

Early View

Research letter

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Additive Value of Lung Ultrasound to Clinical Parameters for Prognosticating COVID-19

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Introduction

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 artifact.¹ A large number of studies have demonstrated that LUS findings are more sensitive than chest X-ray 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 hospitalized adults with COVID-19 beyond traditional clinical assessment.

Methods

Adults (≥ 18 years of age) who tested positive for SARS-CoV-2 on RT-PCR and were admitted to Johns Hopkins Hospital in Baltimore, Maryland enrolled between June 2020 to September 2021. Methods including participant enrollment, lung ultrasound 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 standardized protocol with 6-second 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/m^2), comorbidities (hypertension, cardiovascular disease, cancer, HIV, diabetes, chronic lung disease, liver failure), current tobacco use, white blood count and physiologic parameters within 24 hours of lung ultrasound (maximum respiratory rate, maximum temperature, minimum temperature, maximum heart rate and minimum O₂ saturation), and ordinal baseline COVID severity.⁷

Disease progression was defined by the WHO COVID Scale for Clinical Improvement that classifies disease based off hospitalization 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 were 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 3-fold cross-validated area under the receiver operating characteristic curve (cvAUCs) 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 increasing 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 increasing in $AUC < 0.005$. For each cross-validation step, we performed 100 simulations and used the average cross-validated AUC (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 analyzed in R (v4.0.2) and Stata, version 16.0 (StataCorp LLC, College Station, TX, USA).

Results

Among 264 participants, the median age was 58.9 (interquartile range [IQR], 48.8 to 68.0 years) and 43.2% (n = 114) were female (Table 1). Forty-six participants (17.4%) had baseline moderate disease (WHO COVID 6) requiring high flow nasal cannula (HFNC) or non-invasive positive pressure ventilation (NIPPV) (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 percent A-lines (cvAUC 0.696), minimal oxygen saturation (%) (cvAUC 0.670) and maximum respiratory rate (breaths

per minute) (cvAUC 0.658). For each percent 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 percent 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 optimized cvAUC was 0.748 including minimum oxygen saturation, baseline severity, and percent confluent B lines. Percent 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 percentage of confluent B lines the log odds of disease progression increased 1.85 (SE = 0.91, p = 0.04).

Discussion

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 in a variety of clinical settings and can 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 SIRS (≥ 2 cutoff) C-statistic of 0.55, 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 hospitalization.⁴ While there has 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 lung ultrasound metrics improved the discriminative accuracy of disease progression in each of the three models utilized using a standardized 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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Contribution Statement: TS, PB, DC conceived of the study. EC and CC conducted the analysis. TS and PB wrote the first draft. TS, PB, EC, JP, PH, GL, JE, CC, DC provided critical feedback to the final version.

Table 1. Baseline Demographics

Characteristic	Total (N=264)
Age, median (IQR)	58.56 (48.75, 68.00)
Female, no. (%)	114 (43.18)
Race, no. (%)	
Asian	7 (2.65)
Black	126 (47.73)
White	80 (30.30)
Other	49 (18.46)
Missing	2 (0.75)
Ethnicity, no. (%)	
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)
Median BMI, median (IQR)	30.00 (25.40, 33.15)
Comorbidities, no. (%)	
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)
HIV/AIDS	12 (4.55)
Baseline Severity, no. (%)	
Mild	169 (64.02)
Moderate	46 (17.42)
Severe	49 (18.56)

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