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Lung ultrasound score predicts oxygen requirements in adult patients with COVID 19 pneumonia

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Abstract

Aims: Despite widely used, the ability of lung ultrasound (LUS) to predict oxygen needs in patients with COVID-19 pneumonia is still unclear. The aim of this study is to evaluate the performance of LUS findings for the assessment of oxygen requirements among patients admitted through the emergency department (ED) with COVID-19 pneumonia.

Material and methods: Between 1st November 2021 and 20th November 2021, 80 consecutive patients admitted to the ED of the "Madre Giuseppina Vannini" general hospital with COVID-19 pneumonia underwent bedside LUS within 24 h of admission. A total LUS score, graded 0 (best)-36 (worst) was computed. According to their oxygen requirements, patients were stratified into three groups, as follows: no-oxygen therapy group, venturi mask (VMK) oxygen therapy group, helmet continuous positive airway pressure (CPAP) treatment group. Primary endpoint was the association between LUS score and the need for oxygen therapy.

Results: Overall, 68 (85%) required oxygen therapy, and nearly 60% needed helmet CPAP treatment. Patients in the helmet CPAP group presented significantly higher LUS score compared to the others (CPAP vs VMK: 26.10 ± 3.6 vs 19.5 ± 5.3; $p<0.0001$; CPAP vs no-O2: 26.10 ± 3.6 vs 10.5 ± 5.6; $p<0.0001$).

Conclusions: Among patients with COVID-19 related pneumonia, the LUS score performed at ED admission is associated with the patient's oxygen requirements, further studies are needed to establish the prognostic role of LUS in prediction of bad outcomes.

Keywords: Lung ultrasound; COVID-19 pneumonia; oxygen requirements.

Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been causing a severe disease, named COVID-19, whose rapidly spread worldwide resulted in a pandemic, currently constituting a dire public health emergency [1]. The major morbidity and mortality from COVID-19 is largely due to the viral pneumonia causing severe hypoxia and potentially evolving into acute respiratory distress syndrome (ARDS). At present, available reports suggest that among patients infected with SARS-CoV-2, up to 20% develop a severe disease, depicted by hypoxic respiratory failure and consequent need for oxygenation support, with up to 12% of patients requiring mechanical ventilation [2-9]. Continuous positive airway pressure therapy and mechanical non-invasive ventilation have been used, even if the optimal approach to treatment of severe COVID-19 remains uncertain. [3, 7-9].

In this context of critically ill of COVID-19 patients' overflow, promptly classification is essential to identify the most appropriate therapeutic intervention and follow-up. Consequently, lung ultrasound (LUS), whose role as a helpful and accurate tool in diagnosis of pneumonic alveolar-interstitial syndrome is well known, has become common practice in the clinical management of COVID-19 patients [9-12]. At LUS evaluation, the injured lung patterns in COVID-19 patients may vary from mild to severe interstitial pattern (patchy single to confluent B lines, white lung [13-15]), to alveolar involvement, with small

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and large consolidations, suggestive of either hypo-ventilated or non-ventilated parenchyma. Therefore, some experts have strongly encouraged and developed standardized approaches regarding equipment and LUS acquisition protocol for the management of patients with COVID-19 [14-17].

However, despite since the beginning of the pandemic LUS has been widely used both for diagnosis and evolution monitoring of SARS-CoV-2 pneumonia, few data are currently available on the role of a systematic LUS evaluation for risk stratification, as well as to predict oxygen requirements and outcome in COVID-19 patients [13, 15, 18]. The aim of this study is to evaluate the association between LUS findings at Emergency Department (ED) admission and clinical features, including the need for oxygen therapy, among patients hospitalized with COVID-19 related pneumonia.

Material and Methods

Study design

This is a single-center, prospective study conducted in the ED of "Madre Giuseppina Vannini" General Hospital, a referral center for COVID-19 in Rome, center Italy. We enrolled all the consecutive adult patients admitted to the ED between November 1th 2020 and November 20th 2020 with diagnosis of COVID-19, confirmed by a positive reverse transcriptase polymerase chain reaction assay for SARS-CoV-2 of nasal and pharyngeal swab specimens [19]. All patients underwent to LUS examination and chest computed tomography (CT) scan within 24 hours since ED admission and, to be definitively included in the analysis, had to be received ultrasound and/or radiologic diagnosis of COVID-19-related pneumonia. Patients were not considered if already on orotracheal intubation at ED arrival or who required orotracheal intubation at ED admission, and patients for whom a do not resuscitate order was in place. Patients who did not present ultrasound and/or radiologic signs of pneumonia on chest CT scan were excluded. The study was conducted in accordance with the principles expressed in the Declaration of Helsinki and was approved by the local ethical committee. All patients provided written informed consent.

Study variables

Baseline clinical characteristics at ED admission of each patient included in the analysis were prospectively collected, and included: gender; age; physiological parameters - systolic and diastolic blood pressure, heart rate, respiratory rate, level of consciousness estimated with Glasgow coma scale; major comorbid conditions - diabetes, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), malignancies; laboratory tests - C-reactive protein (CRP), procalcitonin, creatinine, sodium, and potassium levels, hematocrit and white blood cell (WBC) count; blood gas analysis, that was obtained in room air when possible, and in case of severe respiratory distress at a fraction of inspired oxygen (FiO2) adequate for keeping peripheral oxygen saturation (SpO2) at least ≥ 90%. In cases needing ventilator support, the first blood gas sample obtained before ventilation or soon after ventilation start was considered.

Oxygen requirements at ED admission and patient's stratification

Patients included in the analysis were stratified according to their oxygen requirements at ED admission. The evaluations were provided by the emergency physicians, and were based on a set of standardized parameters, including physical examination and blood gas analysis results, as follows: no oxygen therapy for SpO2 ≥ 95% and/or partial pressure of oxygen (PaO2)/FiO2 ratio > 350; venturi mask (VMK) oxygen therapy in the case of PaO2 <70 mmHg, SpO2 <95%, and a RR >24/min; helmet continuous positive airway pressure (CPAP) treatment for a pO2/FiO2 < 200 after at least 1 hour of VMK oxygen therapy with FiO2 of 50%. Thus, enrolled patients were divided in three groups: those who did not need oxygen therapy – no O2 therapy group; those who needed VMK oxygen therapy – VMK group; and those who needed a non-invasive ventilation with helmet CPAP – helmet CPAP group.

Lung Ultrasound

All patients enrolled in the study underwent to bedside LUS within 24 hours of ED admission. The LUS examinations were performed using a six-zone method for each lung, that included a scan of the anterior, antero-lateral, posterior and posterior-lateral segments of the thorax, resulting in a sequence of ultrasound scans of 12 anatomical chest landmarks [18]. LUS was performed with a portable device (Vivid I GE healthcare, Milan, Italy), equipped with a convex transducer (3.5-5 MHz), by four emergency physicians with expertise in LUS recording and interpretation, using a fixed standard 10-cm depth. For every single scan was reported a LUS scoring system ranging from 0 to 3 [14, 20, 21]:

- Score 0: presence of continuous pleural line and regular and horizontal artefacts (A line)

- Score 1: presence of sporadic vertical artefacts, assuming the appearance of bright B lines or small bands of white lung.

- Score 2: B lines and white lung areas are predominant (**Figure 1**);

- Score 2b: presence of small subpleural consolidation (darker area) (**Figure 2**) in the context of predominance of B lines and white lung areas.

- Score 3: presence of largely extended white lung with or without larger consolidations (**Figure 3**).

Moreover, we further attempted to study whether this LUS score was able to predict the need for non-invasive mechanical ventilation with helmet CPAP at ED admission. To this aim, we decided retrospectively to further classify patients into two groups: "risk echo" in which we considered patients who have been attributed a LUS score ≥ 2 in all the 12 segments of the thorax (total score ≥24) and a score of 2b/3 in at least one of these segments; "no-risk echo", in which were included the other patients.

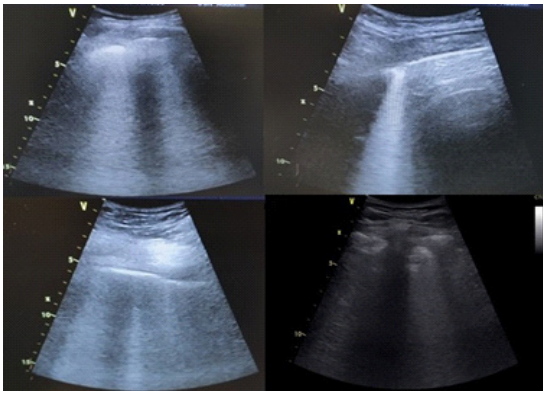

Figure 1: *Pattern 2 with vertical artifacts and white lung confluent area.*

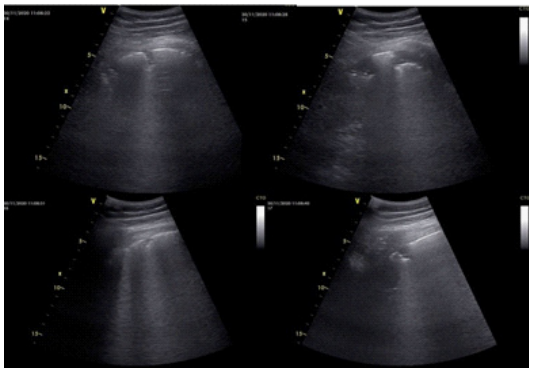

Figure 2: *Pattern 2b with vertical artifacts and anechoic subpleural areas.*

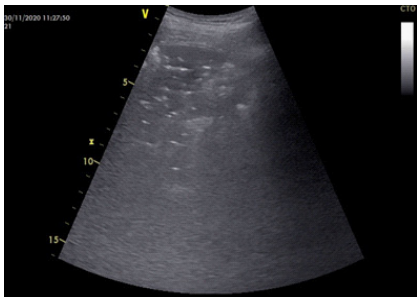

Figure 3: *Pattern 3 with vertical confluent artifact and large lung consolidation.*

Follow-up and outcome

Outcome analysis started at the time of LUS exams. The primary endpoint was the association between the LUS score performed at ED admission and the need for oxygen therapy. Secondary endpoints were to test the association between LUS score and blood gas analysis values, including the PaO2/FiO2 ratio. Electronic health records were used to retrieve information about follow-up (death vs discharge).

Statistical analysis

Data are shown as number and percentage for categorical variables, and mean and standard deviation for continuous variables, as appropriate according to the normal distribution by the Shapiro-Wilk normality test. Differences between groups were assessed either by Fisher's exact test or Chi-square test for categorical variables. Mann–Whitney U test or Kruskal–Wallis test were performed to compare continuous variables. The Pearson correlation coefficient was used to describe the bivariate correlation between variables. P values below 0.05 were considered statistically significant. All analyses were performed with the SPSS software (IBM, Armonk, New York), version 24.

Results

During the study period, 80 patients met the inclusion criteria and were included in the study cohort. Overall, 68 patients (85%) required oxygen therapy, the half of whom needed helmet CPAP treatment. Fourteen patients (17.5%) died during in-hospital stay. Of these, 11 (65%) were on helmet CPAP treatment. None of deceased patients died in ED prior than ward admission. (Table 1) documents the baseline characteristics of patients in each respective group. Patients in helmet CPAP group were older than patients in the other groups, even if the difference was not significant. Not unexpected, most of patients enrolled had higher respiratory rate at admission, that was even higher in helmet CPAP group (18.9 ±

Table 1: *General characteristic of the study population according to the respiratory support (n=80).*

	Study population (n=80)	CPAP helmet (n=40)	VMK (n=28)	No O_2 therapy (n=12)	p*	p**	p***
Age (yrs.), mean (SD)	64(14)	67 (12)	61.8 (17)	59.1 (12.2)	0,16	0,1	0,7
Sex, n (%) *M* *F*	 58(72,5) 22(27,5)	 30 (75) 10 (25)	 20 (71) 8 (29)	 8 (67) 4 (33)	0,7	0,5	0,4
Hypertension, n (%)	27(33,75)	17 (42.5)	8 (28.5)	2 (16.7)	0,4	**0,08**	0,1
Diabets, n(%)	17(21,25)	10(25)	4(14)	3(25)	0,4	0,5	0,8
COPD, n (%)	4(5)	4 (10)	0 (-)	0 (-)	**0,01**	**0,01**	1
Coronary artery disease,n(%)	4(5)	2 (5)	1 (3.5)	1 (8.3)	0,7	0,5	0,5
Malignancies, n (%)	5(6,25)	2 (5)	2 (7.1)	1 (8.3)	0,7	0,8	0,7
GCS/15, mean (SD)	15	15	15	15	NS	NS	NS
Blood pressure (mmHg), mean (SD) *Systolic* *Diastolic*	 125,4±12,7 74,9±8,1	 125 ± 13.8 74 ± 8.3	 125.4 ± 11.7 76.3 ± 7	 126.8 ± 11.9 74.5 ± 9.8	 0.7 0.4	 0.6 0.4	 0.7 0.4
Heart rate (beats per minute), mean (SD)	83±15	82 ± 18.5	85.4 ± 11.8	82.8 ± 9.2	0.4	0.7	0.5
Respiratory rate (breaths per minute), mean (SD)	18±2,4	18.9 ± 2.6	17.6 ± 2.3	16.9 ± 1.4	0.1	**0.01**	0.7
Hematocrit (%), mean (SD)	39,5±4,2	38.7 ± 4.7	40.4 ± 3.8	40.2 ± 3.2	0.2	0.2	1
WBC (x10^3/µL), mean (SD)	7,9±3,4	8.4 ± 3.5	8.3 ± 3.3	5.4 ± 2.3	0.9	**0.01**	**0.02**
Sodium mEq/L, mean (SD)	132±3,7	132 ± 3.5	132 ± 3.9	134 ± 3.4	0.5	0.4	0.2

Potassium mEq/L, mean (SD)	3,9±0,5	4 ± 0.57	3.8 ± 0.6	4 ± 0.3	0.3	0.2	0.3
Creatinine mg/dl, mean (SD)	0,99±0,3	1.03 ± 0.3	0.9 ± 0.2	0.9 ± 0.2	0.1	0.1	0.3
C-reactive protein (mg/dl), mean (SD)	8,7±6,5	10.75 ± 8	7.3 ± 4.7	6 ± 3.4	0.2	0.1	0.5
Procalcitonin (µg/dl), mean (SD)	0,27±0,4	0.34 ± 0.4	0.23 ± 0.4	0.1 ± 0.05	**0.07**	**0.05**	0.9
Mortality, n (%)	13(16,25)	11(27,5)	2(7.1)	0(-)	**0,08**	**0,001**	0,1
	* CPAP vs VMK; ** CPAP vs noO2; *** VMK vs no oxygen therapy						
	Abbreviations: CPAP: Continuous Positive Airway Pressure; VMK: Venturi Mask; SD: Standard Deviation; M: Male; F: Female; COPD: Chronic obstructive Pulmonary Disease; GCS: Glasgow Coma Scale; WBC: White Blood Cells.						

2.6; p 0.01 for CPAP vs no-oxygen therapy group). Patients in helmet CPAP group were more commonly hypertensive and more frequently had diagnosis of COPD compared to other patients. Among comorbidities, diabetes, CAD and malignancy were homogeneously distributed between the three groups. Considering laboratory values, patients who required oxygen therapy, either with VMK or helmet CPAP, showed higher WBC count compared to those who did not require oxygen therapy. Furthermore, patients in helmet CPAP group showed a statistically significant increase in procalcitonin levels compared to the other groups (**Table 1**). CRP mean levels were higher than normal (n.v. 5 mg/L) in all the patients enrolled, with no differences among the groups.

LUS score and oxygen requirements

In our cohort, a higher LUS score was associated with the patient's need for oxygenation support, as well as the need for helmet CPAP treatment (CPAP vs VMK: 26.10 ± 3.6 vs 19.5 ± 5.3; p<0.0001; CPAP vs no-oxygen therapy: 26.10 ± 3.6 vs 10.5 ± 5.6; p<0.0001; (**Table 2, Figure 4**). Furthermore, we found also that attributing a LUS score of 2b-3 at least at one single scan of the chest correlated with the oxygen needs (100% of patients in CPAP helmet group and nearly 70% of patients in VMK oxygen therapy) (**Table 2**). Moreover, a regression analysis showed a linear inverse correlation between mean LUS score and PaO2/FiO2 ratios, as shown in the dispersion diagram in (**Figure 5**).

***Table 2**: Respiratory and LUS characteristics in the study population (n=80).*

	Study population (n=80)	CPAP helmet (n=40)	VMK (n=28)	No O_2 therapy (n=12)	p*	p**	p***
Lus score mean(SD)	21,4±7,1	26 ± 3.6	19.5 ± 5.3	10.5 ± 5.6	< 0.001	< 0.001	<0.001
P/F mean(SD)	230±108	149.4 ± 41.9	287 ± 79.5	394 ± 49.6	<0.001	<0.001	<0.001
pH mean(SD)	7,47±0,05	7.46 ± 0.06	7.48 ± 0.04	7.44 ± 0.02	0.5	0.3	0.4
2b/3 n(%)	61(76,25)	40(100)	19(67)	2(16.6)	0.005	<0.001	<0.001

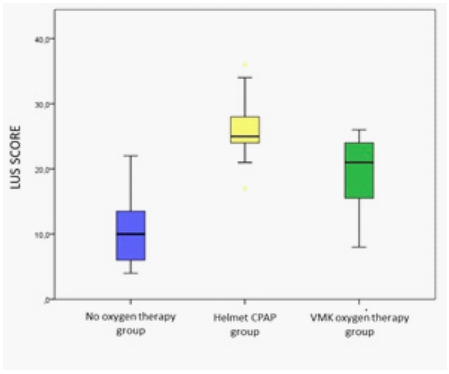

***Figure 4:** Boxplot illustrating the distribution of LUS score with respect to the different oxygen therapies patients underwent.*

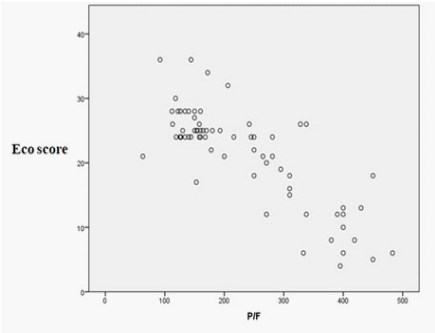

***Figure 5:** Dispersion diagram of the relation between LUS total score and PaO2/FiO2 ratio values.*

PaO2, partial pressure of oxygen; FiO2, fraction of inspired oxygen; ROC, receiver operating characteristics; LUS, lung ultrasound; CPAP, continuous positive airway pressure.

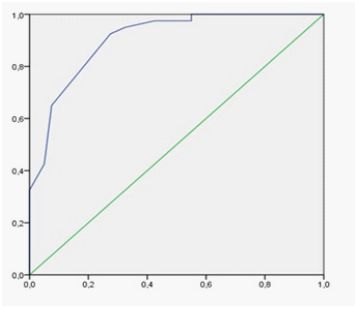

***Figure 6:** ROC Curve analysis of LUS score mean ≥ 24 with respect to patients' need for helmet CPAP treatment.*

Discussion

The main finding of the present study is that, among patients hospitalized with COVID-19 related pneumonia, the LUS score at ED admission is feasible for detecting oxygen requirements, including the need for non-invasive mechanical ventilation with helmet CPAP. The novel SARS-CoV-2 is causing a viral pandemic, whose most relevant clinical feature is the development of hypoxemic lung failure due to the interstitial bilateral pneumonia, with the consequent need for oxygenation support [2-9]. Arterial hypoxemia is mainly due either to ventilation-perfusion mismatch and intrapulmonary shunting, as result of an extensive alveolar damage and exudation, endothelial lesions and coagulation disorders typically depicted in ARDS [22].

Up to date, LUS has emerged as a rapid, unexpensive and easy-to-use tool for evaluation of lung involvement in patients with

suspected or confirmed COVID-19 [13, 16, 20, 21]. However, studies evaluating the sensitivity and specificity of LUS in COVID-19 pneumonia and its ability in detecting patients who will require oxygen therapy are still lacking [18,23]. Furthermore, even if several authors have already assessed the good performance of LUS to detect COVID-19 pneumonia [13-17, 20], very few reports were available on its ability to predict outcomes in COVID-19 patients [15, 18, 23, 24].

In the present study, patients requiring oxygenation support actually had several predictive characteristics of a more severe course of SARS-CoV-2 infection. Indeed, they were older and more commonly hypertensive [2, 3, 5]. Moreover, considering laboratory values, these patients showed higher procalcitonin and CRP levels compared to those who did not require oxygen therapy. In fact, both these markers correlate to inflammation and are not only well-known indexes of severity of pulmonary infections [25], but also of COVID-19 severe respiratory disease, as revealed by recent reports [26, 27]. The LUS score used in this study, performed by Soldati et al. [14] and already validated by an Italian task force of LUS independent experts [28], is actually the first score proposed to assess the severity of lung involvement in COVID-19 related pneumonia. Furthermore, this score is based on LUS patterns already employed in the diagnosis of several lung conditions.

Our analysis showed that patients with higher LUS score at ED admission presented more often oxygen requirements, either with VMK or non-invasive mechanical ventilation with helmet CPAP, as well as higher degree of lung hypoxemic failure, depicted by a lower PaO2/FiO2 ratio. Our results are broadly in accordance with those of Perrone et al. [23] who found that in a cohort of 52 consecutive patients with confirmed SARS-CoV-2 infection, a LUS protocol evaluating 14 anatomic landmarks was associated with established end points of clinical worsening, including need for high-flow oxygen support or ICU admission, and death. Similarly, Lichter et al. [18] showed that a LUS evaluation performed in 120 consecutive patients admitted to a single Center in Tel Aviv due to COVID-19, was not only strongly correlated with the need for invasive mechanical ventilation, but also a strong predictor of mortality in patients hospitalized with COVID-19.

Furthermore, Bonadia et al. [24] in a recent report conducted in an ED setting of 41 COVID-19 patients showed an association between LUS severity at admission and the subsequent need for ICU admission, invasive ventilation and death. The association found in our study between oxygen requirements and LUS findings in COVID-19 patients is in line with what has been found in previous studies conducted by Falgarone et al. [29] who demonstrated that the extension of the lung involvement evaluated by LUS was able to predict with good sensitivity the need for oxygen therapy in setting of 50 patients admitted in a single center in Paris. Our results may really have important clinical implications. Indeed, the use of a relatively simple, unexpensive and non-invasive diagnostic tool, such as LUS, could reliably help to guide early the most appropriate ventilatory support in these patients. Importantly, LUS evaluation may be useful to prioritize ICUs admission of those patients who are at higher risk of requiring mechanical ventilation.

There are several limitations of this study that have to be considered. Firstly, and needless to say, we did not perform the analysis to evaluate the independent predictors of clinical deterioration and death of enrolled patients, as this was not an endpoint of our study. Thus, we definitively could not establish the independent role of LUS in prediction of in-hospital mortality. However, in our cohort, patients who required helmet CPAP treatment since ED admission showed a higher LUS score and higher mortality rate compared to those underwent to VMK oxygen therapy or who do not require oxygen therapy. Therefore, we could speculate that a higher LUS score was associated with higher risk of in-hospital mortality.

Secondly, this is a single-center study which enrolled a small cohort of the only patients with confirmed LUS or chest CT COVID-19-related pneumonia. Patients without signs of lung involvement within 24 hours from ED admission were excluded, and a second LUS examination protocol was not foreseen during ED stay. Thus, on one hand LUS score could have been over-estimated, being evaluated only in patients with signs of lung involvement at ED admission. On the other hand, LUS score could have been under-estimated, since the analysis did not include those patients who developed pneumonia during ED stays. Thirdly, as given for any mono-centric study, both selection and attention bias may have affected our results. On the other hand, the strengths of our study include its prospective design, the standardized ultrasound examination and scoring system used.

Conclusions

Among patients with COVID-19 related pneumonia the LUS score performed at ED admission well correlates with the patients' oxygen requirements. Moreover, in these patients, a standardized and easy-to-use LUS protocol has proven to be a feasible tool not only for the diagnosis and assessment of pulmonary involvement, but also for risk stratification of patients with COVID-19 pneumonia. Further studies are needed to confirm these findings, also to investigate for the presence of an optimal cut-off value of LUS score for clinical use. Lastly, the prognostic performance of LUS will need to be proved by larger studies, in order to definitively establish its independent role in predicting bad outcomes.

Declaration of conflict of interest

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest: All authors declare no conflict of interest for this paper.

Availability of data and material: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability: Not applicable.

Ethics approval: This study was conducted in accordance with the principles expressed in the Declaration of Helsinki and was approved by the local ethical committee.

Consent to participate: Informed consent to participate in this study was obtained from all individual participant included in the study.

Consent for publication: Informed consent for publication in a journal article was obtained from all individual participants included in the study.

Acknowledgments

Authors' contributions: Conceptualization, Methodology, Software, Data curation, Formal analysis, Material preparation, Data collection, Writing - review & editing: ML, BML. Lung ultrasound performing: ML, BML, CC, FP. Conceptualization, Methodology, Data curation, Writing - review & editing, Supervision: PG, SC, PL. All authors contributed to material preparation, read and approved the final manuscript.

References

1. World Health Organization. WHO Coronavirus Disease (COVID-19) Dashboard. https://covid19.who.int/ Accessed on April 11, 2021.

2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395(10223):497-506.

3. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020; 475-481. Erratum in: Lancet Respir Med. 2020; 8(4):e26.

4. Mahase E. Covid-19: most patients require mechanical ventilation in first 24 hours of critical care. BMJ 2020; 368:m1201.

5. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020; 323(13):1239-1242.

6. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW; the Northwell COVID-19 Research Consortium, Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA 2020; 323(20):2052-2059.

7. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. COVID-19 Lombardy ICU Network. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA 2020; 323(16):1574-1581.

8. Wu C, Chen X, Cai Y, Xia J, Zhou X, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA 2020; Intern Med 180(7):934. Erratum in: JAMA Intern Med. 2020; 180(7):1031.

9. Myers LC, Parodi SM, Escobar GJ, Liu VX. Characteristics of Hospitalized Adults With COVID-19 in an Integrated Health Care System in California. JAMA. 2020;323(21):2195-2198.

10. Rinaldi L, Milione S, Fascione MC, Pafundi PC, Altruda C, Di Caterino M, et al. Relevance of lung ultrasound in the diagnostic algorithm of respiratory diseases in a real-life setting: A multicentre prospective study. Respirology 2020; (5):535-542.

11. Lichtenstein DA. Ultrasound in the management of thoracic disease. Crit Care Med. 2020; 35(5):S250-61.

12. Arbelot C, Ferrari F, Bouhemad B, Rouby JJ. Lung ultrasound in acute respiratory distress syndrome and acute lung injury. Curr Opin Crit Care. 2008; 14(1):70-4.

13. Volpicelli G, Lamorte A, Villén T. What's new in lung ultrasound during the COVID-19 pandemic. Intensive Care Med. 2020; 46(7):1445-1448.

14. Soldati G, Smargiassi A, Inchingolo R, Buonsenso D, Perrone T, Briganti DF, et al. Proposal for International Standardization of the Use of Lung Ultrasound for Patients With COVID-19: A Simple, Quantitative, Reproducible Method. J Ultrasound Med 2020; 39(7):1413-1419.

15. Peng QY, Wang XT, Zhang LN. Chinese Critical Care Ultrasound Study Group (CCUSG). Findings of lung ultrasonography of novel corona virus pneumonia during the 2019-2020 epidemic. Intensive Care Med 2020; 5:849-850.

16. Mento F, Perrone T, Macioce VN, Tursi F, Buonsenso D, Torri E, et al. On the Impact of Different Lung Ultrasound Imaging Protocols in the Evaluation of Patients Affected by Coronavirus Disease 2019: How Many Acquisitions Are Needed? J Ultrasound Med 2020. [DOI: 10.1002/jum.15580].

17. Smargiassi A, Soldati G, Torri E, Mento F, Milardi D, Del Giacomo P, De Matteis G, Burzo ML, Larici AR, Pompili M, Demi L, Inchingolo R. Lung Ultrasound for COVID-19 Patchy Pneumonia: Extended or Limited Evaluations? J Ultrasound Med. 2021; 40(3):521-528.

18. Lichter Y, Topilsky Y, Taieb P, Banai A, Hochstadt A, Merdler I, Gal Oz A, Vine J, Goren O, Cohen B, Sapir O, Granot Y, Mann T, Friedman S, Angel Y, Adi N, Laufer-Perl M, Ingbir M, Arbel Y, Matot I, Szekely Y. Lung ultrasound predicts clinical course and outcomes in COVID-19 patients. Intensive Care Med. 2020; (10):1873-1883. Erratum in: Intensive Care Med. 2020 Sep 25.

19. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspect: interim guidance. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance Accessed on April 11, 2021.

20. Soldati G, Smargiassi A, Inchingolo R, Buonsenso D, Perrone T, et al. Is There a Role for Lung Ultrasound During the COVID-19 Pandemic? J Ultrasound Med. 2020; (7):1459-1462.

21. Soldati G, Smargiassi A, Inchingolo R, Buonsenso D, Perrone T, Briganti DF, et al. On Lung Ultrasound Patterns Specificity in the Management of COVID-19 Patients. J Ultrasound Med. 2020; 39(11):2283-2284.

22. Katzenstein AL, Bloor CM, Leibow AA. Diffuse alveolar damage--the role of oxygen, shock, and related factors. A review. Am J Pathol. 1975; 85(1):209-28.

23. Perrone T, Soldati G, Padovini L, Fiengo A, Lettieri G, Sabatini U, et al. A New Lung Ultrasound Protocol Able to Predict Worsening in Patients Affected by Severe Acute Respiratory Syndrome Coronavirus 2 Pneumonia. J Ultrasound Med 2020. [DOI: 10.1002/jum.15548].

24. Bonadia N, Carnicelli A, Piano A, Buonsenso D, Gilardi E, Kadhim C, 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(11):2927-2937.

25. Chalmers S, Khawaja A, Wieruszewski PM, Gajic O, Odeyemi Y. Diagnosis and treatment of acute pulmonary inflammation in critically ill patients: The role of inflammatory biomark-

ers. World J Crit Care Med. 2019; 8(5): 59-71.

26. Covino M, De Matteis G, Santoro M, Sabia L, Simeoni B, Candelli M, et al. Clinical characteristics and prognostic factors in COVID-19 patients aged ≥80 years. Geriatr Gerontol Int. 2020; (7):704-708.

27. Wang L. C-reactive protein levels in the early stage of COVID-19. Med Mal Infect 2020; 50(4):332-334.

28. Roy S, Menapace W, Oei S, Luijten B, Fini E, Saltori C, et al. Deep Learning for Classification and Localization of COVID-19 Markers in Point-of-Care Lung Ultrasound. IEEE Trans Med Imaging 2020; 39(8):2676-2687.

29. Falgarone G, Pamoukdjian F, Cailhol J, Giocanti-Auregan A, Guis S, Bousquet G, et al. Lung ultrasound is a reliable diagnostic technique to predict abnormal CT chest scan and to detect oxygen requirements in COVID-19 pneumonia. Aging (Albany NY) 2020; 12(20):19945-19953.