EM - ORIGINAL



PEGALUS: predictivity of elderly age, arterial gas analysis, and lung ultrasound. A new prognostic score for COVID-19 patients in the emergency department—an observational prospective study

Giorgia Borio^{1,3} · Stefano Tentori^{1,2} · Federica Farolfi^{1,3} · Gloria Vanessa Suma^{1,3} · Paola Rienzo^{1,3} · Annapaola D'ambrosio^{1,3} · Marta Citro^{1,3} · Mariachiara Antonini^{1,3} · Paola Maffi^{2,3}

Received: 14 December 2021 / Accepted: 28 June 2022 / Published online: 27 July 2022 © The Author(s), under exclusive licence to Società Italiana di Medicina Interna (SIMI) 2022

Abstract

Background Periodic surges of COVID-19 patients seeking care in the hospital environment overwhelm systems reduce the availability of resources for treatment of non-COVID-19 cases (Zheng et al. in J Hosp Infect 106:325–329, 2020). Hospital flow and resource management could be greatly enhanced by differentiating patients who are likely at risk of adverse clinical outcomes from those who could safely be discharged after evaluation and managed outside of the hospital setting (Sun et al. in J Infect Dis 223:38–46, 2021).

Herein, we propose a prognostic score named PEGALUS (Predictivity of Elderly age, arterial blood Gas Analysis and Lung UltraSound) that could potentially help clinicians properly and rapidly choose the appropriate allocation of COVID-19 patients admitted to the emergency department (ED).

Methods This observational prospective study enrolled COVID-19 patients who were admitted to the ED of IRCCS San Raffaele Hospital (HSR).

Results 230 COVID-19 patients were enrolled and 30-day follow-up data was collected. Composite outcome was death or need for oro-tracheal intubation (OTI). 50 patients (21.5%) reached the outcome during the observational period. In multi-variate Cox analysis, age, PO_2/FiO_2 ratio, pCO_2 , duration of symptoms, and lung ultrasound evaluation were significantly associated with the adverse outcome. We obtained a new scorecard (PEGALUS) according to the hazard ratio of the identified predictors. PEGALUS score performed well in predicting the composite outcome (AUC 0.866, 95% IC 0.812–0.921; p < 0.001). Kaplan–Meier showed that a PEGALUS score <7 was associated with a good 30-day prognosis (survival rate 97.5%), compared to a PEGALUS score of 7–11 (survival rate 85.9%; p log-rank 0.009) and PEGALUS score > 11 (survival rate 49.3%; p log-rank < 0.001).

Conclusions PEGALUS score performed at the admission can predict adverse outcomes in patients with COVID-19. The systematic application of this score might permit a more accurate and rapid treatment allocation in this setting.

Keywords COVID-19 · POCUS · Lung ultrasound · Emergency

Giorgia Borio, Stefano Tentori, Federica Farolfi, Gloria Vanessa Suma, Paola Rienzo, Annapaola D'ambrosio, Marta Citro, Mariachiara Antonini and Paola Maffi equally contributed to this work.

Giorgia Borio borio.giorgia@hsr.it

- ¹ Emergency Department, IRCCS San Raffaele Hospital, Via Olgettina 60, Milan, Italy
- ² Internal Medicine and Transplantation Unit, IRCCS San Raffaele Hospital, Milan, Italy
- ³ Vita-Salute San Raffaele University, Milan, Italy

Introduction

Periodic surges of COVID-19 patients seeking care in the hospital environment overwhelm systems reduce the availability of resources for treatment of non-COVID-19 cases, place unpredictable demands on inpatient resources, and create increased risk for transmission of the infection to staff or other patients [1].

COVID-19 patient acuity has remained fairly consistent with the majority of patients having somewhat mild symptoms, about 25% experiencing hospitalization, and 5–6% requiring critical care intervention [2]. This suggests that a significant proportion of patients seeking care for COVID-19 at the emergency department (ED) may have less severe presentations of the disease that could potentially be evaluated and managed in the community or in an outpatient setting [3, 4].

Identifying this patient population could reduce the impact of patient surges on ED capacity and inpatient resources [4]. Hospital flow and resource management could be greatly enhanced by differentiating patients who will likely be at risk of adverse clinical outcomes and those who need mechanical ventilation from those who could safely be discharged after evaluation and managed outside of the hospital setting.

Although the pandemic has reduced patient volume in most EDs, the percentage of patients requiring admission rapidly doubled or tripled in many hospitals and continues to fluctuate in tandem with the rate of COVID-19 cases in the community [5, 6].

A number of studies have investigated the role of lung ultrasound (LUS) in predicting worse clinical outcomes including need for intensive care unit (ICU) admission, mechanical ventilation, and even patient death in COVID-19.

In a cohort of 120 patients, Lichter et al. [7] showed that baseline LUS score performed at the time of admission strongly correlates with the eventual need for invasive mechanical ventilation and is a strong predictor of mortality.

In another study performed by Brahier et al. [8], LUS performed in the ED correlates with mortality with AUC 0.76.

Conversely, in a study conducted by Stecher et al. [9], LUS performed at ICU admission failed to predict the outcome of COVID-19 patients.

As our knowledge of the disease progressed, validated tools that predict COVID-19 prognosis in the hospital settings have been proposed by integrating LUS evaluation with clinical and laboratory markers of COVID-19 severity.

In "Prognostic value of bedside lung ultrasound score in patients with COVID-19", Ji et al. [10] found that a lung ultrasound score (LUSS) > 12, older age, and lower lymphocyte count were predictors of adverse events during hospitalization in COVID-19 patients, while in "Lung ultrasound predicts clinical course and outcomes in COVID-19 patients". Lichter et al. [7] demonstrated that LUS can dynamically assess the ventilation status and provide earlier prediction of pulmonary ventilation status and disease deterioration. In the study, LUSS increased progressively according to clinical severity, since clinical deterioration was associated with increased follow-up LUSS (p=0.0009).

Those scores often use data elements that are not immediately available in the ED including lymphocyte count and chest X-ray, or it requires a serial lung ultrasound evaluation which is not always performable in the EDs due to the burden of numbers. In "CLUE: COVID-19 lung ultrasound in emergency department" [11], Manivel et al. proposed a simple protocol based on anatomical parameter: LUSS and a physiological parameter, oxygen requirement at the time of examination, to aid emergency clinicians make disposition decisions of COVID-19 patients. It has to be considered that a clinician's decision on the need for supplemental oxygen is a complex process, involving factors like oxygen saturation, work of breathing, respiratory rate, and pre-existing medical conditions (i.e., chronic obstructive pulmonary disease and heart disease). A single parameter like oxygen saturation or respiratory rate may not represent real-time clinical practice.

We performed an observational retrospective-prospective study assessing the role of a single LUS evaluation performed at the admission to the ED together with arterial blood gas analysis and clinical-pathological findings in predicting the severity of coronavirus disease 2019. Within this context, we propose a new scoring system (Predictivity of Elderly age, arterial blood Gas Analysis and Lung UltraSound, PEGALUS) that could potentially help clinicians properly choose the appropriate treatment allocation in the ED.

Materials and methods

This is a single-center prospective observational study conducted at the IRCCS San Raffaele Hospital (HSR), a 1350-bed tertiary care hospital in Milan, Italy. During the COVID-19 pandemic, the HSR ED was designated as one of the COVID-19 HUB Centers in the region. Therefore, the ED received critical patients delivered by ambulancies to receive advanced medical support (i.e., ECMO), but also self-presented patients.

All participants provided informed consent and the institution research ethics board approved the study (protocol number 196/INT/2020).

We included a convenience sample of patients admitted to the ED from 2020/11/09 to 2021/05/09 with suspected or proven SARS CoV-2 infection and when the study physician sonographer was available to complete lung ultrasound examinations.

Subsequently, patients with negative RT-PCR assay of nasopharyngeal swab or tracheal aspiration specimens were excluded.

Patient demographic characteristics and reported symptoms were collected, and arterial blood gas analysis was performed. Bedside LUS examinations were performed by seven emergency medicine attending physicians with at least 6 month experience in point-of-care emergency ultrasonography. Patients were examined in the sitting position, or in case of clinical deterioration or poor compliance, in the supine, semi-recumbent, or lateral decubitus position. A Philips[®] Sparq Ultrasound machine with 2.5- to 5-MHz convex transducer was used.

The LUS protocol involved the examination of 12 lung regions, six for each hemithorax, delimited by the anterior and the posterior axillary lines and the horizontal line passing through the nipples.

In our study, we validated four LUS patterns (Visual LUS Score, Visual LUSS) to express several degrees of lung involvement in COVID-19 based on a qualitative lung aeration assessment. Those patterns range from normal A lines through confluent B lines and subpleural consolidation, to large consolidations seen in the most severe presentation of the disease. To assess the stage of lung involvement at the time of presentation to ED, we asked the physicians to assign each patient to a pattern (Pattern 1–4), according to ultrasound findings observed in the 12 zones:

- PATTERN 1: lung sliding or discrete B lines (<25% lung involvement)
- PATTERN 2: irregular pleura with multifocal B lines (> 25% lung involvement)
- PATTERN 3: small pleural consolidation with coalescent B lines
- PATTERN 4: consolidation with air bronchogram.

Subsequently, the standard LUSS was calculated by assessing each pulmonary region which is scored according to four ultrasound aeration patterns as proposed by Via et al. [12]. For a given region of interest, points are allocated according to the worst ultrasound pattern observed. The final LUSS is the sum of points in all 12 regions and ranges from 0 to 36 [13]. Then, according to the existing studies in ARDS and other attempts of standardization in COVID-19, the following cut-off were used to categorized LUSS in severity classes depending upon the lung involvement as: mild (LUSS class 1, total score 1–5), moderate (LUSS class 2, total score 6–15), and severe (LUSS class 3, total score > 15), while a normal lung would total 0 points (LUSS class 0) [11].

Routine blood tests included: complete blood count, C-reactive protein (CRP), Lactate DeHydrogenase (LDH), ferritin, electrolytes, and renal and liver function tests. In addition, coagulation profiles with age-adjusted D-dimer (XDP) were performed. Chest X-ray and/or CT-scan were performed according to local protocol.

All the treatments performed in the ED were reported, including medical therapies (steroids, anticoagulation therapy, and antibiotics) and need for oxygen supplementation and/or mechanical ventilation.

A follow-up at 30 days after ED admission was conducted by examining medical records or via telephone call. The primary endpoint of the study was the combination of death



Fig. 1 Flow chart of study identification, inclusion and exclusion criteria

or need for oro-tracheal intubation (OTI) during a 30-day observational period.

Continuous data are expressed as means ± standard deviation, or median with respective interquartile range in the case of a non-normal distribution of the variable. Dichotomous variables are presented as percentages. ANOVA or Mann-Whitney tests were used to compare continuous variables among different groups of patients, whereas Chisquare analysis or Fisher's test was used to compare discrete variables. Univariate and multivariate Cox regression analyses were used to identify variables associated with adverse outcomes. Kaplan-Meier analysis and Log-Rank test were used to compare free-of-events survival among different groups of patients. Receiver-operating characteristics (ROC) analysis was used to examine the performance of new models at predicting adverse outcomes. The curve represents a plot of sensitivity versus 1-specificity. AUC (C-index) was calculated from the ROC curve. The differences between AUC (C-index) were tested using the StAR programme [14]. A two-sided p value < 0.05 was considered to indicate statistical significance. All analyses were performed with SPSS 20.0 software (IBM, Inc., Armonk, NY, USA).

Results

The study population was composed of 233 patients; 2 patients were excluded due to negative RT-PCR assay of nasopharyngeal swab (see Fig. 1). 151 (64.8%) were men and the median age was 62 years (53–77). At the time of presentation to the ED median duration of symptoms was

Among the 233 enrolled patients, 152 (65.2%) needed oxygen therapy and 26 (11.2%) required non-invasive mechanical ventilation (NIMV) during their ED stay. A total of 70 patients (30%) were directly discharged from ED, while 162 (69.6%) were admitted to the wards; 1 patient died in the ED (Table 1 for details).

LUS was performed on each patient and relative findings were reported as explained above (see Materials and methods section). Detailed finding reports are shown in Table 1.

A complete 30-day follow-up was possible for 230 of 233 patients (98.7%). Median time of hospitalization was 12 days (8–23), and 50 patients (21.5%) reached the combined outcome during the observational period. Of these 50 patients, 31 (62%) died, while 19 patients (38%) were intubated. Among those 19 intubated, 7 (36%) died during the 30-day observational period. The combined outcome was achieved after a median of 13, 5 days (the 25% percentile, 75% percentile were 4, 7 days and 20 days).

Three patients were lost at the 30-day follow-up due to an impossibility for the author to contact them.

Univariate Cox regression logistic regression showed that age >65 years and history of hypertension, diabetes, or cardiovascular disease were predictive of a poorer outcome. Similarly, patients who presented with dyspnea, mean arterial pressure (MAP) < 65 mmHg, oxygen peripheral saturation $(SpO_2) < 94\%$, or respiratory rate (RR) > 30/min were at higher risk of worse outcome. A similar trend was also seen for patients presenting symptoms for less than 7 days at the time of ED presentation, even without fulfilling statistical significance.

Interestingly, when performing univariate and multivariate analysis, neither home COVID-19 therapies nor COVID-19 therapies undertaken during the ED stay (LMWH, steroid therapy, antiviral therapies, or immunotherapies) were found statistically significant in determining the primary outcome.

Finally, lower P/F values, hypocapnia $(pCO_2 < 35 \text{ mmHg})$, higher levels of lactic dehydrogenase (LDH), creatinine, and age-adjusted D-dimer were significantly associated with poorer outcomes.

Furthermore, when performing a multivariate Cox analysis model, age higher than 65 years, presence of symptoms for less than 7 days, lower P/F ratio and pCO_2 lower than 35 mmHg remained predictive of adverse outcomes (Table 2).

In univariate Cox regression, LUSS was associated with adverse outcome (hazard ratio 2.837, 95% IC 1.770–4.548; p < 0.001). However, when Kaplan–Meier analysis was performed, only LUSS class 3 showed a significantly lower free-to-events survival with respect to the other classes (63.3% versus 85.9% LUSS 2, 92.3% LUSS 1 and 100% LUSS 0). Moreover, when we added LUSS classification to the multivariate model, it was no longer predictive of adverse outcomes (hazard ratio 1.549, 95% IC 0.918–2.616; p > 0.05).

Visual LUSS (see "Materials and methods" for details) was significantly associated with poorer outcome (hazard ratio 1.574; 95% IC 1.296–1.91; p < 0.001) in univariate Cox regression. Moreover, it seemed to be more accurate in determining adverse outcome, since in Kaplan–Meier analysis, every visual LUSS pattern was associated with a significantly different free-to-event survival with respect to each other (100% Pattern 1, versus 86.3% Pattern 2, versus 73.6% Pattern 3, versus 47.6% Pattern 4). Finally, when we added visual LUSS to the multivariate model described above, it was significantly associated with poorer outcome (hazard ratio 1.25, 95% CI 1.013–1.541; p 0.037; Table 3).

To provide a new score (PEGALUS) based on these clinical, pathophysiological, and echographic datas, we created a new score card by rounding off the hazard ratio of the significant predictors (age > 65 years; duration of symptoms < 7 days, *P/F* classes, $pCO_2 < 35$ mmHg, and visual LUSS) to the nearest 0.5 value. The score for each variable is shown in Table 4. Patient-specific PEGALUS scores were calculated by summing all variable scores (minimum score 0; maximum 21, 5; median 9 [IQR 6, 5–12]).

The PEGALUS score showed to be a good predictor of the composite outcome (AUC 0.866, 95% IC 0.812–0.921; p < 0,001), with a superior predictive power compared with LUS alone (Fig. 2). Best cut-off value according to Youden's index was 11, 25. Kaplan–Meier analysis showed that PEGALUS score <7 was associated with 30 days significantly better prognosis (survival rate 97.5%), compared to PEGALUS score 7–11 (survival rate 85.9%) and PEGALUS score >11 (survival rate 49.3%; Fig. 3).

Discussion

In the context of the COVID-19 pandemic, rapid assessment of disease severity and correct treatment allocation in the emergency department are crucial for increasing surge capacity. The possibility to properly assess the severity of each patient's disease through a simple model based on routinely and promptly available information can permit the identification of patients who need more intensive treatments and of those who could be rapidly and safely dismissed from ED.

Table 1Clinical and laboratorycharacteristics of the patients

Characteristic ($N=233$)	Median (IQR) or $N(\%)$	
Age (years)	62 (53–77)	
Sex (female/male)	82 (35.2%)/151 (64.8%)	
Ethnicity (Caucasians/other)	212 (91%)/21 (8%)	
Comorbidities		
Smoke	88 (37.8%)	
Hypertension	98 (42.1%)	
Diabetes	40 (17.2%)	
Cardiovascular disease	46 (19.7%)	
Chronic respiratory disease	24 (10.3%)	
Chronic kidney disease	19 (8.2%)	
COVID-19 symptoms		
Duration before hospital admission (days)	7 (5–9,5)	
Fever	189 (81.1%)	
Dyspnea	126 (54.1%)	
Cough	130 (55.8%)	
Gastrointestinal	66 (28.3%)	
Other	104 (44.6%)	
Vital signs		
Systolic blood pressure (mmHg)	130 (115–140)	
Diastolic blood pressure (mmHg)	75 (70–85)	
Mean blood pressure (mmHg)	95 (85–100)	
Heart rate (bpm)	88 (80–98)	
RR (bpm)	24 (18–30)	
Arterial blood gas analysis		
pH	7.46 (7.44–7.49)	
$pCO_2 (mmHg) < 35$	170 (73%)	
Lactate > 2 mmol/L	33 (14.3%)	
P/F	305 (246–356)	
<i>P</i> / <i>F</i> > 300	122(52.4%)	
<i>P/F</i> 200–300 (mild acute respiratory distress)	92 (39.5%)	
<i>P/F</i> 100–200 (moderate acute respiratory distress)	14 (6%)	
P/F < 100 (severe acute respiratory distress)	5 (2.1%)	
Blood tests		
White blood cells ($\times 10^{9}/L$)	6.8 (4.9–9.1)	
Lymphocytes ($\times 10^{9}/L$)	0.9 (0.6–1.3)	
Creatine phosphokinase (U/L)	98.5 (56-165.3)	
Lactic dehydrogenase (U/L)	326 (260–434)	
C-reactive protein (mg/L)	50.3 (19.5–105.8)	
Ferritin (ng/mL)	679 (371–1203)	
Pathological age-adjusted D-dimer	138 (59.2%)	
Type of supplemental oxygen during ED stay		
No need for oxygen supplementation	81 (34.8%)	
Nasal cannula	49 (21%)	
Venturi mask	77 (33%)	
Noninvasive ventilation	26 (11.2%)	
ED disposition		
Home discharge	70 (30%)	
Ward admission	162 (69.6%)	
Death in ED	1 (0.4%)	
LUS score	13 (6–20)	

Table 1	(continued)

Lung ultrasound scoring system (LUSS) severity classes according to standard cla	ssification
Early and scoring system (ECSS) severity classes according to standard cha	
LUSS 0	15 (6.4%)
LUSS 1	40 (17.2%)
LUSS 2	79 (33.9%)
LUSS 3	99 (42.5%)
Visual lung ultrasound scoring system (visual LUSS)	
Pattern 1	26 (11.2%)
Pattern 2	75 (32.2%)
Pattern 3	110 (47.2%)
Pattern 4	22 (9.4%)

In the present study, we propose a new risk model and scoring system, named PEGALUS, for the risk stratification of COVID-19 patients in the ED. The PEGALUS model is based on clinical (age, duration of symptoms), pathophysiological (*P*/*F* ratio and pCO_2), and ultrasound parameters, routinely used in the point-of-care approach by emergency physicians.

Several studies have demonstrated that older age represents an important risk factor for mortality in COVID-19 patients [15]. There is current evidence that patients older than 65 years old are at higher risk of worse outcomes. Thus, it is not surprising that in our study age of > 65 years old was found to be an independent negative prognostic factor.

Similarly, a retrospective analysis performed by Huang et al. [16] showed that shorter duration of symptoms (less than 7 days) before admission to ED could be an important

 Table 2
 Predictors of adverse outcome in COVID-19 patients by multivariate Cox proportional hazard model

Variables	Hazard ratio (95% CI)	p value	
Age (>65 years)	3.563 (1.573-8.069)	0.002	
Hypertension	1.230 (0.627–2.413)	ns	
Diabetes	1.377 (0.690–2.748)	ns	
Cardiovascular disease	2.005 (0.994-4.046)	ns	
Dyspnea	1.732 (0.782–3.836)	ns	
Duration of symptoms (<7 days)	2.332 (1.164-4.669)	0.017	
PAM < 65 mmHg	0.693 (0.130-3.702)	ns	
<i>S</i> pO ₂ < 94%	1.327 (0.633–2.782)	ns	
Respiratory rate > 30/min	1.080 (0.517-2.256)	ns	
<i>P/F</i> (Berlino class)	2.074 (1.354–3.179)	0.001	
s	3.346 (1.255-8.919)	0.016	
Serum LDH (>2×upper normal limit)	1.831 (0.858–3.906)	ns	
Serum creatinine (above normal limits)	0.935 (0.456–1.917)	ns	
Age-adjusted XDP (pathological)	1.149 (0.550–2.399)	ns	

 Table 3
 Clinical, pathophysiological, and echographic predictors of adverse outcome in COVID-19 patients by multivariate Cox proportional hazard model

Variables	Hazard ratio (95% CI)	p Value
Age (>65 years)	4.438 (2.160–9.119)	< 0.001
Duration of symptoms (<7 days)	1.626 (0.884–2.992)	0.118
P/F (Berlino class)	2.465 (1.725-3.521)	< 0.001
<i>p</i> CO ₂ (<35 mmHg)	3.491 (1.380-8.828)	0.008
Visual LUSS	1.250 (1.013-1.541)	0.037

Table 4 PEGALUS score system

Variables	Classification	Score	
Age (years)	≤65	0	
	>65	4.5	
P/F (Berlino class)	> 300	0	
	200-300	2.5	
	100-200	5	
	<100	7.5	
$pCO_2 (mmHg)$	<35	3.5	
	≥35	0	
Duration of symptoms	<7	1.5	
	≥7	0	
Visual LUSS pattern	1	0	
	2	1.5	
	3	3	
	4	4.5	



PEGALUS	<	7	7-11		>11	
Score	X ²	p Value	X ²	p Value	\mathbf{X}^2	p Value
< 7			6,798	0,009	53,536	< 0,001
7-11	6,798	0,009			30,757	< 0,001
> 11	53,536	< 0,001	30,757	< 0,001		

Fig. 3 Log-rank (Mantel-Cox) pairwise comparisons



Fig. 2 PEGALUS ROC curve compared to LUSS for predictivity of the composite outcome

prognostic factor for the progression to severe pneumonia in COVID-19. This is probably due to a more aggressive presentation of the disease in those patients, as seen in our study.

COVID-19 is an acute respiratory disease causing interstitial pneumonitis and/or severe acute respiratory syndrome (ARDS) often presenting as hypoxic-normo/hypocapnic (type 1) acute respiratory failure. The severity of hypoxemia is independently associated with in-hospital mortality [17]. In addition, the previous studies have shown that P/F ratio is strictly associated with worse outcomes [18].

Hypoxemia-driven tachypnoea and hyperpnea predict clinical deterioration induced by disease severity and can be responsible for more severe hypocapnia. In this setting, it is not surprising that patients with lower pCO_2 levels were at higher risk of adverse outcomes [19].

In this study, we proposed a different approach to lung ultrasound based on visual estimation of the stage of pulmonary disease in COVID-19 (Visual LUSS). This is comparable to formal methods for the evaluation of LUSS and provides valuable clinical measurements of pulmonary involvement. Visual LUSS could allow quicker and possibly more accurate estimation of the severity of disease in real time. In the present study, visual LUSS performed better than standard lung ultrasound score in predicting COVID-19 outcome; therefore, it was included in the PEGALUS model.

In the present study, the PEGALUS score included promptly available clinical, pathophysiological, and ultrasound predictors, and it performed well at predicting adverse outcomes (death or need for OTI) in COVID-19 patients. We believe that the systematic application of this score at the admission to the ED might permit an accurate and rapid treatment allocation in this setting: patients with PEGALUS score of <7 could be safely managed at home; those with a score between 7 and 11 would need further evaluations; and those with a score of > 11 would need rapid hospitalization and more intensive care support.

Interestingly, in our cohort, median time to reach the outcome was 13, 5 days (4, 7–20 days) after ED admission. PEGALUS score worked well in predicting both early and latest adverse event, suggesting that it might be an important tool to rule out patients who will be likely at risk of death or need for OTI.

There are several limitations of this study that should be highlighted.

The first limitation to this study includes the possibility of selection bias from enrolling a convenience sample of patients with COVID-19 based on the availability of physician sonographer. The potential exclusion of the lower acuity patients and those who were early discharged from the ED may explain the high prevalence of ultrasound findings in our study. However, this potential bias may be less relevant when we consider the adverse outcome in those who had established COVID-19 and had higher severity of the disease. The relatively small number of subjects significantly limits the power of the study to detect more-nuanced findings. This is compounded by the relatively large number of possible ultrasound findings and their combinations. Thus, for this study, we simplified the search space but recognized that a larger data set may yield even more interesting findings.

Therefore, further multi-center studies with larger sample sizes are needed to confirm the potential predictive role of PEGALUS score in COVID-19.

Second, this was an observational prospective study; the limitations of these studies to make causal inference are well known; therefore, the present work could be of limited interest in decision-making. Nevertheless, we believe that our results are relevant to improving the point-of-care approach in COVID-19 patients. The PEGALUS score would need to be validated in the context of a prospective trial, but we believe that the systematic application of the PEGALUS model could immediately help risk-stratify patients presenting to ED with COVID-19 and aid clinicians in making appropriate patient care decisions.

Third, although lung ultrasound is operator-dependent, we did not test for intra-observer variability; to minimize this limitation, lung ultrasound was performed using a standardized procedure and pre-defined scoring methods.

Finally, the actual epidemiologic situation is improving and the availability of anti-SARS CoV-2 vaccination might finally solve the pandemic, making our results of less interest. However, the SARS CoV-2 pandemic is currently far from being declared over, especially in countries where vaccine availability is more scarce. In addition, our findings could potentially be replicated in populations of patients affected by other forms of interstitial disease, and the PEGALUS score might help clinicians in promptly making decisions in these settings, as well.

Conclusions

Despite some limitations, our study demonstrated that lung ultrasound together with promptly available clinical and pathophysiological data might guide clinicians in their decision-making with COVID-19 patients in the emergency department. Further larger studies are needed to confirm these findings and to test the potential application of PEGALUS score in other forms of interstitial pneumonia.

Declarations

Conflict of interest The authors declare that there are no competing interests. This work was not supported by any grant.

Human and animal rights statement The authors states that this research was conducted in accordance with the Helsinki Declaration as revised in 2008.

References

- Zheng C, Hafezi-Bakhtiari N, Cooper V et al (2020) Characteristics and transmission dynamics of COVID-19 in healthcare workers at a London teaching hospital. J Hosp Infect 106(2):325–329. https://doi.org/10.1016/j.jhin.2020.07.025
- Sun H, Jain A, Leone MJ et al (2021) CoVA: an acuity score for outpatient screening that predicts coronavirus disease 2019 prognosis. J Infect Dis 223(1):38–46. https://doi.org/10.1093/infdis/ jiaa663
- Siow WT, Liew MF, Shrestha BR, Muchtar F, See KC (2020) Managing COVID-19 in resource-limited settings: critical care considerations. Crit Care 24(1):167. https://doi.org/10.1186/ s13054-020-02890-x
- Yang BY, Barnard LM, Emert JM et al (2020) Clinical characteristics of patients with coronavirus disease 2019 (COVID-19) receiving emergency medical services in King County, Washington. JAMA Netw Open 3(7):e2014549. https://doi.org/10.1001/ jamanetworkopen.2020.14549
- Baugh JJ, White BA, McEvoy D et al (2020) The cases not seen: patterns of emergency department visits and procedures in the era of COVID-19. Am J Emerg Med. https://doi.org/10.1016/j.ajem. 2020.10.081
- Jeffery MM, D'Onofrio G, Paek H et al (2020) Trends in emergency department visits and hospital admissions in health care systems in 5 states in the first months of the COVID-19 pandemic in the US. JAMA Intern Med 180(10):1328–1333. https://doi.org/ 10.1001/jamainternmed.2020.3288
- 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 (2020) Lung ultrasound predicts clinical course and outcomes in COVID-19 patients. Intensive Care Med 46(10):1873– 1883. https://doi.org/10.1007/s00134-020-06212-1 (Epub 2020 Aug 28. Erratum in: Intensive Care Med. 2020 Sep 25)
- Brahier T, Meuwly JY, Pantet O, Brochu Vez MJ, Gerhard Donnet H, Hartley MA, Hugli O, Boillat-Blanco N (2021) Lung ultrasonography for risk stratification in patients with coronavirus disease 2019 (COVID-19): a prospective observational cohort study. Clin Infect Dis 73(11):e4189–e4196. https://doi.org/10.1093/cid/ ciaa1408
- Stecher SS, Anton S, Fraccaroli A et al (2021) Lung ultrasound predicts clinical course but not outcome in COVID-19 ICU patients: a retrospective single-center analysis. BMC Anesthesiol 21:178. https://doi.org/10.1186/s12871-021-01396-5
- Ji L, Cao C, Gao Y et al (2020) Prognostic value of bedside lung ultrasound score in patients with COVID-19. Crit Care 24:700. https://doi.org/10.1186/s13054-020-03416-1
- Manivel V, Lesnewski A et al (2020) CLUE: COVID-19 lung ultrasound in emergency department. Emerg Med Australas. https://doi.org/10.1111/1742-6723.13546
- Via G et al (2012) Lung ultrasound in the ICU: from diagnostic instrument to respiratory monitoring tool. Minerva Anestesiol 78:1282–1296
- Rouby JJ, Arbelot C, Gao Y, APECHO Study Group et al (2018) Training for lung ultrasound score measurement in critically ill patients. Am J Respir Crit Care Med 198(3):398–401. https://doi. org/10.1164/rccm.201802-0227LE
- Vergara IA, Norambuena T, Ferrada E et al (2008) StAR: a simple tool for the statistical comparison of ROC curves. BMC Bioinform 9:265
- 15. Dessie ZG, Zewotir T (2021) Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies

and 423,117 patients. BMC Infect Dis 21:855. https://doi.org/10. 1186/s12879-021-06536-3

- Bernheim A, Mei X, Huang M et al (2020) Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. Radiology 295:3
- Xie J, Covassin N, Fan Z et al (2020) Association between hypoxemia and mortality in patients with COVID-19. Mayo Clin Proc 95(6):1138–1147. https://doi.org/10.1016/j.mayocp.2020.04.006
- Yanli Gu et al (2021) PaO₂/FiO₂ and IL-6 are risk factors of mortality for intensive care COVID-19 patients. Sci Rep 15(3):353-359
- Zhou F, Yu T, Du R et al (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 395:1054–1062

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.