Intensive Care Med (2020) 46:1707–1713
https://doi.org/10.1007/s00134-020-06186-0

ORIGINAL

Comparative study of lung ultrasound and chest computed tomography scan in the assessment of severity of confirmed COVID-19 pneumonia

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Abstract

Purpose: The relationship between lung ultrasound (LUS) and chest computed tomography (CT) scans in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia is not clearly defined. The primary objective of our study was to assess the performance of LUS in determining severity of SARS-CoV-2 pneumonia compared with chest CT scan. Secondary objectives were to test the association between LUS score and location of the patient, use of mechanical ventilation, and the pulse oximetry (SpO_2)/fractional inspired oxygen (FiO_2) ratio.

Methods: A multicentre observational study was performed between 15 March and 20 April 2020. Patients in the Emergency Department (ED) or Intensive Care Unit (ICU) with acute dyspnoea who were PCR positive for SARS-CoV-2, and who had LUS and chest CT performed within a 24-h period, were included.

Results: One hundred patients were included. LUS score was significantly associated with pneumonia severity assessed by chest CT and clinical features. The AUC of the ROC curve of the relationship of LUS versus chest CT for the assessment of severe SARS-CoV-2 pneumonia was 0.78 (CI 95% 0.68–0.87; $p < 0.0001$). A high LUS score was associated with the use of mechanical ventilation, and with a SpO_2/FiO_2 ratio below 357.

Conclusion: In known SARS-CoV-2 pneumonia patients, the LUS score was predictive of pneumonia severity as assessed by a chest CT scan and clinical features. Within the limitations inherent to our study design, LUS can be used to assess SARS-CoV-2 pneumonia severity.

Keywords: SARS-CoV-2, Chest computed tomography, Lung ultrasound, Diagnostic accuracy

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Introduction

Severe acute respiratory syndrome from coronavirus 2 (SARS-CoV-2) can be identified by a chest computed tomography (CT) scan [1, 2], typically showing ground-glass opacities, consolidation and interlobular septal thickening [3]. CT scanning has recently been shown to predict prognosis in these patients [4]. However, the use of chest CT scan is associated with adverse events and increased resource consumption [5, 6], and especially during this pandemic, the safety of transferring patients for CT scan remains uncertain at both individual and collective levels [7].

Lung ultrasound (LUS) has a high diagnostic accuracy for interstitial syndrome and alveolar consolidation, which is superior to chest radiograph [8, 9]. LUS has been recommended for the diagnosis and management of pneumonia [10], even during a previous viral pandemic [11]. During the current coronavirus disease 2019 (COVID-19) pandemic, LUS might reduce in-hospital transfers, the exposure of healthcare workers, and the risk of contamination of medical devices [12].

The main pattern of SARS-CoV-2 pneumonia using LUS is interstitial syndrome [13]. However, pneumonia may show different features using different diagnostic methods [3, 14]. To date, there has been case report [15], but few studies, comparing LUS with chest CT scan in patients with SARS-CoV-2 pneumonia.

The primary objective of our study was to assess the performance of LUS in determining COVID-19 pneumonia severity as assessed by chest CT scan. The secondary objectives were to test the association between LUS score and clinical features including the location of the patient, mechanical ventilation and pulse oximetry (SpO_2)/fractional inspired oxygen (FiO_2) ratio.

Methods

Design

This multicentre observational study was conducted in four university hospitals. We performed a retrospective analysis comparing the result of LUS examinations and chest CT, performed as part of routine care, in a convenience sample of patients in either the Emergency Department (ED) or the Intensive care unit (ICU). The ED and ICUs were located in different institutions.

Ethical considerations

The study was approved by the Committee for Research Ethics of the French Society of Anesthesia and Intensive Care Medicine (CERAR IRB000102542020-062). In accordance with French law, patients were informed regarding the use of their data for publication [16].

Population

We included adult patients admitted to the ED or ICU with confirmed SARS-CoV-2 infection, diagnosed by acute dyspnoea ($SpO_2 < 94\%$ and/or breathlessness [17]) together with a positive polymerase chain reaction (PCR) test in a nasopharyngeal or bronchoalveolar sample, who had a LUS exam at admission as well as a chest CT within the 24 h following the LUS.

Take-home message

Lung ultrasound is a possible alternative to chest CT scan, especially in resource-constrained environment, for the diagnosis of SARS-CoV-2 pneumonia severity. Given its high availability at the bedside, it may be widely used during the pandemic

Clinical features

At inclusion, each patient had a standard medical history and examination, monitoring of heart and respiratory rate, blood pressure and SpO_2, and arterial blood gas analysis.

For patients who were breathing spontaneously, FiO_2 was calculated as follows: $FiO_2 = (21 + 3^*$ oxygen flow (L/min)/100) [18].

For the purposes of analysis, we defined a low SpO_2/FiO_2 ratio as < 357 and high SpO2/FiO2 ratio as ≥ 357. This cut-off was chosen as it is equivalent to a PaO_2/FiO_2 ratio of 300 mmHg [19].

LUS and chest CT examination

LUS was performed within the first 2 h after admission. LUS was performed by imaging 12 lung regions, modified for critical illness. Thus, we imaged the posterior areas behind the posterior axillary line rather than in the paravertebral areas to avoid turning completely the patient [20]. LUS examinations were performed by emergency physicians or intensivists in charge of the patient [21, 22]. The skill of the operators was rated as follows [21]:

- Level 3 operator; LUS academic teacher with several publications in the field
- Level 2 operator; more than 25 supervised procedures and 200 non-supervised procedures
- Level 1 operator; at least 25 supervised procedures and less than 200 non-supervised procedures

Chest CT was performed at an appropriate time during the clinical course using a 128-slice CT (OPTIMA CT660, GE Healthcare, Chicago, Illinois, US) in the supine position, with the patient instructed to hold their breath after a deep inspiration. Most CT scans were non-contrast, low-dose chest CT.

Further details of the diagnostic procedures are available in the Electronic Supplemental Material (ESM 1).

Sample size considerations

The sample size calculation was performed to determine whether an area under the curve (AUC) of ≥ 0.80 was achieved for a receiver operator characteristic (ROC) plot of LUS versus chest CT scan. Based on the unpublished data, with a precision of 10% and an expected proportion of severe pneumonia on chest CT scan of 40%, the sample size required was 87. Taking into account the potential for incomplete data from LUS or chest CT scans, we included 100 patients.

Statistical analysis

The characteristics of the patients are summarized as medians and interquartile ranges for continuous variables, and as numbers and percentages for qualitative variables. Comparisons of patients' characteristics, CT and ultrasound parameters were performed between patients managed in the ED versus the ICU. The LUS score was compared between the three severity grades (mild, moderate, and severe pneumonia) on CT scan using an ANOVA test. The receiver operator characteristic (ROC) curve and AUC estimates were determined for the relationship of LUS score and CT scan to diagnose severity of pneumonia. The optimal threshold for best discrimination between non-severe and severe pneumonia was calculated using the Youden index. Sensitivity (Se), specificity (Sp), negative predictive value (NPV), positive predictive value (PPV) and DA are provided with their 95% confidence intervals (CIs). A grey zone represents a predictive test of low accuracy, that is, the Se and Sp are both < 90% [23]. Se and Sp curves were constructed to calculate the grey zone for an LUS score that was inconclusive for predicting severe pneumonia [24]. ROC and AUC, the optimal thresholds, Se, Sp, NPV, PPV and DA were determined for LUS score to diagnose consolidation, interstitial syndrome, pleural effusion and pleural irregularity according to the chest CT findings and use of mechanical ventilation. Mean LUS scores were compared between low and high SpO_2/FiO_2 ratios. For all calculations, R software (R Development Core Team) and SPSS Statistics for Windows, Version 20.0 (IBM, Armonk, NY) were used. The significance level was set at $p < 0.05$.

Results

Patient features

Figure 1 presents the flowchart of the study. Among the 412 patients presenting with suspected SARS-CoV-2 infection in the ED, 207 were symptomatic with dyspnea. Of these symptomatic patients, 77 underwent LUS exam followed by a chest CT scan within the next 24 h and were included in the ED group. Among the 87 patients admitted to the ICU during this period, 23 fulfilled the inclusion criteria and were included in the ICU group. Thus, 100 patients (200 hemi-thoraces) were analyzed. The demographic and clinical data of the patients are summarized in Table 1.

Descriptive analysis

LUS was performed by Level 3, Level 2 and Level 1 operators in 37%, 53% and 10% of cases, respectively. A descriptive analysis of chest CT scan and LUS findings is reported in (Table 2).

Primary outcome

The LUS score was significantly associated with chest CT scan severity ($p < 0.0001$; Table 3). The AUC of the ROC curve of the relationship of LUS versus chest CT for the assessment of severe SARS-CoV-2 pneumonia was 0.78 (CI 95% 0.68–0.87; $p < 0.0001$; Fig. 2a). The maximum Youden index was 0.50. The LUS score gray zone (score of 13–23) with inconclusive values included 38 patients (38%) (Fig. 2b). An LUS score > 23 predicted severe SARS-CoV-2 pneumonia diagnosed by chest CT scan with a Sp > 90% and a PPV of 70% in 23 patients. An LUS score < 13 excluded severe SARS-CoV-2 pneumonia diagnosed by chest CT scan with a Se > 90% and an NPV of 92% in 39 patients. Thirty-eight patients (38%) were in the gray zone.

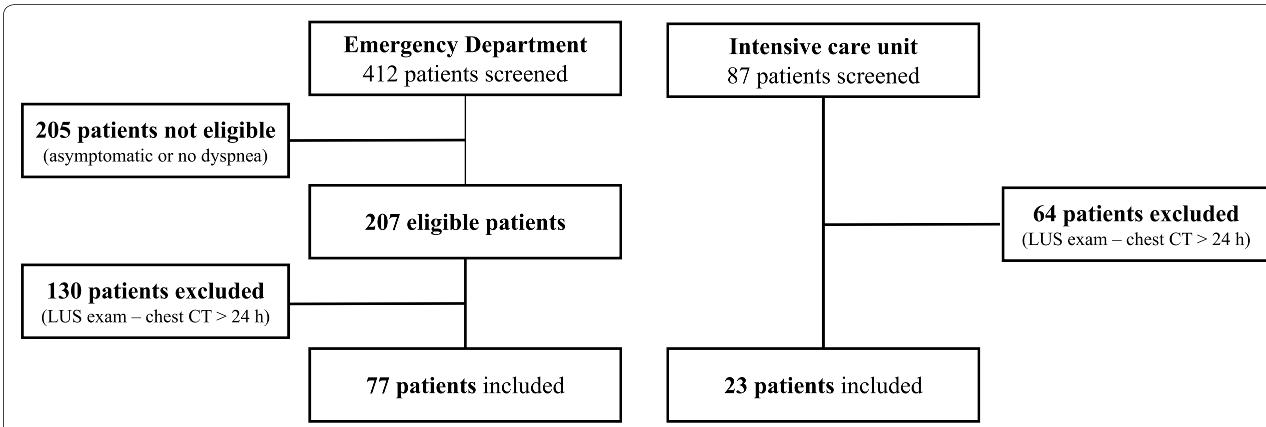

Fig. 1 Study flowchart

Table 1 Baseline clinical data

Patient information	All $n = 100$	ED $n = 77$	ICU $n = 23$	*P* value
Characteristics				
Age, median (IQR), years	61 (54–77)	60 (51–78)	69 (55–73)	0.49
Sex				
Men (%)	65 (65)	45 (58)	20 (87)	0.01
Women (%)	35 (35)	32 (42)	3 (13)	
BMI > 30 kg/m (%)	17 (17)	11 (14)	6 (26)	0.21
Co-morbidities				
Hypertension (%)	24 (24)	12 (16)	12 (52)	0.0003
Coronary disease (%)	11 (11)	5 (7)	6 (26)	0.02
Heart failure (%)	16 (16)	13 (17)	3 (13)	0.66
COPD (%)	10 (10)	8 (10)	2 (9)	0.81
Chronic kidney disease (%)	2 (2)	1 (1)	1 (4)	0.41
Liver disease (%)	1 (1)	0	1 (4)	0.23
Diabetes (%)	16 (16)	7 (9)	9 (39)	0.002
Immunodepression (%)	1 (1)	1 (1)	0	0.58
Cancer (%)	7 (7)	4 (5)	3 (13)	0.2
Clinical features				
MAP, median (IQR), mmHg	90 (81–99)	92 (83–100)	84 (75–98)	0.16
Heart rate, median (IQR), bpm[1]	91 (82–104)	91 (82–104)	91 (82–105)	0.82
Respiratory rate, median (IQR), bpm[2]	23 (18–28)	22 (18–28)	26 (20–30)	0.20
SpO_2, median (IQR), %	95 (93–97)	96 (93–98)	93 (91–94)	0.0001
Oxygen rate flow, median (IQR), L/min	2 (0–6)	0 (0–4)	9 (6–30)	0.002
Mechanical ventilation, n (%)	7 (7)	0	7 (30)	< 0.0001
PaO_2, median (IQR), mmHg	76 (66–88)	77 (65–90)	76 (67–82)	0.66
SpO_2/FiO_2 ratio, median (IQR)	335 (233–452)	428 (292–457)	184 (133–244)	< 0.0001
Delay between ultrasound exam and chest CT scan, median (IQR), hours	4 (3–7)	4 (3–6)	3 (1–10)	0.5

Data are expressed as *n* (%) of participants, unless otherwise indicated

BMI body mass index; *COPD* chronic obstructive pulmonary disease; *MAP* mean arterial pressure; *SpO_2* pulse oximetry; *PaO_2* arterial oxygen partial; *FiO_2* fractional inspired oxygen; *IQR* interquartile range; *CT* computed tomography, *ED* emergency department; *ICU* intensive care unit

[1] bpm: beats per minute

[2] bpm: breath per minute

Secondary outcomes

The Se, Sp, PPV, NPV and DA of LUS for the chest CT scan diagnosis of alveolar consolidation, interstitial syndrome, pneumothorax, pleural effusion and pleural irregularity are reported in ESM Table S1. LUS score was associated with clinical status at the time of examination. The LUS score was significantly higher in the mechanically ventilated patients (28 ± 5 vs. 14 ± 8; $p < 0.0001$). All the mechanically ventilated patients had an LUS score > 19. The ROC curve of LUS for mechanical ventilation was 0.92. The LUS score was significantly higher in the patients with a SpO_2/FiO_2 ratio < 357 (19 ± 8 vs. 11 ± 8; $p < 0.0001$).

Discussion

Our results show that the severity of SARS-CoV-2 pneumonia assessed by LUS is highly associated with severity as assessed by chest CT scan. Thus, LUS could replace chest CT scan for the initial assessment of lung involvement in most of confirmed symptomatic SARS-CoV-2 patients.

A chest CT scan is the gold standard to assess the severity of pneumonia in patients with SARS-CoV-2 [25]. An international consensus statement concluded that ‘In a resource-constrained environment, imaging is indicated for medical triage of patients with suspected SARS-CoV-2 who present with moderate-severe

Table 2 CT and LUS findings

Findings	CT $n = 100$	LUS $n = 100$	*P* value
Interstitial syndrome			
Absent	8 (8)	4 (4)	0.134
Unilateral	5 (5)	11 (11)	
Bilateral	87 (87)	85 (85)	
Consolidation			
Absent	48 (48)	68 (68)	0.002
Unilateral	16 (16)	17 (17)	
Bilateral	36 (36)	15 (15)	
Pleural effusion			
Absent	89 (89)	94 (94)	0.122
Unilateral	7 (7)	6 (6)	
Bilateral	4 (4)	0	
Pneumothorax	0	0	–
Pleural irregularity	15 (15)	32 (32)	0.005

Data are expressed as n (%) of participants unless otherwise indicated

CT computed tomography; *ED* emergency department; *ICU* intensive care unit

clinical features and a high pre-test probability of disease' [26]. However, there are risks and logistical limitations to the use of CT. The transfer of unwell patients risks adverse events [5, 6], there is increased potential exposure to the virus of all the healthcare providers involved in the transfer, and there may be a lack of scanning capacity if there is a high number of patients presenting. Unlike CT scan, LUS has the advantages that it is available at the point of care, it may be performed by suitably skilled physicians in the ED or ICU, and there is negligible cost to each individual examination [27]. The same trends were previously reported for the H1N1 pandemic [11], and our results confirm similar utility of LUS to assess the severity of SARS-CoV-2 pneumonia. In addition, due to the high incidence of thromboembolic events [28, 29], LUS should be incorporated into multiorgan ultrasound assessment to detect both venous thrombosis [30, 31] and signs of acute right heart failure [32].

The discrepancy between LUS and CT scan results lies in the middle region, or gray zone, of LUS scores. From these results, we suggest that chest CT scan would not be required if an initial LUS examination found a score < 13 (mild disease) or > 23 (severe disease), but only in the 38% of cases with an intermediate score between 13 and 23. Furthermore, LUS exams were not performed exclusively by expert operators, and it might be assumed that improving the level of expertise would have improved the accuracy. In contrast, chest CT scans were all interpreted by senior radiologists with a high level of expertise.

LUS scores differed according to clinical status of our highly select population. Patients in the ICU had a higher SpO_2/FiO_2 ratio ≥ 357. Furthermore, all the patients having mechanical ventilation had an LUS score > 19.

Our study has several limitations. First, we included a convenience sample of patients with dyspnoea and confirmed PCR, which represents only a small percentage of the many cases of pneumonia observed during the pandemic. The chest CT scan and LUS were not performed simultaneously, but the median delay between chest CT scan and LUS was four hours. As previously described [20], we used a modified LUS technique that did not scan the paravertebral areas. If this introduced any alteration in the diagnostic accuracy, it would be expected to have reduced identification of pulmonary consolidation, and hence the assessed degree of severity.

We wished to ensure that patients who were studied had both significant and proven SARS-CoV-2 infection. The delay in getting test results has led to situations where CT scan is being used as the primary investigation to diagnose and triage patients. As a positive PCR test was one of the inclusion criteria for our analysis, we cannot comment on whether our findings would apply to patients who had an expedited scan on this basis.

We suggest that further research should assess the generalisability of the low and high thresholds suggested above for replacement of CT scan by LUS as a tool to assess pneumonia severity, and the use of LUS as a predictor of the clinical course and a guide to ongoing management [33, 34].

Table 3 Correlation: LUS score according to chest CT scan severity

Chest CT scan severity	Patients	LUS score mean ± SD	95% CI for Mean		LUS score min	LUS score max	*P* value
			Lower bound	Upper bound			
Minimal damage	18	8 ± 7	4	11	0	22	< 0.0001
Moderate damage	43	14 ± 8	11	16	0	30	
Severe damage	39	20 ± 8	18	23	5	34	

CT computed tomography; *LUS* lung ultrasound; *CI*: confidence interval, *SD* standard deviation

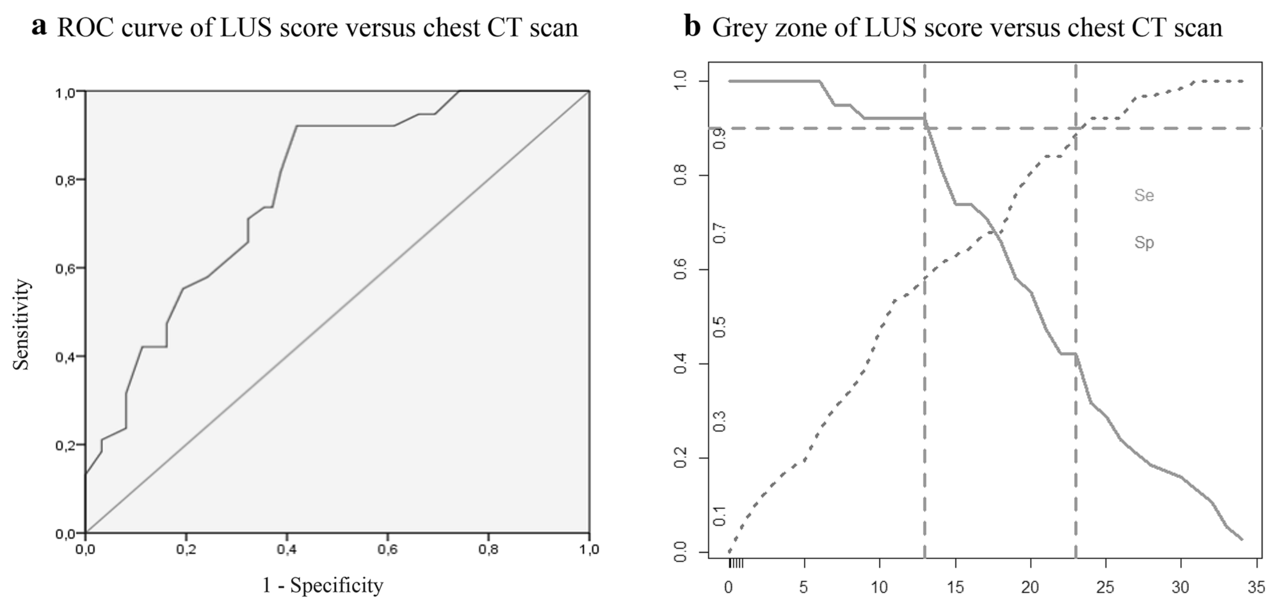

Fig. 2 Diagnostic accuracy of LUS score for the detection of severe SARS-CoV-2 pneumonia assessed by chest CT scan. **a** ROC curve of LUS score versus chest CT scan. AUC = 0.78 (CI 95% 0.68–0.87; $p < 0.0001$), (**b**) Gray zone of LUS score versus chest CT scan. Solid line: Se (Sensitivity). Dotted line: Sp (Specificity)

Conclusion

In patients with proven SARS-CoV-2 pneumonia, LUS score is associated with severity as assessed by chest CT scan and clinical features.

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-020-06186-0) contains supplementary material, which is available to authorized users.

Abbreviations

AUC: Area under curve; COVID-19: Coronavirus disease 2019; CI: Confidence interval; CT: Computed tomography; DA: Diagnostic accuracy; ED: Emergency department; ESM: Electronical Supplemental Material; FiO_2: Fractional inspired oxygen; ICU: Intensive care unit; LUS: Lung ultrasound; NPV: Negative predictive value; PaO_2: Arterial oxygen partial; PCR: Polymerase chain reaction; PPV: Positive predictive value; ROC: Receiver operating characteristic; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; Se: Sensitivity; Sp: Specificity; SpO_2: Pulse oximetry.

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Acknowledgements

We wish to thank Mike Kinsella for his help in editing the manuscript. We thank Eloïse Cercueil for her help in patient recruitment.

Author contributions

The corresponding author (LZ) attests that all listed authors meet the authorship criteria and that no others meeting the criteria have been omitted. LZ: Contributions: This author helped design and conduct the study, analyze the data and write the manuscript. Thibaut Markarian: Contributions: This author helped design and conduct the study, analyze the data and write the manuscript. AL: Contributions: This author helped conduct the study, analyze the data and write the manuscript. CT: Contributions: This author helped conduct the study. NM: Contributions: This author helped conduct the study. MB: Contributions: This author helped analyze the data and write the manuscript. KB: Contributions: This author helped analyze the data and write the manuscript. GB: Contributions: This author helped conduct the study and write the manuscript. GM: Contributions: This author helped conduct the study. GD: Contributions: This author helped conduct the study. LB: Contributions: This author helped write the manuscript. PM: Contributions: This author helped conduct the study. BA: Contributions: This author helped conduct the study. KC: Contributions: This author helped conduct the study, analyze the data and write the manuscript. MB: Contributions: This author helped conduct the study, analyze the data and write the manuscript. ML: Contributions: This author helped design the study and write the manuscript.

Compliance with ethical standards

Conflicts of interest

LZ and TM received fees for teaching ultrasound to GE healthcare customers.

Publisher's Note

Received: 28 April 2020 Accepted: 16 July 2020
Published online: 29 July 2020

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