Additive value of lung ultrasound to clinical parameters for prognosticating COVID-19

Received: 24 Oct 2022
Accepted: 18 Feb 2023

To the Editor:

Lung ultrasound (LUS) is an inexpensive, point-of-care assessment used for identifying and risk-stratifying respiratory conditions [1]. Traditional findings such as A-lines signify a normal pleural interface, whereas B-lines signify fluid at the interstitial space resulting in characteristic artefact [1]. A large number of studies have demonstrated that LUS findings are more sensitive than chest radiograph and are associated with respiratory disease progression, including the presence of B-lines and consolidations [2, 3]. However there have been limited studies related to LUS combined with clinical factors to predict outcomes in COVID-19 [4, 5]. Using unsupervised learning techniques, we evaluated the additive prognostic value of POCUS parameters to predict disease progression among hospitalised adults with COVID-19 beyond traditional clinical assessment.

Adults (⩾18 years of age) who tested positive for SARS-CoV-2 on reverse transcriptase PCR and were admitted to Johns Hopkins Hospital in Baltimore, Maryland, were enrolled between June 2020 to September 2021. Methods including participant enrolment, LUS acquisition and quality assurance and control have been previously described [6]. Ethical approval was obtained from the Johns Hopkins University Institutional Review Board (IRB00245545).

Trained research assistants obtained LUS using a Lumify S4 phased array probe (Philips, Amsterdam, Netherlands) and standardised protocol with 6-s clips from 12 zones with six lung zones on each side [7]. Clinical parameters for the risk model included age, gender, body mass index ($kg \cdot m^{-2}$), comorbidities (hypertension, cardiovascular disease, cancer, HIV, diabetes, chronic lung disease, liver failure), current tobacco use, white blood count, physiological parameters within 24 h of LUS (maximum respiratory rate, maximum temperature, minimum temperature, maximum heart rate and minimum O_2 saturation) and ordinal baseline COVID severity [7].

Disease progression was defined by the World Health Organization (WHO) COVID Scale for Clinical Improvement that classifies disease based on hospitalisation status and severity (0–10) [8]. Date of death was determined through medical chart review and review of the regional health information exchange [6]. Independent study personnel masked to clinical information, identified pleural line changes, pleural effusions, consolidations, lung sliding (yes/no), A-lines and B-lines (percentage of lung zones) [6].

We used logistic regression models and three-fold cross-validated area under the receiver operating characteristic curves (cvAUC) to identify the prognostic accuracy of the most important variables in three separate models for sensitivity. The first model fitted single predictor logistic regression models to determine the top single predictors. The second model was built by forward selection including both clinical and LUS parameters with a predefined stopping rule of increase in AUC <0.005 at both stages to assess the additive accuracy of each variable [9]. The third model was built by two-stage forward selection including clinical parameters at the first stage, followed by LUS parameters with a predefined stopping rule of increase in AUC <0.005. For each cross-validation step, we performed 100 simulations and used the average cvAUC across simulations as the result. Two clinical parameters and one LUS parameter were obtained in the third model using the predefined stopping rule. Data were analysed in R (v4.0.2) and Stata, version 16.0 (StataCorp LLC, College Station, TX, USA).

Shareable abstract (@ERSpublications)
The inclusion of LUS with simple, point-of-care clinical parameters have potential to improve COVID-19 prognostication above that from standard clinical care delivery. https://bit.ly/3InePYK

Cite this article as: Siddharthan T, Blair PW, Cui E, *et al*. Additive value of lung ultrasound to clinical parameters for prognosticating COVID-19. *ERJ Open Res* 2023; 9: 00564-2022 [DOI: 10.1183/23120541.00564-2022].

Among 264 participants, the median age was 58.6 (interquartile range (IQR) 48.8–68.0) years and 43.2% (n=114) were female (table 1). 46 participants (17.4%) had baseline moderate disease (WHO COVID 6) requiring high-flow nasal cannula or noninvasive positive pressure ventilation (table 1). 10% (n=27) of participants progressed to higher WHO COVID disease states.

When assessing single predictors, the most discriminative risk factors were lower % A-lines (cvAUC 0.696), minimal oxygen saturation (%) (cvAUC 0.670) and maximum respiratory rate (breaths·min^{-1}) (cvAUC 0.658). For each % increase in A-lines the log odds of disease progression decreased by 1.99 (SE 0.67, p=0.004). When using forward selection, inclusion of % A-lines, minimum oxygen saturation and baseline severity produced a cvAUC of 0.737, although in this model a dose–response relationship between A-lines and likelihood disease progression was not observed. Finally, when using two-stage forward selection, the optimised cvAUC was 0.748 including minimum oxygen saturation, baseline severity and % confluent B-lines. % confluent B-lines had the highest level of prediction compared to the other risk factors included in the composite model using two-stage forward selection. For each increase in % of confluent B-lines the log odds of disease progression increased 1.85 (SE=0.91, p=0.04).

LUS findings were additive to clinical parameters for predicting worsening acute respiratory failure due to COVID-19 pneumonia. The results demonstrate that easily obtained, point-of-care LUS confluent B-lines, oxygen saturation and current severity level accurately predict disease progression. There was a dose-dependent response between LUS findings and the likelihood of disease progression more so than other clinical parameters. The baseline score incorporated important clinical data to provide a comprehensive predictive model and demonstrated value from LUS findings independent of disease severity for prognostication.

Prognostic scores have been used to predict disease morbidity and mortality in a range of clinical settings and can be used for triage to assist in determination of escalation of care. In each model, LUS parameters independently were associated with COVID progression and provided additive benefit beyond regularly obtained clinical parameters. The present model with oxygen saturation, % confluent B-lines and baseline severity outperformed that of a systemic inflammatory response syndrome (⩾2 cut-off) C-statistic of 0.55,

TABLE 1 Baseline demographics (n=264)

Age years	58.56 (48.75–68.00)
Female	114 (43.18)
Race	
Asian	7 (2.65)
Black	126 (47.73)
White	80 (30.30)
Other	49 (18.46)
Missing	2 (0.75)
Ethnicity	
Hispanic	44 (16.67)
Non-Hispanic	220 (83.33)
Smoking	
Never	149 (56.44)
Current	23 (8.71)
Former	80 (30.30)
Missing	11 (4.16)
Body mass index kg·m^{-2}	30.00 (25.40–33.15)
Comorbidities	
Cancer	25 (9.47)
Congestive heart failure	87 (32.95)
COPD	96 (36.36)
Hypertension	196 (74.24)
Liver disease	54 (20.45)
Diabetes	112 (42.42)
Baseline severity	
Mild	169 (64.02)
Moderate	46 (17.42)
Severe	49 (18.56)

Data are presented as median (interquartile range) or n (%).

which was previously described in this cohort [6]. Additionally, by using individual lung fields rather than a summative score, the derived prognostic baseline score can be extended to individuals with a more limited scan due to mechanical ventilation and patients at varying levels of severity during hospitalisation [4]. While there have been numerous studies outlining the utility of LUS for acute respiratory failure prognostication, dissemination has been limited due to the variability of protocols, anatomical locations for the exam, probe type and settings, and data interpretation [10]. We found that the inclusion of LUS metrics improved the discriminative accuracy of disease progression in each of the three models utilised using a standardised scanning protocol, which demonstrates the additive value of lung imaging.

The inclusion of LUS with simple, point-of-care clinical parameters has the potential to improve prognostication beyond standard clinical care delivery and may have value in settings where standard chest imaging is not readily available.

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Provenance: Submitted article, peer reviewed.

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Author contributions: T. Siddharthan, P.W. Blair and D.V. Clark conceived of the study. E. Cui and C. Crainiceanu conducted the analysis. T. Siddharthan and P.W. Blair wrote the first draft. T. Siddharthan, P.W. Blair, E. Cui, J. Pearce, P. Herrera, G. Liu, J. East, C. Crainiceanu and D.V. Clark provided critical feedback to the final version.

Support statement: This project was supported by Joint Program Executive Office (JPEO-EB) W911QY-20-9-0004 (2020 OTA) and the Johns Hopkins University School of Medicine COVID-19 Research Fund. Funding information for this article has been deposited with the Crossref Funder Registry.

Conflict of interest: The authors have no conflict of interest to declare.

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