the pandemic, the HC-FMUSP ED has been designated exclusively to the reception and care of patients with COVID-19.

The study protocol was approved by the local Ethics Committee (opinion number 3.990.817; CAAE: 30417520.0.0000.0068), which also waived the need for written informed consent. The present report adheres to the STROBE guidelines.

Selection Of Participants:

Patients aged 18 years and older who were admitted to the ED with suspected or confirmed COVID-19 were considered eligible. Patients who had advance directives (do not intubate or do not resuscitate) and pregnant women were excluded.

Patients who did not test positive for COVID-19 by reverse-transcriptase polymerase chain reaction (RT-PCR) assay of nasopharyngeal swab or tracheal aspiration specimens were also excluded (Fig. 1).

Interventions:

After selection, patients were asked for permission to be included in the study. Once permission has been granted, a researcher interviewed the patient and collected data using a standardized form in the TeamScope® software environment (TeamScope, BV). The following variables were collected: age, sex, day of illness, admission to the Emergency Department, and signs and symptoms on admission.

A second, blinded investigator who was not involved in patient care was called in to perform the lung ultrasound. Due to the investigators’ limited availability, scans were performed only from Monday through Thursday, from 8:00 a.m. to 8:00 p.m. The investigators were aware of the presenting symptoms and the most visible physical signs, but were blinded to all the other clinical information, including radiologic findings.

Subsequently, a third investigator prospectively completed a second questionnaire in the RedCap® software environment (Vanderbilt University) with the following variables collected from electronic medical records: chest CT findings, hospitalization outcome (including hospital discharge and death), need for ICU referral, and need for invasive mechanical ventilation.
Chest CT was performed only for clinical purposes, independently of the study protocol. Blinded attending radiologists reported chest CTs as consistent or inconsistent with the most typical pattern described in COVID-19, which includes ground-glass opacities, sometimes with superimposed interlobular septal thickening (crazy paving), consolidations and reversed halo, presenting a bilateral multilobar distribution, predominantly peripheral, with mild predilection for the posterior regions and lower lobes), and gave a visual estimate of the extent of parenchymal involvement (greater or lesser than 50%).

**Luss Protocol**

We performed transthoracic lung ultrasound with a Sonosite Edge II portable ultrasound system and a 2-to 5-MHz convex probe. The investigators were four emergency medicine attending physicians with at least 5 years’ experience in point-of-care emergency ultrasonography.

The patient was preferably examined in the sitting position. When this position could not be maintained due to clinical deterioration or poor compliance, the examination was performed in the supine or semi-recumbent position. The posterior lung fields were scanned in the sitting position or, when not feasible, by turning the patient onto lateral decubitus on both sides successively.

The Lung Ultrasound Score (LUSS) protocol involves the examination of 12 lung regions: upper and lower parts of the anterior, lateral, and posterior aspects of the left and right chest wall. Each region was scored according to four ultrasound aeration patterns: 0 points for normal aeration, characterized by the presence of lung sliding with horizontal A lines and, occasionally, one or two isolated vertical B lines; 1 point in the presence of moderate loss of lung aeration (either multiple well-defined and spaced B1 lines, issued from the pleural line or from small juxtapleural consolidations and corresponding to interstitial edema, or coalescent B2 lines, issued from the pleural line or from small juxtapleural consolidations, present in a limited portion of the intercostal space and corresponding to localized alveolar edema); 2 points for severe loss of lung aeration, characterized by multiple coalescent vertical B2 lines issued either from the pleural line or from juxtapleural consolidations, detected in the whole area of one or several intercostal spaces and corresponding to diffuse alveolar edema; and 3 points for complete loss of lung aeration, resulting in consolidation and characterized by the presence of tissue pattern containing either hyperechoic punctiform images representative of static air bronchograms, or hyperechoic tubular images representative of dynamic air bronchograms. For a given region of interest, we allocated points according to the worst ultrasound pattern observed. The final LUSS is the sum of points in all 12 regions, and ranges from 0 to 36.

**Outcomes**

The primary endpoint of the study was death from any cause by 20 July 2020. Secondary endpoints were any ICU admission and endotracheal intubation for respiratory failure by 20 July 2020. We chose this date solely to expedite communication of our findings.
Analysis

Data are presented as percentages for categorical variables and mean ± standard deviations for continuous variables. All data were tested for normality using the Kolmogorov–Smirnov test. When distribution was normal, a two-tailed Student's t-test was used. Logistic regression was performed to explore the associations of LUSS with intubation, ICU admission, and mortality. We calculated the area under the receiver operating characteristic (ROC) curve for each regression and accepted statistical significance at \( p \leq 0.05 \). All analyses were performed in Stata 13 software (College Station, TX, USA).

Results

CHARACTERISTICS OF STUDY SUBJECTS:

During the study period, 1606 consecutive patients were admitted to our ED. Of these, 506 patients were confirmed to have COVID-19 by RT-PCR, of whom 180 were enrolled (Fig. 1). The median age was 60 years, and 105 patients (58%) were men. Clinical and laboratory characteristics of the patients are summarized in Table 1.
Table 1  
Baseline characteristics of patients, vital signs, and laboratory results at admission

| Characteristic (N = 180)                             | Median (IQR) or N (%) |
|------------------------------------------------------|-----------------------|
| Age (y)                                              | 60 (49–70)            |
| Sex                                                   |                       |
| Female                                               | 75 (42%)              |
| Male                                                 | 105 (58%)             |
| Comorbidities                                        |                       |
| Hypertension                                         | 98 (55%)              |
| Diabetes                                             | 69 (39%)              |
| Congestive heart failure                             | 25 (14%)              |
| Chronic respiratory disease                          | 15 (8%)               |
| Chronic and end-stage renal disease                  | 11 (6%)               |
| Duration of symptoms before hospital admission (days)| 7 (5–10)              |
| Oxygen saturation < 93% **                           | 78 (43%)              |
| Oxygen saturation – Median (IQR)                      | 93 (90–96)            |
| Received supplemental oxygen at triage               | 136 (76%)             |
| Type of supplemental oxygen                          |                       |
| Nasal cannula                                        | 53 (30%)              |
| Nasal cannula oxygen flow                            | 2.8 ± 1.4 L O₂/min    |
| Venturi mask (FiO₂ = 50%)                            | 1 (1%)                |
| Non-rebreather mask                                  | 35 (19%)              |
| Non-rebreather mask oxygen flow                      | 11.9 ± 3.5 L O₂/min   |
| Mechanical ventilation                               | 47 (27%)              |
| Mechanical ventilation FiO₂                          | 86.5 ± 21.8%          |
| Respiratory rate > 24 breaths/min**                  | 91 (51%)              |

*IQR: interquartile range; LUSS: lung ultrasound score

* Mean ± standard deviation

** Most of these patients did not tolerate removal of supplemental oxygen to measure at room air.
### Characteristic (N = 180)

| Characteristic                                      | Median (IQR) or N (%) |
|-----------------------------------------------------|-----------------------|
| Respiratory rate – Median (IQR)                     | 25 (20–30)            |
| Heart rate > 100 beats/min                          | 53 (29%)              |
| Heart rate – Median (IQR)                           | 92 (80–103)           |
| PaO2/FiO2 on admission, median (IQR)                | 120 (64–230)          |
| LUSS*                                               | 18.7 ± 6.8            |

IQR: interquartile range; LUSS: lung ultrasound score

* Mean ± standard deviation

** Most of these patients did not tolerate removal of supplemental oxygen to measure at room air.

### Main Results

All patients underwent LUSS on the day of Emergency Department admission. The average LUSS was 18.7, with a standard deviation of 6.8.

Among the 170 patients who reached a definitive outcome at the study endpoint, 109 (64%) were discharged alive and 61 (36%) died; the remaining 10 patients were still in hospital.

As of 20 July 2020, 74 patients (56%) had been treated in the ICU, and 52 (39%) received invasive mechanical ventilation. Forty-seven patients were already intubated at admission or were intubated shortly after admission, before lung ultrasound could be performed, and were excluded from intubation and ICU analysis. The mean time between lung ultrasound and intubation was 2.1 ± 1.9 days with a median of 2 days.

Among the 142 patients who underwent chest CT on admission, LUSS was consistently associated with evidence of COVID-19 on CT. COVID-19 pneumonia involving > 50% of lung parenchyma on chest CT was predictive of all-cause mortality. The mean LUSS in patients with < 50% involvement on chest CT was 15 ± 6.7, vs. 21 ± 6.0 in those with > 50% involvement (p < 0.001).

Duration of symptoms before admission did not correlate with LUSS. We also performed a univariate analysis with symptoms at admission and laboratory tests, and found no correlation with mortality in our patients. However, age and bilateral lung involvement > 50% on chest CT were accurate predictors of death (Fig. 3).

As observed in Figs. 2 and Table 2, LUSS was able to predict death, endotracheal intubation, and ICU admission. ROC curves were also plotted to define useful cutoffs for LUSS scores, as shown in Table 3.
Table 2
LUSS and Outcomes in Patients with COVID-19.

| Primary Outcome          | Patients        | LUSS (mean ± SD) | OR (95%CI)     | p**   |
|--------------------------|-----------------|------------------|----------------|-------|
| Deceased                 | 61 / 170 (36%)  | 21.6 ± 4.9       | 1.13 (1.07–1.21)* | < 0.001 |
| Discharged alive         | 109 / 170 (64%) | 16.7 ± 4.9       |                |       |
| Secondary Outcomes       |                 |                  |                |       |
| Intubated                | 52 / 133 (39%)  | 21.3 ± 4.9       | 1.17 (1.09–1.26) | < 0.001 |
| Not intubated            | 81 / 133 (61%)  | 15.2 ± 7.1       |                |       |
| Admitted to ICU          | 74 / 133 (56%)  | 20.0 ± 5.9       | 1.14 (1.07–1.21) | < 0.001 |

*Adjustment for age did not change results.

**p-values calculated by Student’s t-test.

Table 3
LUSS and Outcome Cutoffs

|                             | LUSS cutoff | Sensitivity | Specificity |
|-----------------------------|-------------|-------------|-------------|
| Discharged alive            | < 16        | 40%         | 90%         |
| Deceased                    | ≥ 26        | 23%         | 90%         |
| Not intubated during hospital stay | < 15   | 41%         | 90%         |
| Intubated during hospital stay | ≥ 25   | 27%         | 93%         |
| Not admitted to ICU         | < 13        | 31%         | 91%         |
| Admitted to ICU             | ≥ 25        | 22%         | 93%         |

Discussion

The COVID-19 pandemic has brought to Emergency Departments around the world a flock of patients complaining of fever, cough, and dyspnea. Proper assessment of the severity and extent of pulmonary involvement is of paramount importance to select patients who will be admitted to hospital wards or ICUs, and thus to ensure adequate management of overwhelmed healthcare resources.

To date, this is the first study to demonstrate that lung ultrasound using the LUSS protocol in the Emergency Department, is a reliable instrument to evaluate patients with COVID-19 pneumonia, can be used to predict endotracheal intubation and mortality, and, therefore, is a useful tool for indicating whether in-hospital treatment and ICU admission will be necessary.
Several published papers have reported the use of clinical and laboratory tests for initial evaluation of COVID-19 patients. For example, the combined results of D-dimer and IL-6 assays showed high sensitivity and specificity in a Chinese study with 43 patients \(^4\); however, these measurements (particularly IL-6) are not widely available, and results can be considerably delayed. Time is not a luxury we have at crowded emergency departments in the best of circumstances, and even less so during the COVID-19 pandemic.

Chest radiography is not sensitive, particularly in the early stages of the disease, while lung CT has been the gold standard for diagnosis of COVID-19 pneumonia. The most common CT pattern has usually been described as one of bilateral ground-glass opacities, with interspersed areas of consolidation. In more severe cases, bilateral multiple lobular areas of consolidation are found \(^11\). Nonetheless, CT is not as widely available, particularly in rural areas or developing countries. Moreover, transporting patients from the emergency room to the CT scanner can be a difficult and risky task, considering that many patients are under ventilatory support, and increases the risk of healthcare personnel contamination.

Taken together, these findings demonstrate that bedside ultrasound is a viable instrument to evaluate pneumonia severity in COVID-19 patients. Transthoracic lung ultrasound is a noninvasive, easily repeatable, and useful diagnostic tool for bedside use in critically ill patients. The use of LUSS to quantify and monitor lung aeration has been described in critically ill patients with ARDS \(^21\). In COVID-19 patients, contrary to what has been described in ARDS, interstitial patterns and consolidations contribute almost equally to lack of aeration \(^22\). Rather, the severity of respiratory impairment seems to be related to the overall proportion of lung tissue showing ground-glass opacities \(^23\).

In the present study, all lung ultrasounds were performed on the day of patient admission. Duration of symptoms before hospital admission was not significantly correlated with LUSS and did not predict outcomes. Age was an independent predictor of death; however, LUSS remained significantly correlated with death, ICU admission, and endotracheal intubation despite adjustment for age or days of symptoms.

Some limitations of this study must be mentioned. First, it was a single-center study, conducted at a large academic hospital in São Paulo, Brazil. Second, there are potential sources of error in assessing B lines. This depends on the type of probe, wavelength emission frequency, and filter technique used for artifact suppression. To minimize this, lung ultrasound was performed only by physicians who had ample experience with the method. Third, the absence of data on patients who remained hospitalized at the date of final data collection may have biased the findings. It would have been better to wait for all patients to achieve a definite outcome; however, since our results are already significant and we believe they are relevant, we chose to sacrifice these data for the sake of reporting our findings more quickly. Last but not least, the level of expertise required to detect small changes in LUSS, together with operator dependence, may limit the clinical applicability of bedside transthoracic lung ultrasound.

In spite of these limitations, we report that LUSS is a good tool to predict death or endotracheal intubation in patients with COVID-19 pneumonia. This finding is very useful and can help emergency physicians who have to rapidly decide about the disposition of their patients in the Emergency Department.
Conclusion

In this study, LUSS was a good predictor of death, ICU admission, and endotracheal intubation in patients with COVID-19. The study provides support for further research, ideally combining clinical, laboratory, and imaging parameters, to estimate the risk of poor outcomes from COVID-19 infection.

Declarations

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was approved by the local Ethics Committee (CAPpesq, number 3.990.817; CAAE: 30417520.0.0000.0068), which also waived the need for written informed consent.

CONSENT FOR PUBLICATION

All authors have read and approved the submission of the manuscript. The manuscript has not been published and is not being considered for publication elsewhere, in whole or in part, in any language.

AVAILABILITY OF SUPPORTING DATA

The data that support the findings of this study are available from the corresponding author JCGA upon reasonable request.

COMPETING INTERESTS

The authors declare they have no conflicts of interest that might constitute an embarrassment to the publication of this article.

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AUTHORS' CONTRIBUTIONS

JCGA, JFMM, and HPS conceived of the presented idea. JCGA, JFMM, SCCR, and RABN performed the lung ultrasound. The COVID USP Registry Team conducted patient interviews and collected data from medical records. JCGA and JFMM ran statistical analyses. JCGA, JFMM, CGB, VPC, FLN, RABN, LOM, and HPS wrote the manuscript. All authors provided critical feedback and helped shape the research, analysis, and manuscript.

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**Figures**
Figure 1

Diagram of Patient Flow Through the Study * Lung ultrasound was performed only from Monday through Thursday, from 8:00 a.m. to 8:00 p.m. a. 47 were already intubated before the LUSS protocol was performed. b. As of 20 July 2020, 10 patients remained in hospital.
Figure 2

ROC Curves and Outcomes. a. For LUSS versus Death. b. For LUSS versus Intubation. c. For LUSS versus ICU Admission.
COVIDSCORE = 3 x LUSS + Age