Prognostic value of lung ultrasound score performed in the Emergency Department in COVID-19 patients: a prospective multicenter study in central Italy

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Abstract

Lung ultrasound (LUS) is an essential tool for respiratory disease differential diagnosis at Emergency Department (ED), due to easy applicability and safety. During Sars-Cov 2 pandemic, LUS was widely used in every setting. This study aims to demonstrate the prognostic role of LUS independently of other factors and the identification of an LUS score cut-off to be applied in the ED. A multi-center prospective study was conducted on 285 patients, 123 from Pisa University Hospital, 162 from S. Maria Misericordia Hospital of Perugia. All patients received LUS examination by expert sonographers within 48 hours of admission with the same methodology. Univariate logistic analysis demonstrated that LUS is a mortality predictor, OR 2.8 (CL1.5-5.1). Using LUS score cut-off 1.3, the OR was 6.7 (CL2.7-1.6). In multivariate logistic analysis, LUS score significantly predicted death, independently of other factors. ROC curves comparison demonstrated that the introduction of LUS score <1.3 to a multifactorial model improved the association with mortality (AUC 0.76vs0.84, p=0.04). LUS combined with clinical, anamnestic, laboratory, and blood gas parameters, would allow an effective prognostic stratification in Sars-Cov2 patients at ED.

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Introduction

The lung is the main target organ of the coronavirus disease identified in 2019 (COVID-19). The disease typically manifests as bilateral interstitial pneumonia with predominantly postero-inferior distribution, in which chest computed tomography (CT) is the gold standard for diagnosis.[1,2]

Timely recognition and prognostic stratification of the disease allow early therapeutic procedures implementation, to prevent the most fearsome complications such as respiratory failure up to Acute Respiratory Distress Syndrome (ARDS).[3]

Lung ultrasound (LUS) is a tool widely used in the Emergency Department (ED) due to its safety, manageability, and efficacy in the first evaluation of many respiratory diseases.[4] During the worldwide Sars-Cov2 pandemic, LUS gained a fundamental role in diagnosis[5] related to the ultrasound patterns characterizing COVID-19 pneumonia, such as patchy distributed B-lines, "light beam" or subpleural consolidations.[6,7] The use of numerical scores and topographic evaluation techniques allows a quantitative analysis of lung involvement.[8] This approach is also made available and appropriate for LUS to monitor both during hospitalization[9] and follow-up.[10]

The evaluation of the patient with Sars-Cov 2 infection by ED physicians is based on anamnestic, clinical, laboratory, and blood gas analysis. Numerous studies identified factors that strongly predict an unfavorable outcome, including male gender, comorbidities, lymphopenia, increasing inflammation markers, and blood gas parameters, in particular arterial oxygen partial pressure/fractional inspired oxygen ratio (P/F).[11,12]

Unfortunately, some systematic reviews and meta-analyses showed that the currently proposed models, based on these generic and thus not disease-specific prognostic factors, are at elevated risk of bias and have low performance, mainly because of high heterogeneity and lack of prospective design.[13,14]

An appropriate early assessment of the severity of disease with risk stratification allows identifying correct hospitalization settings and therapeutic strategies.[15] Chest imaging, either with chest CT or with LUS, is a cornerstone of the prognostic evaluation of the patient with COVID-19 pneumonia, given that many studies have shown that greater lung involvement predicts the need for intensive care, complications, or death.[16,17]

Aim of the study

The goal of our study was to verify whether the LUS score could predict mortality, independently of other known prognostic factors. Secondary objectives were to verify whether an early involvement of the anterior chest areas is a negative prognostic factor; to identify an effective LUS score cut-off for rapid risk stratification to be applied in the ED; to assess whether the inclusion of LUS in the context of clinical-laboratory evaluation can improve prognostic stratification.

Materials and Methods

Setting and study design

We conducted a prospective study in two hospitals of central Italy, University Hospital of Pisa and S. Maria Misericordia Hospital of Perugia. The 2 centers belong to the same geographical area and have a similar catchment area, approximately 100,000 inhabitants.

The research followed the Declaration of Helsinki ethical principles and the international standards of Good Clinical Practice. The local Ethics Committee approved the protocol (protocol number 17828). Written informed consent was obtained from all the patients.

Study population

We enrolled a total of 285 patients (123 in Pisa and 162 in Perugia) admitted to the ED between March 2020 and March 2022.

All the subjects presented acute respiratory symptoms consistent with COVID-19 (fever, cough, dyspnoea, cold) and were positive for the nasopharyngeal molecular swab for Sars-CoV-2. Pneumonia was not an inclusion criterion for the study and enrolment was anterior to or concurrent with imaging. The exclusion criteria were chronic fibrosis, advanced lung cancer, and dialysis.

For each patient, we collected demographic data (age, sex), comorbidities, clinical presentation and course of the COVID-19 disease, data registered during ED stay such as vitals, laboratory tests, arterial blood gas analysis, ventilatory strategy (high flow nasal cannula HFNC, non-invasive ventilation NIV, orotracheal intubation (OTI), hospitalization setting, outcomes.

We performed standardized LUS with the topographic scheme and standardized report on all enrolled patients within 48 hours of admission, in the ED, or the first days of hospitalization. We excluded patients who, due to clinical needs, or technical or organizational problems due to the pandemic, did not undergo LUS with adequate methods and reporting within the scheduled times.

LUS topographic scheme and scoring

We adopted a 16-area scanning scheme (8 scans for each hemi-thorax) reduced to 12 areas (6 areas for each hemi-thorax) in patients whose clinical conditions did not allow complete mobilization and exploration of more posterior areas (Figure 1).

We used convex probes (frequency 2.5-5 MHz) along the intercostal spaces with the transverse approach. The focus was set on the pleural line and the progressive TGC (time gain compensation) was adjusted to optimize the image. Each area was evaluated independently, assigning a numerical value based on lung aeration (with increasing numerical scores as the lung aeration decreased). The score was derived by the one usually used in ARDS,[18] with a score of 0 in case of normal aeration (only A-lines or less than 3 separated B-lines per area); and a score of 1 in case of 3 or more B-lines or coalescent B-lines occupying ≤ 50% of the screen; score 2 for coalescent B-lines occupying > 50% of the screen; and score 3 for consolidation. A final LUS score was indexed since it was obtained from the sum of all single values divided by the number of all explored areas.

Anterior thoracic involvement was defined by the presence of LUS scores > 1 in at least 3 of the 4 anterior lung areas (R1 to R4 and L1 to L4).

Each exam was reviewed by expert sonographers (GB, SD) to verify the methodology and scoring assignment. All sonographers had undergone and successfully passed a LUS training on B-lines and a dedicated LUS training on COVID-19 findings. The B-lines inter-observer variability was examined by intraclass correlation coefficient (ICC) on 50 previously acquired LUS videos evaluated by an expert reader (LG).

Statistical analysis

Data are expressed as mean ± standard deviation, median, and interquartile range (IQR) for continuous numeric variables and as percentages for categorical variables. Differences between groups were analyzed with a parametric test (Student's T test) for normally distributed variables and a non-parametric test (Mann-Whitney U test) for non-normally distributed variables. $\chi 2$ test was used for comparisons between variables expressed in the form of frequencies. Receiving Operator Curves (ROC) were used to identify the best cut-off values of the LUS aeration score and their diagnostic accuracy in mortality prediction. Regression coefficient (β) and odds ratio (OR) with the corresponding 95% confidence interval

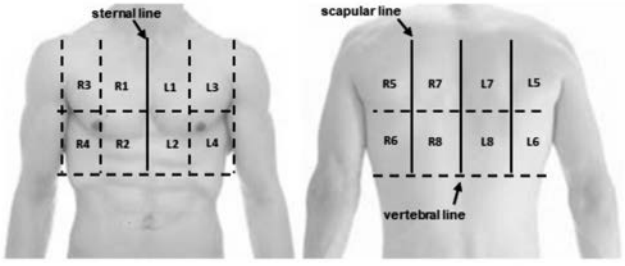

Figure 1. Topographic scheme adopted in the study.

(CI) were assumed as outputs of the logistic regression models. A p-value of 0.05 was considered statistically significant. Comparisons between ROC curves derived from difference evaluation models were made by De Long's test.

Results

We analyzed 285 patients (123 of Pisa, 162 of Perugia) with a mean age of 62.5 ± 14.9 years, of which 182 (63.9%) were male, and 103 (36.1%) were female. The most frequent clinical presentations upon admission to the ED were fever (n=205, 71.9%), cough (n=138, 48,4%), and dyspnoea (n=165, 58%). The days between the onset of symptoms and hospital admission were on average 7.4±5.4.

Table 1 shows the baseline characteristics, comorbidities, and outcomes of the two study center populations compared. Data showed no significant differences in the two subgroups, except for the mean age, which was higher in the Pisa group.

Univariate logistic analysis showed that the indexed LUS score was a significant predictor of death with an Odds Ratio (OR) of 2.8. A cut-off of 1.3 for the LUS score was identified through the ROC curve, with the best combination of sensitivity, equal to 70%, and specificity, equal to 73%.

Anterior thoracic involvement, defined as a LUS score ≥ 1 for at least 3 of the 4 anterior areas, at LUS examination performed within 6 days of symptom onset, was also predictive of death. The univariate logistic regression analyses of the LUS score are shown in Table 2.

We also evaluated the correlation between the LUS score indexed with P/F, demonstrating an inverse relationship between the 2 parameters (R-squared 0.09, R-0.31, p>0.001). This relationship is confirmed by subdividing the population based on the P/F cut-off value of 200, demonstrating higher mean indexed LUS score values in the group with altered P/F (16.77±9.6 *vs* 12.39±8.4, p-value 0.008). Subsequently, we verified mortality predictive power of clinical, laboratory blood gas indicators, already validated in literature.[19-21] The results of these analyses, performed as univariate logistic regression, are shown in Table 3.

Finally, we used the variables probed in previous tests in different multivariate logistic regression models (Table 4). Among clinical-laboratory parameters, the most impacting variable was the P/F<200, with an OR of 6.8. Our results showed that the LUS score, as introduced in multivariate regression models, maintained the ability to significantly predict death (Table 4).

Finally, we verified the accuracy in predicting death in three models, through a comparison of ROC curves. Figure 2 shows a significant improvement in the accuracy thanks to the LUS score introduction, with a corresponding increase in the area under the curve (AUC).

The best evaluation model was the one that included clinical-laboratory parameters, LUS, and age, with AUC= 0.92.

Discussion

LUS provided a key tool in the management, diagnosis, and monitoring of patients during the Sars-Cov2 pandemic.[8]

The present study demonstrated an association of the standardized LUS score with mortality in patients hospitalized for COVID-19, both when indexed LUS was considered as continuous value or with the cut-off of 1.3 (OR of respectively 2.8 and 6.7).

Multivariate logistic regression analysis demonstrated that the LUS score is an independent predictor of death in COVID-19

Table 1. Populations' features in the two subgroups.

	Tot; n=285 (%)	Perugia; n= 162 (%)	Pisa; n=123 (%)	p
Age	62.5 ± 14.9	60.8 ± 12.7	64.6 ± 17.2	0.006
Male sex	182 (63.9)	100 (61.7)	82 (66.7)	0.39
Smoke	50 (17.7)	25 (15.4)	25 (20.8)	0.24
Asthma	15 (5.3)	6 (3.7)	9 (7.3)	0.18
COPB	19 (6.7)	7 (4.3)	12 (9.8)	0.07
Hypertension	134 (47)	80 (49.4)	54 (43.9)	0.35
Chronic cardiac disease	27 (9.5)	12 (7.4)	15 (12.2)	0.17
Diabetes	49 (17.2)	29 (17.9)	20 (16.3)	0.72
Dyslipidaemia	52 (18.3)	31 (19.1)	21 (17.1)	0.65
Obesity	33 (14.5)	21 (13.0)	12 (18.5)	0.29
ICU	22 (7.8)	12 (7.4)	10 (8.4)	0.75
ETI	16 (5.6)	12 (7.4)	4 (3.3)	0.13
Death	27 (9.7)	18 (11.1)	9 (7.7)	034

COPD, chronic obstructive pulmonary disease; ICU, Intensive care unit; ETI, Endotracheal intubation.

Table 2. LUS univariate regression logistic analysis.

	Odds ratio	CL	Beta	p
Indexed LUS score	2.8	1.5-5.1	1	0.001
LUS cut-off=1,3	6.7	2.7-16	1.9	<0.001
Early anterior lung involvement	3.4	1.1-10	1.2	0.03

CL, confidence limits.

patients, compared to other powerful prognostic factors. Its significance is maintained in different models, even in the presence of age. Importantly, the ROC curves demonstrated that the introduction of LUS into the prognostic model results in a significant improvement in the accuracy of the evaluation (p value=0.04).

Several authors showed that lung ultrasound has a central role in the diagnosis and monitoring of COVID-19 patients. Some authors suggest that lung ultrasound with scoring may have a role in identifying the patient's prognosis, alone or associated with other indicators.[17,22-25]

Sacco *et al.* demonstrated, in a single-center population with a similar size, a correlation between LUS score and P/F, also confirmed by our results. Furthermore, the LUS score proved to effectively predict death, with sensitivity and specificity values like those of our study, although independence from other factors was not demonstrated.[22]

A meta-analysis and a systematic review of the prognostic role of the LUS score have been published on the subject.[26,27] In May 2021 Song G et al., in their meta-analysis including 16 studies for a total of 1541 covid patients, showed that the LUS score was higher in non-survivors than in survivors.[26] However, the studies included in this meta-analysis were highly heterogeneous, including small populations, did not describe when lung ultrasounds were performed during the hospital route, and above all these studies did not adjust for possible confounding factors. In 2022 Gil-Rodríguez *et al.* published a systematic review showing that a high LUS score is associated with developing unfavorable outcomes, including 66 studies for a total of 4687 patients.[27] Only 7 of the studies included in this systematic review evaluated the role of LUS score in the prediction of mortality. Particularly in three of them,[28-30] the authors compared LUS scores between survivors and non-survivors, and in four the authors directly correlated LUS scores with death.[16,31-33] Only two of them adjusted for possible confounding factors: Garcia de Alencar *et al.*[34] adjusted for age and Wangüemert Pèrez *et al.*[35] for sex and age-adjusted Charlson index. Numerous studies have demonstrated that the typical distribution of COVID-19 pneumonia is mantle, patchy, and prevalent in the lung posterior fields, with a typical evolution over time in

Table 3. Clinical-laboratory parameters univariate regression logistic analysis.

	Odds ratio	CL	Beta	p
Age > 65	18.7	4.3-8.0	2.9	<0.001
Male sex	5.1	1.5-17.3	1.6	<0.001
Neutrophils (%)	1.2	1.06-1.3	0.2	0.002
Lymphocytes (%)	0.9	0.8-1	-0.1	0.002
L < 20%	4.7	1.08-20.4	1.6	0.03
CRP	1	0.99-1.007	0.0003	0.93
CRP > 6.5	2.7	1.1-6.4	1	0.02
P/F > 200	8.8	3.6-21.3	2.2	<0.001
Lactate	1.9	1.2-2.8	0.6	0.002
Lactate <1.3	3.6	1.4-9	1.3	0.005

L, lymphocytes; CRP, C-reactive protein.

Table 4. Multivariate regression logistic models compared.

	Odds ratio	CL	Beta	p
Model 1: C-L p				
Female sex	0.3	0.1-1.2	-1.16	0.08
L < 20%	1.4	0.3-6.8	0.3	0.68
CRP > 6.5	1.9	0.6-6.6	0.6	0.31
P/F < 200	6.8	2.4-19.4	1.9	<0.001
Lat > 1.3	2.3	0.8-6.4	0.8	0,11
Model 2: C-L p + LUS				
Female sex	0.2	0.1-0.9	0.7	0.03
L < 20%	1.4	0.3-7.3	0.9	0.7
CRP > 6.5	2	0.6-7.1	0.6	0.3
P/F < 200	5.4	1.8-16.4	0.6	0.002
Lat > 1.3	2,5	0.9-7.5	0.6	0.09
LUS > 1.3	6.7	2.2-20.3	0.6	<0.001
Model 3: C-L p + LUS + age				
Female sex	0.2	0.04-0.8	3.1	0.03
L < 20%	1	0.2-6.1	0.03	0.9
CRp > 6.5	2.2	0.5-9.3	0.8	0.3
P/F < 200	7.3	1.9-28.6	1.9	0.004
Lat > 1.3	2.1	0.6-7.6	0.7	0.3
LUS > 1.3	8.5	2.3-30.8	2.1	0.001
Age > 65	21.7	4-116.7	3.08	<0.001

C-L p, clinical-laboratory parameters; LUS, lung ultrasound; CRP, C-reactive protein.

terms of extension and consolidation.[6] Our study shows that pulmonary involvement extended to lung anterior areas from the early stages, is a strong predictor of mortality, as already suggested by Castelao *et al.*[36] This confirms the observation relating to the clinical and imaging evolution observed in Sars-Cov 2 disease, in which the implementation of therapeutic actions in the early stages of the disease is crucial for the good outcome of the patient.

The main strength of our study is that we showed that the LUS score can predict mortality also after adjusting for the main variables currently considered as severity disease predictors, whether they are patient pre-existing characteristics (age, gender), laboratory indicators (inflammation index, lactate) or respiratory parameters (P/F ratio). Also, most of the studies in both the meta-analysis and the systematic review included a population's sample size smaller than ours.

Our population consisted of two numerically similar groups from hospitals in the same geographical and catchment area. The patients were homogeneous in terms of anamnestic characteristics, management, hospitalization setting, and ventilatory strategy.

The methodology was rigorous through topographic evaluation and numerical reporting scheme by trained operators, supervised by expert sonographers, despite the urgency conditions in which LUS examinations were performed. Furthermore, the choice of the indexed score allowed an accurate examination of all patients including critically ill patients, in which the chest could not be fully evaluated.

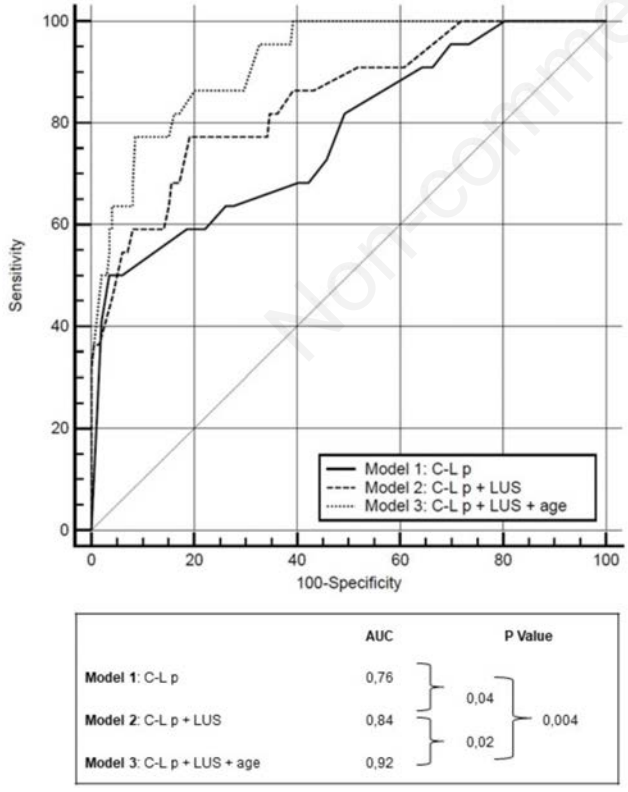

Figure 2. Comparison between the ROC curves of the 3 models. C-L p, clinical-laboratory parameters; LUS, lung ultrasound.

Limitations

US findings, despite a standardized methodology, are sometimes nonspecific. They could be attributable to pathological phenomena other than Sars-Cov2 pneumonia, such as lung congestion of cardiogenic origin, which can also be correlated to a negative prognosis. For reasons related to the pandemic situation, which did not allow a complete evaluation in all cases, the subjects are not consecutive.

Another limitation of the study was the partial discrepancy of the methodology applied, given that 12 quadrants were explored in some subjects and 16 in others. However, this choice considered the emergency needs and allowed even very critical patients to be included in the study, in which LUS necessarily had to be performed quickly and without mobilization.

Conclusions

Our study demonstrates that LUS applied with a topographic standardized scanning scheme and numerical reporting predicts mortality in patients hospitalized for COVID-19. The combination of the indexed LUS score with a cut-off of 1.3 to other clinical, anamnestic, laboratory, and blood gas analytical parameters, guarantees an accurate prognostic stratification in the patient affected by Sars-Cov2 disease. Testing for anterior thoracic involvement early in the disease history is also useful in predicting outcomes. Thus, LUS should be an indispensable element of diagnostic, monitoring, and prognostic evaluation in low-resource care settings.

References

1. Li Y, Xia L. Coronavirus Disease 2019 (COVID-19): role of chest CT in diagnosis and management. AJR Am J Roentgenol 2020;214:1280-6.
2. Islam N, Ebrahimzadeh S, Salameh JP, et al. Thoracic imaging tests for the diagnosis of COVID-19. Cochrane Database Syst Rev 2021;3:CD013639.
3. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020;8:420-2.
4. Bellone A, Etteri M, Maino C, et al. The role of bedside ultrasound in the diagnosis and outcome of patients with acute respiratory failure. Emerg Care J 2013;9:e2.
5. Volpicelli G, Gargani L, Perlini S, et al. Lung ultrasound for the early diagnosis of COVID-19 pneumonia: an international multicenter study. Intensive Care Med 2021;47:444-54.
6. Volpicelli G, Gargani L. Sonographic signs and patterns of COVID-19 pneumonia. Ultrasound J 2020;12:22.
7. Vetrugno L, Bove T, Orso D, et al. Lung ultrasound and the COVID-19 "pattern": not all that glitters today is gold tomorrow. J Ultrasound Med 2020;39:2281-2.
8. Gargani L, Soliman-Aboumarie H, Volpicelli G, et al. Why, when, and how to use lung ultrasound during the COVID-19 pandemic: enthusiasm and caution. Eur Heart J Cardiovasc Imaging 2020;21:941-8.
9. Vetrugno L, Bove T, Orso D, et al. Our Italian experience using lung ultrasound for identification, grading and serial follow-up of severity of lung involvement for management of patients with COVID-19. Echocardiography 2020;37:625-7.
10. Barbieri G, Gargani L, Lepri V, et al. Long-term lung ultrasound follow-up in patients after COVID-19 pneumonia

hospitalization: A prospective comparative study with chest computed tomography. Eur J Intern Med 2023;110:29-34.
11. Zheng Z, Peng F, Xu B, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. J Infect 2020;81:e16-e25.
12. Grasselli G, Greco M, Zanella A, et al. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. JAMA Intern Med 2020;180:1345-55.
13. Wynants L, Van Calster B, Collins GS, et al. Prediction models for diagnosis and prognosis of covid-19: systematic review and critical appraisal. BMJ 2020;369:m1328.
14. Chu K, Alharahsheh B, Garg N, Guha P. Evaluating risk stratification scoring systems to predict mortality in patients with COVID-19. BMJ Health Care Inform 2021;28:e100389.
15. Bima P, Pivetta E, Baricocchi D, et al. Lung ultrasound improves outcome prediction over clinical judgment in COVID-19 patients evaluated in the emergency department. J Clin Med. 2022;11:3032.
16. Lichter Y, Topilsky Y, Taieb P, et al. Lung ultrasound predicts clinical course and outcomes in COVID-19 patients. Intensive Care Med 2020;46:1873-83.
17. Ravetti CG, Vassallo PF, de Barros GM, et al. Lung ultrasound can predict the clinical course and severity of COVID-19 disease. Ultrasound Med Biol 2021;47:2090-6.
18. Bouhemad B, Mongodi S, Via G, Rouquette I. Ultrasound for "lung monitoring" of ventilated patients. Anesthesiology 2015;122:437-47.
19. O'Driscoll M, Ribeiro Dos Santos G, Wang L, et al. Age-specific mortality and immunity patterns of SARS-CoV-2. Nature 2021;590:140-5.
20. Li T, Zheng F, Cheng F. The function of myeloid-derived suppressor cells in COVID-19 lymphopenia. Int Immunopharmacol 2022;112:109277.
21. Bonaventura A, Mumoli N, Mazzone A, et al. Correlation of SpO. Intern Emerg Med 2022;17:1769-75.
22. Secco G, Delorenzo M, Salinaro F, et al. Lung ultrasound presentation of COVID-19 patients: phenotypes and correlations. Intern Emerg Med 2021;16:1317-27.
23. Boccatonda A, Grignaschi A, Lanotte AMG, et al. Role of lung ultrasound in the management of patients with suspected SARS-CoV-2 infection in the emergency department. J Clin Med 2022;11:2067.
24. Boccatonda A, Cocco G, Ianniello E, et al. One year of SARS-CoV-2 and lung ultrasound: what has been learned and future perspectives. J Ultrasound 2021;24:115-23.
25. Smargiassi A, Soldati G, Torri E, et al. Lung ultrasound for COVID-19 patchy pneumonia: extended or limited evaluations? J Ultrasound Med 2021;40:521-8.
26. Song G, Qiao W, Wang X, Yu X. Association of lung ultrasound score with mortality and severity of COVID-19: a meta-analysis and trial sequential analysis. Int J Infect Dis 2021;108:603-9.
27. Gil-Rodríguez J, Pérez de Rojas J, Aranda-Laserna P, et al. Ultrasound findings of lung ultrasonography in COVID-19: A systematic review. Eur J Radiol 2022;148:110156.
28. Rojatti M, Regli IB, Zanforlin A, et al. Lung ultrasound and respiratory pathophysiology in mechanically ventilated COVID-19 patients-an observational trial. SN Compr Clin Med 2020;2:1970-7.
29. Bosso G, Allegorico E, Pagano A, et al. Lung ultrasound as diagnostic tool for SARS-CoV-2 infection. Intern Emerg Med 2021;16:471-6.
30. Bonadia N, Carnicelli A, Piano A, et al. Lung ultrasound findings are associated with mortality and need for intensive care admission in COVID-19 patients evaluated in the emergency department. Ultrasound Med Biol 2020;46:2927-37.
31. Recinella G, Marasco G, Tufoni M, et al. Clinical role of lung ultrasound for the diagnosis and prognosis of coronavirus disease pneumonia in elderly patients: a pivotal study. Gerontology 2021;67:78-86.
32. Boero E, Rovida S, Schreiber A, et al. The COVID-19 Worsening Score (COWS)-a predictive bedside tool for critical illness. Echocardiography 2021;38:207-16.
33. Bitar ZI, Shamsah M, Maadarani O, et al. Lung ultrasound and sonographic subpleural consolidation in COVID-19 pneumonia correlate with disease severity. Crit Care Res Pract 2021;2021:6695033.
34. de Alencar JCG, Marchini JFM, Marino LO, et al. Lung ultrasound score predicts outcomes in COVID-19 patients admitted to the emergency department. Ann Intensive Care 2021;11:6.
35. Wangüemert Pérez AL, Figueira Gonçalves JM, Hernández Pérez JM, et al. Prognostic value of lung ultrasound and its link with inflammatory biomarkers in patients with SARS-CoV-2 infection. Respir Med Res 2021;79:100809.
36. Castelao J, Graziani D, Soriano JB, Izquierdo JL. Findings and prognostic value of lung ultrasound in COVID-19 pneumonia. J Ultrasound Med 2021;40:1315-24.