

# Prognostic performance of lung ultrasound score in patients presenting to the emergency department with respiratory complaints or suspected infection independent of final diagnosis

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## Abstract

In patients presenting to the Emergency Department (ED) with acute respiratory symptoms or suspected infection, Lung Ultrasound (LUS) may serve as a valuable diagnostic tool. Its use and clinical applicability markedly increased since the SARS-CoV-2 pandemic. The aim of this study was to evaluate whether LUS can predict 30-day mortality or Intensive Care Unit (ICU) admission in patients presenting to the ED and to develop a prognostic model. We conducted a bicentric observational cohort in two Italian EDs. Two scores were analyzed, the overall LUS score and the anterolateral LUS score. Multivariable logistic regression models were developed, and their performance was assessed using the area under the receiver operating characteristic curve (Area Under the Curve, AUC) and validated with concordance indices (C-indexes). Four hundred and thirty-four patients were enrolled. The median time from symptom onset to ED presentation was 4 days (IQR 6). The primary final diagnosis was SARS-COV2 infection in 32% of cases, other respiratory diseases in 15%, heart failure in 9%. The composite outcome occurred in 68 patients (15.7%). The empirically estimated AUC of the LUS score was 67%. A prognostic model including age, overall LUS score, time from symptom onset, history of diabetes, chronic kidney disease, and cancer within the previous 5 years showed a C-index of 70.8%. This study suggests that, in patients presenting to the ED with respiratory symptoms, the LUS score may have a prognostic value regardless of the final diagnosis established at the end of the diagnostic work-up performed in the ED.

**Key words:** lung ultrasound, prognosis, dyspnea, emergency department.

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## Introduction

In patients presenting to the Emergency Department (ED) with acute respiratory symptoms or suspected infection, Lung Ultrasound (LUS) can be used as a bedside tool to diagnose pulmonary conditions such as consolidation due to pneumonia, diffuse interstitial syndrome due to interstitial pneumonia as in Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV2) infection, or acute heart failure.<sup>1-8</sup>

Several studies have suggested that the LUS score, a tool used to assess the extent of pathological involvement of the lung surface, may be useful for predicting the prognosis of patients with acute heart failure, Acute Respiratory Distress Syndrome (ARDS), and SARS-COV2 infection.<sup>2,9-12</sup> However, most of these studies were conducted in patients with an already established diagnosis. To date, no studies have evaluated the prognostic performance of LUS in patients presenting with respiratory symptoms and/or suspected infection regardless of the final diagnosis.

With the increasing availability of portable ultrasound devices, many physicians now perform LUS at the time of ED presentation in patients with dyspnea, cough, respiratory failure and/or fever, immediately after history taking and physical examination, but before a final diagnosis is established.<sup>13-17</sup> In this setting, it is important to determine whether LUS may also provide prognostic information in the ED, in addition to its diagnostic utility. Furthermore, it would be valuable to assess whether patient prognosis correlates with the extent of pathological lung involvement, irrespective of the underlying disease. This is particularly relevant because mixed conditions, such as pneumonia and heart failure, often coexist. The aim of this study was to assess whether LUS can predict 30-day mortality or ICU admission in patients presenting to the ED with respiratory symptoms and/or suspected infection, regardless of the final diagnosis. In addition, the study sought to develop a prognostic model incorporating clinical, demographic, and sonographic variables.

## Materials and Methods

### Study setting and enrolment criteria

This prospective, bicentric observational cohort study was conducted in two Italian EDs, the Careggi University Hospital, Florence, and the Città della Salute e della Scienza di Torino, Turin. Before study initiation, approval was obtained from both the respective Ethics Committees (authorization n. 17104 and CS3/23, respectively). Patients or their legal representatives provided informed consent, and the study was conducted in accordance with the principles of the Declaration of Helsinki for clinical research involving human subjects. From March 2020 to April 2020, all consecutive ED outpatients were eligible for inclusion if they met the following criteria: i) age  $\geq 18$  years; ii) presenting to the ED with dyspnea, cough, oxygen saturation  $\leq 94\%$  on room air, respiratory rate  $\geq 20$  breaths/minute, need for supplemental oxygen or ventilation support (for patients with a pre-existing chronic respiratory disease, worsening dyspnea or respiratory failure within the previous 24 hours qualified for inclusion); and/or fever (temperature  $\geq 37.5^\circ\text{C}$ ); iii) LUS performed in all chest regions according to the study protocol (see after) at the time of ED presentation. Exclusion criteria were: i) patient's refusal to participate in the study, and ii) patient lost to follow-up after ED discharge.

### Lung ultrasound score

A standardized LUS examination was performed at ED presentation by an ED physician experienced in LUS. All physicians involved had completed an accredited ultrasound training course (WINFOCUS, the Italian Society of Emergency Medicine or an equivalent course) and had already performed at least 40 LUS examinations before the study.<sup>18,19</sup> Operators were blinded to the result of other imaging and laboratory tests, although they were aware of the patient's presenting symptoms. Whenever possible, LUS was performed with the patient in the sitting position. If this was not feasible because of the patient's clinical condition or poor compliance, the examination was performed in the supine or semi-recumbent position.

The sonographic evaluations were carried out using a portable ultrasound device with a convex transducer preset, 3.5–6.0 MHz. The focus was set at the level of the pleural line, and the depth was adjusted to 8–10 cm according to patient size. The probe was positioned perpendicular to the ribs, and each area was examined for at least one complete respiratory cycle. The LUS protocol included 12 lung regions, six for each hemithorax, including anterior, lateral, and posterior fields as identified by sternum, anterior, and posterior axillary lines. Each field was further divided into upper and lower regions (Figure 1). Each region was scored according to four ultrasound aeration patterns: Score 0: normal aeration (A-lines present and/or no more than two B-lines); Score 1: moderate loss of aeration (three or more well-spaced B-lines); Score 2: severe loss of aeration (coalescent B-lines); Score 3: complete loss of aeration (tissue-like pattern).

For each patient, the worst ultrasound pattern observed in each region was recorded to determine the total score (Figure 2).<sup>20–24</sup>

For analysis, two measurements were considered, i) the overall LUS score, calculated as the sum of the scores of all 12 lung regions (range 0–36); and ii) the anterolateral LUS score, calculated as the sum of the anterior and lateral regions only (range 0–24). Pleural effusion was recorded but not included for the score calculation.

## Outcomes

We analyzed the association between the severity of pulmonary involvement at ED admission, as assessed by the LUS score (both overall and anterolateral), and the occurrence of an adverse outcomes. The primary outcome was a composite of all-cause mortality and ICU admission within 30 days of the index ED visit. Outcome were assessed by reviewing the medical records of admitted patients or, for discharged patients, by contacting all enrolled patients through a structured telephone interview 30 days after the ED visit. For patients reporting additional ED visits or hospital admissions, the relevant dates were recorded and medical records were reviewed. For deaths occurring during follow-up among non-hospitalized patients, information was obtained from family members, primary care physicians, or emergency medical services, when available.

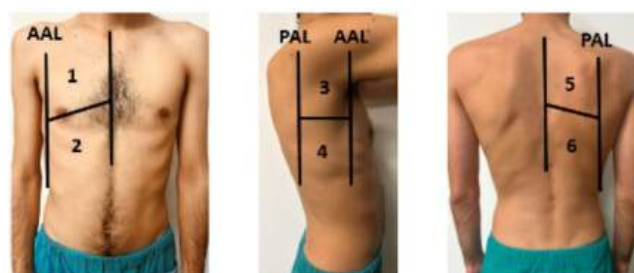
### Statistical analysis

Continuous and categorical variables were reported as medians and Interquartile Ranges (IQR), or counts and percentages, as appropriate.

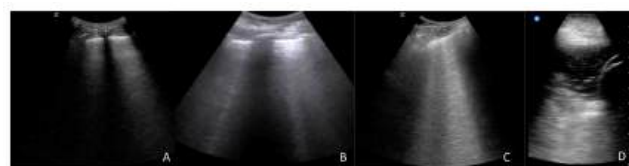
Multi-variate models were used to assess the causal association between the outcome and several potential predictors, including medical history, symptoms at ED presentation, and LUS score.

In addition, the diagnostic accuracy [*i.e.*, sensitivity, specificity, and the AUC, the area under the of Receiver Operating characteristic Curve (ROC)] was assessed for both the multivariable model and for the LUS score alone.

The Liu method was used to identify the optimal cutoff maximizing sensitivity and specificity on the ROC curve for the LUS score.



**Figure 1.** Zones evaluated using lung ultrasound (PSL, parasternal line; AAL, anterior axillary line; PAL, posterior axillary line): zones 1 and 2 are upper and lower anterior areas, 3 is the superior-lateral area, 4 is the inferior lateral area, 5 and 6 are upper and lower posterior areas.



**Figure 2.** Lung ultrasound patterns as categorized in the LUS score: panel A normal aeration (score 0), panel B moderate loss of aeration (some B-lines, score 1), panel B severe loss of aeration (coalescent B-lines, score 2), and complete loss of aeration (tissue-like pattern, score 3).

The models were internally validated with 5000 bootstrap samples to obtain bias-corrected discrimination estimates using a concordance index (C-index). Model performance was compared across the different models. Calibration was assessed by visually inspecting plots of predicted versus observed outcomes.

Analyses were performed using STATA 17.0 SE (Stata Corp) and RStudio 2023.06.2+561 (The R Foundation for Statistical Computing). The authors had full access to the data and take full responsibility for the integrity. All authors have read and approved the manuscript as written.

## Results

A total of 441 patients underwent LUS according to the study protocol. Two were excluded because they declined to participate, and 5 were lost to follow-up. Thus, 434 patients were finally included (Figure 3). Of these, 229 (53%) were female, with a median age is 64 (IQR 34) like reported in Table 1. The median time from symptom onset to the ED presentation was 4 days (IQR 6). The primary final diagnoses were SARS-COV2 infection in 139 cases (32%), other non-COVID-19 respiratory conditions in 65 (15%), heart failure in 40 (9%), pulmonary embolism in 15

(3%), sepsis without respiratory involvement in 79 (18%), and other conditions in 96 (22%).

The composite outcome occurred in 68 patients (15.7%), including 19 died (4.4%) and 49 ICU admission (11.3%).

LUS examinations were performed by 50 operators (35 residents and 15 attending physicians). Pathological findings (B-line pattern and/or consolidations, *i.e.*, LUS score  $\geq 1$ ) were observed in 280 patients (64.1%). The median overall LUS score for the entire cohort was 2 (IQR 7), and the median anterolateral LUS score was 0 (IQR 4). The regions showing pathological findings (LUS  $\geq 1$ ) in more than 30% of patients were the right posteroinferior and inferolateral regions, bilaterally.

Among patients who experienced the outcome, the median overall LUS score was 8 (range 0-26), and the median anterolateral LUS score was 4.5 (range 0-20; Table 2 and Figure 4). Both the overall and the anterolateral LUS score at admission were significantly associated with the outcome, with an OR of 1.14 (95% CI 1.10-1.19) and of 1.18 (95% CI 1.12-1.24), respectively.

A multivariate logistic regression model, including age, gender, overall LUS score, history of chronic kidney disease, cancer of any type within the last 5 years, and diabetes confirmed the independent association between the LUS score and the outcome (OR 1.14, IQR 1.09-1.19; Table 3).

Table 4 reports the sensitivity, specificity, and AUC for the

**Table 1.** Characteristics of enrolled patients.

| Patients                                  | "No death/No ICU admission | Death/ICU admission | All             | p      |
|-------------------------------------------|----------------------------|---------------------|-----------------|--------|
| Age, median (IQR)                         | 60.4 (27.5)                | 80.7 (15.6)         | 64 (33.8)       | <0.001 |
| Gender, female – no. (%)                  | 196 (89.8)                 | 33 (10.2)           | 229 (53)        | 0.462  |
| Coexisting Conditions – no. (%)           |                            |                     |                 |        |
| Hypertension (%)                          | 138 (36.2)                 | 29 (60.4)           | 167 (39)        | <0.001 |
| Diabetes (%)                              | 40 (10.5)                  | 13 (27.1)           | 53 (12)         | <0.001 |
| Atrial Fibrillation (%)                   | 47 (12.3)                  | 12 (25)             | 59 (14)         | <0.001 |
| Coronary Artery Disease (%)               | 43 (11.3)                  | 10 (20.8)           | 53 (12)         | <0.001 |
| Asthma (%)                                | 21 (5.5)                   | 1 (2.1)             | 22 (5)          | 0.609  |
| Chronic Obstructive Pulmonary Disease (%) | 30 (7.9)                   | 7 (14.6)            | 37 (9)          | 0.573  |
| Chronic Kidney Disease (%)                | 14 (3.7)                   | 7 (14.6)            | 21 (5)          | 0.003  |
| Stroke (%)                                | 29 (7.6)                   | 5 (10.4)            | 34 (8)          | 0.384  |
| Tumor (%)                                 | 45 (11.8)                  | 15 (31.3)           | 60 (14)         | 0.001  |
| Presenting Symptoms – no. (%)             |                            |                     |                 |        |
| Cough                                     | 158 (41.5)                 | 16 (33.3)           | 174 (40)        | 0.102  |
| Dyspnea                                   | 153 (40.2)                 | 27 (56.3)           | 180 (41)        | 0.03   |
| Chest Pain                                | 20 (10.1)                  | 0 (-)               | 20 (4)          | 0.085  |
| Sore throat                               | 39 (10.2)                  | 3 (6.3)             | 42 (10)         | 0.763  |
| Fever                                     | 227 (59.6)                 | 34 (70.8)           | 261 (60)        | 0.094  |
| Myalgia                                   | 11 (2.9)                   | 1 (2.1)             | 12 (3)          | 1.000  |
| Asthenia                                  | 64 (16.8)                  | 6 (12.5)            | 70 (16)         | 0.827  |
| Headache                                  | 23 (6)                     | 0 (-)               | 23 (5)          | 0.201  |
| Anosmia                                   | 19 (5)                     | 0 (-)               | 19 (4)          | 0.320  |
| Ageusia                                   | 25 (6.6)                   | 0 (-)               | 25 (6)          | 0.138  |
| Nausea                                    | 7 (1.8)                    | 1 (2.1)             | 8 (2)           | 1.000  |
| Vomiting                                  | 12 (3.2)                   | 3 (6.3)             | 15 (3)          | 0.445  |
| Diarrhea                                  | 56 (14.7)                  | 3 (6.3)             | 15 (3)          | 0.069  |
| Vital Signs – no. (IQR)                   |                            |                     |                 |        |
| Systolic Blood Pressure (mmHg)            | 130 (IQR 25)               | 120 (IQR 45)        | 130 (IQR 25)    | 0.004  |
| Diastolic Blood Pressure (mmHg)           | 80 (IQR 25)                | 70 (IQR 20)         | 80 (IQR 19)     | <0.001 |
| Heart Rate (beats per minute)             | 88 (IQR 23)                | 96 (IQR 25)         | 88 (IQR 23)     | 0.04   |
| Oxygen Saturation (%)                     | 97 (IQR 3)                 | 94 (IQR 7)          | 97 (IQR 4)      | <0.001 |
| Respiratory Rate (breaths per minute)     | 18 (IQR 6)                 | 25 (IQR 12)         | 18 (IQR 8)      | <0.001 |
| Body Temperature (Celsius degrees)        | 36.5 (IQR 1.2)             | 36.8 (IQR 1.1)      | 36.5 (IQR 1.2)  | 0.04   |
| PF                                        | 276.2 (IQR 195.5)          | 233.3 (IQR 162)     | 262 (IQR 190.5) | 0.007  |

overall and anterolateral LUS scores, empirically estimated using the Liu method. Figure 5 shows the ROC curves, with an AUC of 67% for the overall LUS score and 66% for the anterolateral LUS score. When the analysis was restricted to patients presenting with respiratory symptoms only (*i.e.*, cough or shortness of breath), 282 patients were included, 47 of whom experienced the outcome (16.7%). Among these, 15 patients (5.3%) died, and 32 (11.3%) were admitted to the ICU. In these 47 patients, the median overall LUS score was 8 (range 0-26), and the anterolateral LUS score was 4 (range 0-20).

Figure 6 shows the nomogram of the prognostic model, which includes age, overall LUS score, time from symptom onset, and a history of diabetes, chronic kidney disease, or cancer within the previous 5 years. In addition, we evaluated a second model including the anterolateral LUS score instead of the overall LUS score, and a third model without any LUS variable. The C-index of the three models was 70.8%, 69.8%, and 67%, respectively. Model calibrations are shown in Figure 7.

Discussion

This observational bi-centric study tested the hypothesis that LUS may have not only a diagnostic but also a prognostic value in patients presenting to the ED with respiratory symptoms, such as fever, cough, dyspnea, or respiratory failure, regardless of the final diagnosis.

The diagnostic accuracy of LUS for several conditions, including pneumonia and heart failure, has already been shown in several studies.<sup>3,5,7,8,25-28</sup> In contrast, less data are available regarding its potential prognostic value.

Our study suggests that superficial pathological lung involvement detected by bedside LUS is associated with worse outcomes in patients presenting to the ED with respiratory symptoms. However, the discriminative ability of the LUS score alone was only moderate, indicating that LUS should be interpreted as a complementary tool for early risk stratification rather than as a standalone prognostic marker. Indeed, each 1-point increase in the LUS score was associated with a 14% higher risk of death or ICU admission within 30 days (95% IC 9-19%), irrespective of the final diagnosis. This finding was not only statistically significant in univariate analysis but also remained robust in the multivariable model, which included readily available clinical and demographic variables such as age, gender, history of renal failure, diabetes, and cancer.

These findings may have relevant implications for patient management, as LUS is easy to learn, to perform, and to interpret even in the ED setting.<sup>7,15,29-31</sup> A median overall LUS score of 8 was observed among patients who experienced a 30-day outcome after ED evaluation, and the prognostic model including the overall LUS score showed a better calibration than a similar model without it, although the C-indexes were relatively close.

The score used in the present study, the LUS score, was origi-

nally proposed several years ago in critical care for the bedside assessment of lung aeration.<sup>24</sup> However, it was only extensively adopted and used during the SARS-CoV-2 pandemic.<sup>32,33</sup>

In 2020, Bonadia and co-authors evaluated the role of LUS score in COVID-19 patients presenting to the ED.<sup>34</sup> They used a 14-zone scanning protocol and a similar scoring system, with greater emphasis on the pleural line abnormalities, as proposed by

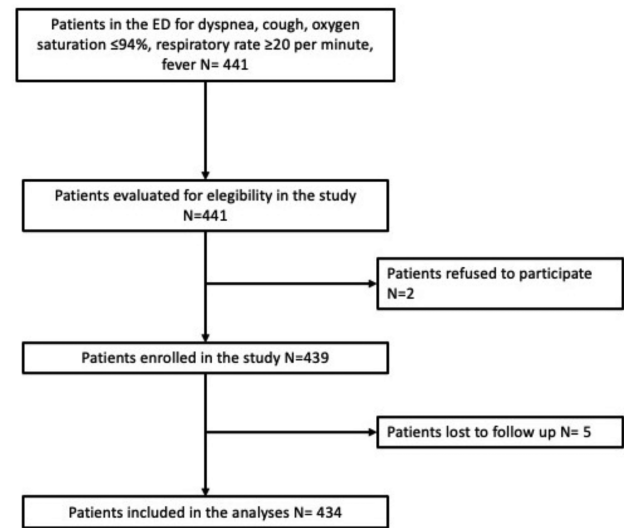


Figure 3. Flow chart of participants in the study.

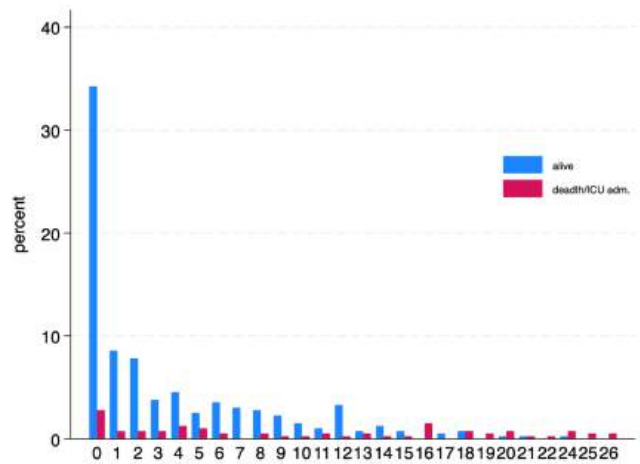


Figure 4. Distribution of LUS scores among patients who survived and were not admitted to ICU and those who experienced the composite outcome (*i.e.*, death and/or ICU admission).

Table 2. Lung ultrasound score and outcome.

|                                      | Death/ICU admission | Death    | No death/No ICU admission |
|--------------------------------------|---------------------|----------|---------------------------|
| Total score – median (range)         | 8 (0-26)            | 5 (0-16) | 11 (0-24)                 |
| Anterolateral score – median (range) | 4.5 (0-20)          | 2 (0-18) | 6 (0-20)                  |

P value for median difference between who experienced the composite outcome (*i.e.*, Death/ICU admission) and those who didn't (*i.e.*, No death/No ICU admission) for total and for anterolateral score is <0.001; P value for Death vs No death/No ICU admission for total score is 0.09; P value for Death vs No death/No ICU admission for anterolateral score is 0.12.

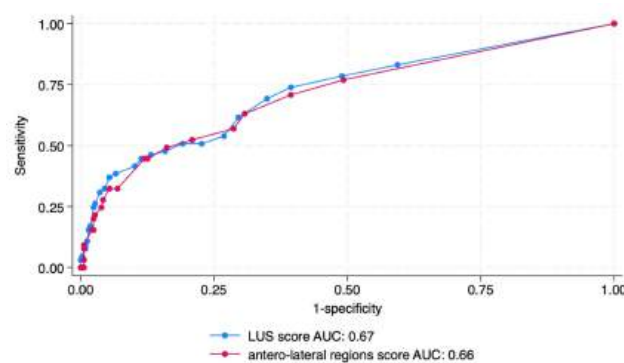
Soldati *et al.*<sup>35</sup> Among 41 patients enrolled, a median of 6 pathological areas was reported (IQR 6), with a substantial difference between patients who subsequently died (100%, IQR 81.5%) and those who were discharged (50%, IQR 27%).<sup>34</sup> In addition, Secco *et al.* described different LUS phenotypes in COVID-19 patients and reported correlations between ultrasound presentation and clinical features, further supporting the potential role of LUS in the early stratification of patients with acute respiratory disease.<sup>36</sup>

These findings supported the predictive value of LUS score, although the cohort was limited to patients infected by SARS-CoV2.<sup>34,36,37</sup>

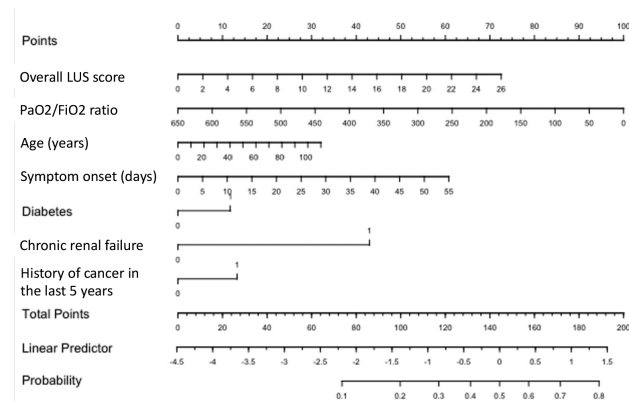
Benchoufi and co-authors recently published a similar multi-center cohort study conducted in France during the first wave of the SARS-CoV2 pandemic.<sup>30</sup> They analyzed 328 patients enrolled across 8 centers and applied a simplified 8-zone LUS score to test the association between lung involvement at ED presentation and subsequent clinical deterioration, defined as ICU admission, invasive mechanical ventilation, or death within 28 days.<sup>30</sup> In this study, the authors reported a higher AUC than in our cohort, likely because of the more extensive pulmonary involvement observed during the first wave of SARS-CoV-2 pandemic. In addition, the study was restricted to patients with COVID-19, and no prognostic score integrating the LUS findings with other clinical variables was proposed.

In our study, both diagnostic and prognostic performance of LUS were tested using two different approaches, the conventional 12-zone LUS score and a simplified score including only the antero-lateral regions (0-24 points), similar to that adopted by Benchoufi *et al.*<sup>30</sup> The latter approach is faster and may be more practical than the full LUS score, as it requires assessment of fewer regions and does not require the patient to sit upright for posterior scanning. However, in our cohort it showed a slightly lower AUC, a lower C-index, and poorer calibration than the overall LUS score.

The results of our study are broadly consistent, although somewhat less strong, than those reported in other studies of patients



**Figure 5.** Area under the ROC curve of overall LUS score and the antero-lateral regions score.



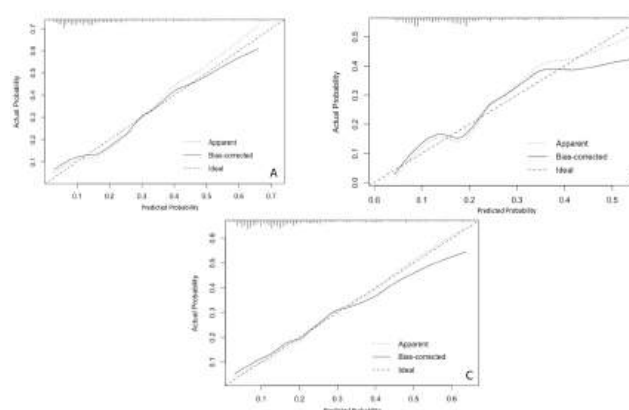
**Figure 6.** Nomogram of the prognostic model including the LUS score.

**Table 3.** Multivariate analysis for risk of death and/or ICU admission in 30 days after first evaluation.

| Independent variable                 | OR   | 95% CI    |
|--------------------------------------|------|-----------|
| Age                                  | 1.00 | 0.99-1.01 |
| Gender                               | 1.00 | 0.56-1.82 |
| LUS score                            | 1.14 | 1.09-1.19 |
| Days from symptoms onset             | 1.02 | 0.98-1.06 |
| Renal failure                        | 2.93 | 0.91-10.6 |
| Cancer, any type during last 5 years | 2.11 | 1.00-4.42 |
| Diabetes                             | 1.83 | 0.83-4.01 |

**Table 4.** Best empirical sensitivity, specificity, AUC for LUS variables estimated using Liu method.

| Best estimated cut off   | Sensitivity | Specificity | AUC  |
|--------------------------|-------------|-------------|------|
| LUS score, 3.5           | 0.69        | 0.65        | 0.67 |
| Anterolateral score, 2.5 | 0.60        | 0.72        | 0.66 |



**Figure 7.** Calibration of both prognostic models evaluated. Panel A shows calibration of a model including age, LUS score, symptom onset, history of diabetes, chronic renal failure, and cancer in the last 5 years; panel B shows the calibration of a model with age, symptom onset, history of diabetes, chronic renal failure, and cancer in the last 5 years; panel C shows the same model as panel A but using antero-lateral zone scores instead of the overall LUS score.

with heart failure, pneumonia, ARDS, and SARS-CoV-2 infection, in which LUS was associated with increased risk, with OR ranging from approximately 1.1 to 1.9.<sup>38–41</sup> This difference may be at least partly explained by the intrinsic nature of B-lines, which are sonographic artifacts reflecting increased lung density.<sup>42</sup> Some acute conditions frequently encountered in the ED, such as COPD exacerbations or sepsis without pulmonary involvement, may have a poor prognosis but are not typically characterized by B-lines.<sup>43,44</sup>

## Limitations

Our study presents some limitations.

First, in both participating centers all operators underwent an extensive training in POCUS before taking part in the study. Since POCUS training is not uniform worldwide, this may raise concerns regarding generalizability. However, several national and international societies recommend that a relatively limited number of supervised examinations may be sufficient to achieve a basic skill level in LUS adequate for clinical use of the LUS score.<sup>17,18</sup>

Second, both centers were university hospitals. This may have influenced the overall use of LUS, particularly during the SARS-CoV-2 pandemic, when ultrasound was extensively used for both training and research purposes, potentially limiting the external validity of the findings. In addition, the composite outcome included ICU admission which may have been influenced by local organizational factors and resource availability. In the Italian hospital system, and especially during the first COVID-19 wave, several patients requiring non-invasive ventilatory support were managed in high-dependency units rather than in the ICU. This may limit the comparability of our outcome definition with that used in other healthcare systems, and the issue was likely amplified during the first wave because of the large number of patients requiring ventilatory support.

Third, the study enrollment period coincided with the first wave of the SARS-CoV-2 pandemic. This extraordinary context may have influenced both patient selection and disease severity. In particular, the epidemiological and clinical characteristics of that phase differed from those of subsequent pandemic waves and from the current ED population.

Another limitation is the potential inter-observer variability in LUS acquisition and interpretation. Although all operators had completed accredited training and had previous experience in LUS, ultrasound remains an operator-dependent technique. Therefore, some degree of variability among the 50 operators, including both residents and attending physicians, cannot be excluded and may have partially affected study findings.

## Conclusions

The results of this observational study suggest that, in patients presenting to the ED with respiratory symptoms, the extent of superficial pathological lung involvement assessed by the LUS score may have a prognostic value, regardless of the final diagnosis established after clinical, laboratory, and imaging tests performed in the ED.

Further studies, conducted not only in academic hospitals but also in centers of different level of care, are needed to confirm these findings.

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