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LUNG ULTRASOUND SEVERITY INDEX: DEVELOPMENT AND USEFULNESS IN PATIENTS WITH SUSPECTED SARS-COV-2 PNEUMONIA—A PROSPECTIVE STUDY

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Abstract—Coronavirus disease 2019 (COVID-19) has spread across the world with a strong impact on populations and health systems. Lung ultrasound is increasingly employed in clinical practice but a standard approach and data on the accuracy of lung ultrasound are still needed. Our study’s objective was to evaluate lung ultrasound diagnostic and prognostic characteristics in patients with suspected COVID-19. We conducted a monocentric, prospective, observational study. Patients with respiratory distress and suspected COVID-19 consecutively admitted to the Emergency Medicine Unit were enrolled. Lung ultrasound examinations were performed blindly to clinical data. Outcomes were diagnosis of COVID-19 pneumonia and in-hospital mortality. One hundred fifty-nine patients were included in our study; 66% were males and 63.5% had a final diagnosis of COVID-19. COVID-19 patients had a higher mortality rate (18.8% vs. 6.9%, p = 0.04) and Lung Ultrasound Severity Index (16.14 [8.71] vs. 10.08 [8.92], p < 0.001) compared with non-COVID-19 patients. This model proved able to distinguish between positive and negative cases with an area under the receiver operating characteristic (AUROC) equal to 0.72 (95% confidence interval [CI]: 0.64–0.78) and to predict in-hospital mortality with an AUROC equal to 0.81 (95% CI: 0.74–0.86) in the whole population and an AUROC equal to 0.76 (95% CI: 0.66–0.84) in COVID-19 patients. The Lung Ultrasound Severity Index can be a useful tool in diagnosing COVID-19 in patients with a high pretest probability of having the disease and to identify, among them, those with a worse prognosis. (E-mail: soccorsa.sofia@ausl.bologna.it) © 2021 World Federation for Ultrasound in Medicine & Biology. All rights reserved.

Key Words: Lung ultrasound, Point-of-care-ultrasound, SARS-COV-2 pneumonia, Prognostication, Emergency department.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) encompasses a wide range of clinical manifestations caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel human betacoronavirus first isolated in December 2019 in Wuhan, China (Coronaviridae Study Group of the International Committee on Taxonomy of Viruses 2020). Since then, SARS-CoV-2 infection has rapidly spread across the world, and on January 30th, 2020, the World Health Organization declared an International Public Health Emergency (World Health Organization 2020). The pandemic has had a huge impact on the health systems and people of affected countries, causing a strong increase in demand for care and heavy social and economic consequences. Although SARS-CoV-2 has pleiotropic actions (Gupta et al. 2020), its main target is the lung. Through initial alveolar damage, the infection can result in mild, moderate or severe pneumonia. Therefore, chest imaging, and in particular computed tomography (CT), became a milestone in the diagnosis of COVID-19 (Han et al. 2020), especially in the early stages of the pandemic, because of the poor availability and reliability of microbiological diagnostic...
Sofia et al. 2020; Tan et al. 2020; Vetrugno et al. 2020; (Bonadia et al. 2020; Dargent et al. 2020; Lu et al. 2020; pathways of SARS-CoV2 pneumonia. The latest reports potentially useful tool in the context of the current pan-

hospital mortality of patients with respiratory distress involvement, in relation to COVID-19 diagnosis and in-

designed to measure the quality and extent of lung ultrasound (US), having an acknowledged role in the diagnosis and staging of many lung diseases (Volpicelli et al. 2012), has been repeatedly evoked as a potentially useful tool in the context of the current pandemic and has been included in many clinical diagnostic pathways of SARS-CoV2 pneumonia. The latest reports (Bonadia et al. 2020; Dargent et al. 2020; Lu et al. 2020; Sofia et al. 2020; Tan et al. 2020; Vetrugno et al. 2020; Xing et al. 2020; Yasukawa and Minami 2020) claim its beneficial use in such a context. However, published studies are generally based on score systems that do not consider the patchy US appearance of SARS-CoV-2 pneumonia caused by the different patterns displayed in the same area. In our opinion, this issue could be relevant to better assessment of lung US diagnostic characteristics in SARS-CoV-2 pneumonia.

This study aimed to propose and validate the Lung Ultrasound Severity Index (LUSI), a novel US score designed to measure the quality and extent of lung involvement, in relation to COVID-19 diagnosis and in-hospital mortality of patients with respiratory distress admitted for suspected COVID-19.

METHODS

Study design

This observational prospective study was conducted in the Emergency Medicine Unit (EMU) of Maggiore Hospital, Largo Bartolo Nigrisoli, Bologna, Italy. All patients aged >18 y consecutively admitted to our EMU between March 6, 2020, and April 5, 2020, for suspected COVID-19 as the main disease underwent a standard Lung US examination and were included in our study if informed consent was given. According to our institutional protocol, a “suspected COVID-19” is a patient with respiratory distress, fever, cough, anosmia or dysgeusia, with or without lung abnormalities, in which SARS-CoV-2 infection is a possible cause of the clinical picture. The study was conducted in accordance with the Declaration of Helsinki. All lung US examinations were acquired and interpreted individually by an emergency medicine physician or an emergency medicine resident, both with at least 5 y of experience in emergency US, including chest US. Patients admitted to the EMU during the working hours of one of the two operators were recruited for the present study. The local institutional ethics committee approved the study protocol. Each patient underwent a lung US examination on admission to the EMU, with the operators blind to clinical, radiological and laboratory data. Then lung US records acquired by one of the two operators were reviewed blindly by the other to assess inter-observer variability. Past medical records, vital signs, laboratory findings and in-hospital death of the included patients were retrospectively collected. Clinical presentation, vital signs and laboratory data refer to the admission in the emergency department (ED). Anion blood gas analysis (ABGA) occurred close to the lung US examination, at most 8 h before or later. COVID-19 is a microbiological diagnosis. The diagnostic standard was the reverse transcription polymerase chain reaction (RT-PCR) assay to detect SARS-CoV-2 RNA on the nasopharyngeal swab. If the swab was not diagnostic and a high suspicion for COVID-19 persisted, it was repeated at least three times. Patients with repeated negative swabs, low clinical suspicion and another underlying cause of respiratory distress were considered COVID-19 negative.

Lung US scanning technique

Included patients underwent a standard lung US examination as follows: three areas were defined for each hemithorax, bounded by the sternal marginal, anterior axillary, the posterior axillary and the dorsal marginal lines. Each area was further subdivided into upper and lower sectors, delimited by the third intercostal space in the front and side areas and by the lower scapular edge in posterior areas. Thus, 12 thoracic areas were defined, numbered from 1 to 6 on each side of the chest (Fig. 1). The whole extension of all areas was scanned, with the probe moved continuously from border to border. Patients were in a sitting position when examined. A video at least 6-s long was recorded for each of the 12 areas defined. All scans were performed using the Esaote MyLab XPRO30 (Esaote, Genoa, Italy) with a convex probe at a 10 ± 3 cm scan depth focused on the pleural line. The convex probe is the most common in emergency departments and enables exploration of large thoracic areas. Moreover, a lower-frequency probe, reducing US attenuation, allows better visualization of all lung ultrasonographic findings, from A-lines to major parenchymal consolidation and pleural effusion. During lung US examinations, all locally indicated personal protective equipment was used, including a disposable cap, a filtering facepiece 2, a protective suit, two pairs of disposable latex gloves and disposable shoe covers. The facility was sanitized before and after each exam with a 0.05% sodium hypochlorite solution.

Lung ultrasound findings

Main US findings (A-lines, B-lines, and consolidations) were defined according to the International Consensus Conference on Lung Ultrasound (Volpicelli 2012). After each scan, all findings were
recorded according to the area examined on a lung US datasheet. Each finding accounted for a different score, to measure various degrees of alveolar aeration impairment, as follows:

- A-pattern: A-lines without other artifacts, 0 points (Fig. 2)
- Isolated B-lines: one or no more than three distant, well-isolated B-lines, 1 point (Fig. 3)
- Isolated subpleural consolidation: in a context of A-pattern, presence of one consolidation <2 cm with a posterior vertical artifact, extending to the bottom of the screen without fading and moving synchronously with lung sliding, 1.5 points (Fig. 4)
- Non-confluent B-lines: multiple B-lines that do not completely erase A-lines, 2 points (Fig. 5)
- Confluent B-lines: multiple B-lines that completely erase A-lines, 3 points (Fig. 6)
- Confluent subpleural consolidations (CSpCs): multiple consolidations <2 cm in depth with a posterior vertical artifact, 4 points (Fig. 7)
- Parenchymal consolidation >2 cm: subpleural consolidation >2 cm in-depth, 5 points (Fig. 8)
- Pleural effusion: anechoic fluid within the pleural space, 0 points (Fig. 9).
Scores of each area were added to calculate a regional Lung Ultrasound Severity Score (rLUSS). The Lung Ultrasound Severity Score (LUSS) was obtained by summing all rLUSS values. The number of different US patterns found in each area defined the regional Lung Ultrasound Heterogeneity Score (rLUHS). The regional Lung Ultrasound Severity Index (rLUSI) was computed as rLUSS/rLUHS for each area. Finally, the LUSI was calculated as the sum of all rLUSI values, and the Lung Ultrasound Severity Score (LUSS) was obtained by summing all rLUSS values.

**Lung US severity index**

Fig. 4. Isolated subpleural consolidation. The *red arrow* indicates an isolated subpleural consolidation.

Fig. 5. Non-confluent B-lines. *Red arrows* indicate two B-lines moving from the pleural line, non-completely erasing the posterior pleural reverberations (*green arrow*).

Fig. 6. Multiple confluent B-lines completely erasing the posterior pleural reverberation of the pleural line. The *red arrow* indicates the pleural line with a “with-lung” appearance.

Fig. 7. Multiple subpleural consolidations. *Red arrows* indicate the thickening of the irregular pleural line with a posterior “with-lung appearance” because of the presence of trapped air.

Ultrasound Heterogeneity Score (rLUHS). The regional Lung Ultrasound Severity Index (rLUSI) was computed as rLUSS/rLUHS for each area. Finally, the LUSI was calculated as the sum of all rLUSI values, and the Lung Ultrasound Severity Score (LUSS) was obtained by summing all rLUSS values.

Fig. 8. Large subpleural consolidation. The *red arrow* indicates the pulmonary consolidation and the “hepatic-like” aspect of the lung. The *green arrow* indicates the air bronchograms: hyperechogenic artifact caused by the presence of trapped air.

Fig. 9. The *red arrow* indicates the anechoic free fluid in the thoracic cavity, above the diaphragm on the right side of the body. The *red star* indicates the liver.
Ultrasound Heterogeneity Score (LUHS) was calculated as the sum of all \( rLUHS \) values. See Table 1 for the LUSI record sheet and calculator.

Statistical analysis

Normally distributed data were expressed as the mean and standard deviation; non-normally distributed data were described as the median and interquartile range; categorical data were reported as absolute number and percentage. Normally distributed data were compared via an independent sample \( t \)-test. Non-normally distributed data were compared via a Mann–Whitney \( U \)-test. Pearson’s \( \chi^2 \)-test was used to compare categorical dependent variables among at least two independent groups. The correlation between two independent parametric continuous variables was determined using Pearson’s correlation. Receiver operator characteristic (ROC) curves were determined for the relationship of LUSS, LUHS and LUSI with the severity of pneumonia. The optimal threshold for best discrimination was calculated using the Youden index. Inter-observer reliability of LUSI was assessed with Cohen’s \( \kappa \). Statistical analyses were performed using SPSS Version 23 (Apache Software Foundation, Chicago, IL, USA) and MedCalc Version 14.8.1 for Windows (MedCalc Software Ltd.).

RESULTS

Clinical characteristics of all patients

One hundred fifty-nine patients were included in the study; their mean age was 64.6 y, and 66% were male. Forty-nine percent had respiratory failure (P/F ratio \(< 300 \) mm Hg) on admission; 63.5% of patients were positive on the standard test RT-PCR for SARS-CoV-2 and received a final diagnosis of COVID-19. ABGAs revealed higher pH values and lower pCO\(_2\) levels and P/F ratios in the COVID-19 group (Table 2). Twenty-three (14.5%) of the included patients died during the study lag, 19 of the 23 (82%) were from the COVID-19 group. Among COVID-19 patients, those who died were older and had a higher heart rate, higher respiratory rate and lower blood oxygenation at presentation compared with surviving COVID-19 patients.

Lung US characteristics of all patients

The included patients resulted in a total of 3779 six-second videos recorded, with a mean of 23.8 videos for each patient. The mean duration of examination was 8.05 min. The emergency medicine physician and emergency medicine resident had high concordance (Cohen’s \( \kappa = 0.958 \), 95% confidence interval [CI]: 0.906–0.981). Regarding lung US findings, COVID-19 patients had significantly fewer A-pattern areas and a larger number of areas with confluent B-lines and CSPCs. The patchy distribution of the lung US findings—measured as lung US heterogeneity—appeared as a constant in all lung US images. LUSS, LUSI and LUHS were calculated for all patients, with means of 29.95, 13.96 and 21.6, respectively. COVID-19 patients had higher LUSS, LUSI and LUHS values. Dead COVID-19 patients had a higher LUSS and LUSI values compared with survivors, while there were no significant differences in LUHS (Table 2). Moreover, both LUSI and LUSS exhibited a strong inverse correlation with P/F, with Pearson’s \( r \) values of \(-0.61 (p < 0.001) \) and \(-0.599 (p < 0.001) \), respectively, while LUHS had a weak correlation with P/F (\(-0.386, p\)
### Table 2. Clinical characteristics and outcomes of the included patients

|                        | All patients | COVID-19 patients | p Value | COVID-19 patients | p Value |
|------------------------|--------------|--------------------|---------|-------------------|---------|
|                        | Total N = 159 | No COVID-19 (N = 58) | COVID-19 (N = 101) |                   |         |
| Demographics           |              |                    |         |                   |         |
| Men, N (%)             | 105 (66)     | 34 (58.6)          | 71 (70.3) | 0.135             |         |
| Age, mean (SD), y      | 64.59 (16.63) | 65.4 (19.51)       | 64.13 (14.85) | 0.67              |         |
| Vital signs, mean (SD) |              |                    |         |                   |         |
| Heart rate, ppm        | 93.9 (18.28) | 98.45 (20.49)      | 91.33 (16.46) | 0.02              |         |
| Respiratory rate/min   | 20.63 (5.51) | 21.84 (6.35)       | 19.94 (4.87)  | 0.06              |         |
| Systolic blood pressure, mm Hg | 123.51 (18.45) | 126.27 (22.5) | 121.95 (15.61) | 0.2              |         |
| Diastolic blood pressure, mm Hg | 73.5 (10.09) | 73.95 (11.11) | 73.25 (9.51)  | 0.68              |         |
| Body temperature, °C   | 37.61 (0.98) | 37.47 (1.04)       | 37.7 (0.94)   | 0.16              |         |
| Anion blood gas analysis, mean (SD) |              |                    |         |                   |         |
| pH                     | 7.44 (0.05)  | 7.43 (0.05)        | 7.46 (0.04)  | <0.001            |         |
| pCO₂                   | 36.28 (6.41) | 38.9 (7.76)        | 34.9 (5.12)  | <0.001            |         |
| pO₂                    | 89.99 (33.99)| 97.1 (38.21)       | 86.3 (31.14) | 0.06              |         |
| Lactate                | 1.06 (0.5)   | 1.14 (0.61)        | 1.03 (0.43)  | 0.24              |         |
| p/F                    | 281 (104.18) | 318 (109.25)       | 261 (96.33)  | <0.001            |         |
| HCO₃                   | 25 (3.83)    | 25 (4.53)          | 24 (3.41)    | 0.18              |         |
| Lung ultrasound characters |              |                    |         |                   |         |
| No. of lung US scans, mean (SD) | 23.77 (7.02) | 21.41 (5.74)       | 25.12 (7.18) | 0.001             |         |
| Length of lung US scan, mean (SD), min | 8.05 (2.88) | 7.53 (2.66)        | 8.35 (2.98)  | 0.087             |         |
| Areas with A-pattern, median (IQR), N | 11 (10–12) | 12 (11–12)        | 11 (9–12)   | 0.01              |         |
| Areas with isolated B-lines, median (IQR), N | 2 (1–4) | 2 (0.75–4)        | 2 (1–4)    | 0.46              |         |
| Areas with isolated subpleural consolidations, median (IQR), N | 1 (0–2) | 1 (0–2)          | 1 (0–2)    | 0.095             |         |
| Areas with non-confluent B-lines, median (IQR), N | 0 (0–2) | 0.5 (0–2)        | 0 (0–2)    | 0.85              |         |
| Areas with confluent B-lines, median (IQR), N | 0 (0–1.25) | 0 (0–0.25)       | 0 (0–2)    | 0.014             |         |
| Areas with confluent subpleural consolidations, median (IQR), N | 4 (2–6) | 2 (0–4)          | 5 (3–7)    | <0.001            |         |
| Areas with pulmonary consolidation >2 cm, median (IQR), N | 0 (0–1) | 0 (0–1)        | 0 (0–1)    | 0.89              |         |
| Areas with pleural effusion, median (IQR), N | 0 (0–1) | 0 (0–1.5)       | 0 (0–1)    | 0.38              |         |
| Lung Ultrasound Severity Score, mean (SD) | 29.95 (18.25) | 22.62 (18.37)     | 34.16 (16.89) | <0.001            |         |
| Lung Ultrasound Severity Index, mean (SD) | 13.96 (9.25) | 10.08 (8.92)      | 16.14 (8.71) | <0.001            |         |
| Lung Ultrasound Heterogeneity Score, mean (SD) | 21.64 (5.53) | 19.84 (5.72)     | 22.67 (5.17) | 0.002             |         |
| Outcomes               |              |                    |         |                   |         |
| Total deaths, N (%)    | 23 (14.5)    | 4 (6.9)            | 19 (18.8)   | 0.04              |         |

IQR = interquartile range; p/F = partial pressure of oxygen/fraction of inspired oxygen.

< 0.001). With respect to the diagnosis of COVID-19, LUSI had an area under the receiver operating characteristic (AUROC) of 0.72 (95% CI: 0.64–0.78) with 63% sensitivity and 75% specificity for LUSI >13 (the best single cutoff), a sensitivity of 95% for a LUSI >2 and a specificity of 95% for a LUSI >26. However, no differences were noted in the AUROCs for LUSI, LUSS and LUHS (see Table 3).

Relative to in-hospital mortality, LUSI had the best AUROC: 0.81 (95% CI: 0.73–0.86), significantly greater than those of LUSS (difference between AUROCs equal to 0.062, p = 0.004) and LUHS (difference between AUROCs of 0.177, p < 0.001). LUSI has an odds ratio (OR) of 1.14, suggesting an increase of 14% in mortality risk for each point. The best Youden index was associated with a cutoff of 14.5, with sensitivity and specificity of 90% and 65.67%, respectively, while a cutoff of 4 had 95% sensitivity and a cutoff of 26 had 95% specificity.

**In-hospital deaths related to lung US characteristics in patients with COVID-19**

The number of acquired scans and length of US examination were similar in patients with COVID-19.
who died during in-hospital stay and survivors. COVID-19 patients who died had a smaller number of areas with A-pattern and a larger number of areas with nonconfluent B-lines, confluent B-lines and CSpCs.

The LUSI and LUSS were also higher in dead COVID-19 patients than in the survivors, but there were no differences in LUHS. Considering only the patient population with the final diagnosis of COVID-19, LUSI, LUSS and LUHS correlate with the P/F ratio impairment, even when data are adjusted for comorbidities (Pearson’s $r = -0.613$ [$p < 0.001$], $-0.569$ [$p < 0.001$] and $-0.284$ [$p = 0.01$], respectively). LUSI had the best AUROC for in-hospital mortality, equal to 0.76 (95% CI: 0.66—0.84), significantly greater than that of LUSS (difference between AUROCs of 0.07, $p = 0.018$) and LUHS (difference between AUROCs equal to 0.18, $p = 0.001$). LUSI had an OR of 1.124, with an increase of 12.4% in mortality risk for each point of the LUSI. The best Youden index was associated with a cutoff of 24, with sensitivity and specificity of 63.16% and 90.12% respectively, and a positive likelihood ratio of 6.7, while a cutoff >0 had 95% sensitivity and a cutoff of 30 had 95% specificity.

All lung US data are summarized in Tables 2 and 3.

### Table 3. Diagnostic and prognostic characteristics of the lung ultrasound scores

|                  | AUROC (95% CI) | Cutoff  | Sensitivity (%) | Specificity (%) | Odds ratio (95% CI) |
|------------------|---------------|---------|----------------|-----------------|---------------------|
| **In relation to in-hospital mortality** |               |         |                |                 |                     |
| LUSI             | 0.805 (0.735—0.864) | 14      | 90.91          | 65.67           | 1.14 (1.076—1.207) |
|                  | 3.63          | 95      |                | 15.67           |                     |
|                  | 26            | 40.91   |                | 95              |                     |
| LUSS             | 0.733 (0.657—0.8) | 37      | 65.22          | 73.53           | 1.045 (1.018—1.073) |
|                  | 11            | 95      |                | 16.9            |                     |
|                  | 57            | 20.87   |                | 95              |                     |
| LUHS             | 0.576 (0.495—0.654) | 20      | 69.57          | 48.53           | 1.037 (0.958—1.122) |
|                  | 13            | 95      |                | 8.31            |                     |
|                  | 31            | 4       |                | 95              |                     |
| **In relation to in-hospital mortality, COVID-19 patients only** |               |         |                |                 |                     |
| LUSI             | 0.76 (0.66—0.84) | 24      | 63.16          | 90              | 1.124 (1.052—1.2)   |
|                  | 0             | 95      |                | 1.23            |                     |
| LUSS             | 0.69 (0.59—0.78) | 37      | 68.42          | 68.29           | 1.042 (1.009—1.076) |
|                  | 0             | 95      |                | 1.22            |                     |
|                  | 58            | 21.58   |                | 95              |                     |
| LUHS             | 0.51 (0.41—0.61) | 20      | 68.42          | 37.8            | 1.005 (0.913—1.108) |
|                  | 12            | 95      |                | 2.38            |                     |
|                  | 31            | 5.26    |                | 95              |                     |
| **In relation to COVID-19 diagnosis** |               |         |                |                 |                     |
| LUSI             | 0.72 (0.64—0.78) | 13      | 63             | 75              | 1.09 (1.042—1.141)  |
|                  | 2             | 95      |                | 14.8            |                     |
|                  | 26            | 14.8    |                | 95              |                     |
| LUSS             | 0.69 (0.62—0.76) | 26      | 68.32          | 68.97           | 1.04 (1.019—1.062)  |
|                  | 7             | 95      |                | 24.14           |                     |
| LUHS             | 0.65 (0.57—0.73) | 17      | 88.12          | 37.93           | 1.11 (1.036—1.181)  |
|                  | 14            | 95      |                | 20.78           |                     |
|                  | 31            | 4.85    |                | 95              |                     |

AUROC = area under the receiver operating characteristic curve; LUSS = Lung Ultrasound Severity Score; LUSI = Lung Ultrasound Severity Index; LUHS = Lung Ultrasound Heterogeneity Score.

### DISCUSSION

Our study population is similar to those of other studies (Goyal et al. 2020; Wang et al. 2020; Wu et al. 2020; Zhou et al. 2020). Although many laboratory markers of inflammation strongly correlate with COVID-19 diagnosis and in-hospital mortality and only some lung US signs do the same, neither laboratory nor US signs, if individually evaluated, can correctly establish a final diagnosis. Only the integration of different clinical, laboratory and US features could suggest the correct diagnosis, as reported for many diseases (i.e., pulmonary edema, acute respiratory distress syndrome, bacterial or viral causes of pneumonia, contusions and others), where a similar loss of aeration in subpleural air spaces generates the same US signs. In lung diseases, a typical distribution and the association of different lung US or patterns could suggest the presence of a definite disease (Copetti et al. 2008; Volpicelli et al. 2012; Bekgoz et al. 2019; Weile et al. 2020).

Several authors have argued that lung US is potentially helpful in distinguishing between COVID-19 and non-COVID-19 patients in emergency departments (Bar et al. 2020; Narinx et al 2020; Tan et al. 2020) with
high inter-observer agreement (Yassa et al. 2020), representing a valid diagnostic aid in the management of patients with COVID-19 pneumonia (Dargent et al. 2020; Nouvenne et al. 2020; Zhao et al. 2020; Zieleskiewicz et al. 2020), which is also potentially able to reduce the number of health care providers exposed to possible contamination (Mongodi et al. 2020).

Recently Islam et al. (2021) reported an 86.4% (95% CI: 72.7–93.9) US pooled sensitivity and a 54.6% (95% CI: 35.3–72.6) US pooled specificity for the diagnosis of COVID-19 pneumonia. Moreover, they emphasize that data required to properly evaluate the diagnostic performance of various index tests are lacking and suggest future studies targeting positive US findings and improving transparency and reporting to allow a more effective data extraction. Despite a large number of published studies on lung US, there is no consensus on the evaluation of lung US artifacts and on the best way to grade pulmonary involvement in the setting of suspected COVID-19 patients admitted to the EMU. Each proposed lung US grading score lacks validation studies in large populations and different clinical settings and comparison with other imaging methods. Researchers should make every effort to reach an agreement on a standard of reference in the conduct, reporting and grading of pulmonary involvement in SARS-CoV-2 pneumonia. Most of the published studies are simply reports of locally used protocols without a clear population of validation (Manivel et al. 2020) and/or with a limited number of patients, mostly including only COVID-19 or selected patients (Bar et al. 2020; Bonadia et al. 2020). Moreover, these studies analyze some scores based on LUSS or only B-lines to evaluate lung US diagnostic accuracy (Haak et al. 2020; Schmid et al. 2020) or its prognostic value (Lichter et al. 2020), with variable results.

RT-PCR testing is used to diagnose a current infection, but its utility as a reference standard is constrained by its limited sensitivity (71%–98%). Chest CT is being widely used in the setting of suspected and confirmed cases of COVID-19; however, a recent Cochrane Systematic Review reported a pooled sensitivity equal to 87.9% (95% CI: 84.6–90.6) and specificity equal to 80% (95% CI: 74.9–84.3) for the diagnosis of SARS-CoV-2 pneumonia. According to the authors of the Systematic Review, these findings indicate that high-resolution CT is not able to differentiate COVID-19 from other causes of respiratory illness (Islam et al. 2021). An interesting observation came from Mongodi et al. (2017) whereby “the coalescence of B lines alone to define the severe loss of aeration is not suitable for non-homogeneous lung pathologies (acute respiratory distress syndrome, contusion), potentially leading to overestimation of aeration loss by lung US, thus suggesting that a modified and more detailed lung US scoring system could be more appropriate in such and similar diseases. Moreover, as already reported by Volpicelli et al. (2012), a semiquantitative approach to the definition of lung involvement on lung US is more precise than a qualitative one that evaluates only the presence of the worst pulmonary abnormality in each thoracic area.

Moving from these considerations, we decided to build a lung US model that could semiquantitatively represent the extent of lung involvement and could include the typical patchy appearance of SARS-CoV-2 pneumonia, reporting clearly all data regarding the technical aspects of the lung US examination and all data regarding the accuracy of the model, and testing it only with respect to the RT-PCR results, the only universally accepted standard reference for the diagnosis of COVID-19.

In our study, A-pattern and CSpCs were the two pulmonary signs that most differed in distribution between COVID-19 and non-COVID-19 patients, the former being most common in non-COVID-19 and surviving COVID-19 patients and the latter in COVID-19 and deceased patients. B-Lines in various degrees and aggregations did not differ between COVID-19 and non-COVID-19 patients; however, B-lines were more widespread in COVID-19 patients who died. That could be explained by the greater alveolar damage in these patients, caused by both infection (as in early phases of disease) and cytokine storm, possibly enhanced by coexisting comorbidities. As the inflammation progresses, B-line areas are complicated with the appearance of subpleural thicknesses as confluent subpleural consolidations. Conversely, consolidations larger than 2 cm are infrequent and do not differ significantly between groups, thus appearing not to be related to COVID-19 etiology.

Even if early B-lines or coalescent B-lines alone could not be used to distinguish between COVID-19 and non-COVID-19 patients, their irregular distribution throughout the lung along with CSpCs may reflect the patchy distribution of SARS-CoV-2 pneumonia as a diffuse pulmonary inflammatory syndrome at different stages of evolution and probably set up the elements enabling the capacity of LUHS and LUSI to distinguish between COVID-19 and non-COVID-19 patients.

The goal of LUSI is to better describe the coexistence of different lung lesions in the same lung area: in this way we have determined that this new scoring system, considering the coexistence of higher severity lesions with the presence of A-pattern areas, can better discriminate between patients with COVID-19 and those without and, with respect to only the COVID-19 patients, better identifies patients who will experience in-hospital mortality when compared with LUSS, the simple sum of the lung US findings. LUHS is the sum of the number of different US patterns found in each area—again, a simple but straightforward way to measure the
typical “patchy distribution” of SARS-CoV-2 pneumonia. LUSI puts together the strengths of both LUSS and LUHS, allowing for better prognostic ability, as reflected by the significantly higher AUROC value of LUSI. Moreover, the inclusion of this type of evaluation, on one hand, slightly complicates the calculation of the score, and on the other hand, includes and enriches the information coming from the different lung patterns. The dichotomous use of the scores allows them to be used more easily; however, LUSI can provide a lot of information along with the whole range of possible values regarding both the risk of COVID-19 and the short-term prognosis at the same time: In patients with possible COVID-19, an LUSI <2 has negative likelihood ratios of 0.25 for COVID-19 diagnosis and 0.29 for in-hospital mortality, excluding both in low pretest risk patients. Vice versa, a patient with an LUSI of 14 has positive likelihood ratios of 2.35 for COVID-19 and 2.3 for in-hospital mortality, indicating that the patient has a significantly higher risk of COVID-19 and poor prognosis.

Limitations
This study has several limitations. Its monocentric nature influences the mortality rate estimated with our local diagnostic and therapeutic algorithms. The study design was prospective and blinded only in collecting lung US findings; clinical data were recorded retrospectively. However, examiners could not be considered fully blinded to the patients: patients were admitted in the EMU only if suspected of having COVID-19, configuring the examiners, who were blinded to the clinical histories and diagnostic studies performed. We considered ABGAs closest to LUS examination; however, a few hours of oxygen support and ventilation could modify the P/F ratio. All lung examinations were made by clinicians experienced in lung US, and an evaluation of intra-observer variability is lacking. Finally, because of the lack of a standard of reference for lung US evaluation of SARS-CoV2 pneumonia in the determination, reporting and grading of the degree of pulmonary involvement on lung US, the score attributed to each lung US finding and the way in which LUSI is calculated were decided arbitrarily by the authors. Moreover, the correspondence between lung US findings and chest CT was not evaluated.

CONCLUSIONS
According to our results, LUSI has high diagnostic accuracy with respect to COVID-19 diagnosis and prognosis in both broad populations of patients with suspected COVID-19 and considering only COVID-19 patients. In such an epidemiological scenario, in which a huge number of patients are admitted for the same disease, early differentiation of patients with highly infectious disease from patients with other causes of respiratory distress is essential. While laboratory exams, nasopharyngeal swabs and high-resolution CT could take several hours to yield fundamental information, lung US can be performed in less than 10 min and LUSI can identify patients at higher risk of both COVID-19 disease and in-hospital mortality, resulting in better decisions on further imaging, urgent therapies and patient destination. Our study was performed in an EMU with a clear diagnostic and therapeutic protocol. Further studies are needed to understand the role of LUSI in achieving different clinical goals, such as in monitoring treatment or progression of the disease or in other epidemiological and medical settings.

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