THORACIC ULTRASOUND

Thoracic Ultrasound in COVID-19: Use of Lung and Diaphragm Ultrasound in Evaluating Dyspnea in Survivors of Acute Respiratory Distress Syndrome from COVID-19 Pneumonia in a Post-ICU Clinic

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Abstract

Introduction Dyspnea is a common symptom in survivors of severe COVID-19 pneumonia. While frequently employed in hospital settings, the use of point-of-care ultrasound in ambulatory clinics for dyspnea evaluation has rarely been explored. We aimed to determine how lung ultrasound score (LUS) and inspiratory diaphragm excursion (DE) correlate with patient-reported dyspnea during a 6-min walk test (6MWT) in survivors of COVID-19 acute respiratory distress syndrome (ARDS). We hypothesize higher LUS and lower DE will correlate with dyspnea severity.

Study Design and Methods Single-center cross-sectional study of survivors of critically ill COVID-19 pneumonia (requiring high-flow nasal cannula, invasive, or non-invasive mechanical ventilation) seen in our Post-ICU clinic. All patients underwent standardized scanning protocols to compute LUS and DE. Pearson correlations were performed to detect an association between LUS and DE with dyspnea at rest and exertion during 6MWT.

Results We enrolled 45 patients. Average age was 61.5 years (57.7% male), with average BMI of 32.3 Higher LUS correlated significantly with dyspnea, at rest ($r = +0.41$, $p = <0.01$) and at exertion ($r = +0.40$, $p = <0.01$). Higher LUS correlated significantly with lower oxygen saturation during 6MWT ($r = -0.55$, $p = <0.01$) and lower 6MWT distance ($r = -0.44$, $p = <0.01$). DE correlated significantly with 6MWT distance but did not correlate with dyspnea at rest or exertion.

Conclusion Higher LUS correlated significantly with patient-reported dyspnea at rest and exertion. Higher LUS significantly correlated with more exertional oxygen desaturation during 6MWT and lower 6MWT distance. DE did not correlate with dyspnea.

Keywords COVID-19 · Diaphragm Excursion · Dyspnea · Lung Ultrasound Score · Post-ICU clinic · Thoracic Lung Ultrasound

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Abbreviations

ARDS	Acute respiratory distress syndrome
BMI	Body Mass Index
Cm	Centimeters
COVID-19	Coronavirus Disease 2019
DE	Diaphragm Excursion
DL_{CO}	Diffusion capacity of carbon monoxide
FiO2	Fraction of inspired oxygen
HFNC	High-flow nasal cannula
IQR	Inter Quartile Ratio
LUS	Lung ultrasound score
MHz	Megahertz
mMBD	Modified Borg Dyspnea Scale
(n)	Number
NRB	Non-rebreather mask
(p)	P value

(r)	Pearson correlation coefficient
SOFA	Sequential Organ Failure Assessment
SD	Standard deviation
TUS	Thoracic ultrasound score
6MWT	6-minute walk test

Background

Acute respiratory distress syndrome (ARDS), the most severe form of viral pneumonia caused by COVID-19, has strained healthcare systems worldwide [1]. While improvements in critical care led to better survival from COVID-19 ARDS, health care systems were required to confront a new and complex population of ICU survivors [2].

Survivors of critically ill COVID-19 experience symptoms overlapping with the post-intensive care syndrome, in which patients experience long-term physical, neurocognitive, and mental health debility related to their critical illness [3]. Dyspnea is one of the most common persistent symptoms following COVID-19 [4, 5], especially in the post-critically ill; severe lung injury, prolonged advanced respiratory support and high-dose corticosteroids may all be contributory. Indeed, clinicians treating survivors of COVID-19 ARDS with dyspnea must consider multiple potential contributors to this symptom complex including the coexistence of systemic and neuromuscular debility secondary to critical illness neuromyopathy, pre-existing cardiopulmonary comorbidities along with any potential specific post-viral consequences [6, 7].

Thoracic ultrasound (TUS) has become an indispensable tool for the rapid diagnosis and therapeutic management of acute respiratory failure in critically ill patients [8–10]. In addition to the acute evaluation, there is growing literature in lung ultrasound's capability in profiling distinct diseases of respiratory failure, such as characterizing pleural abnormalities in ARDS, identifying B-lines and pleural irregularity in interstitial lung disease, and measuring diaphragm thickening or excursion as assessments for neuromuscular weakness in respiratory failure commonly seen in mechanically ventilated patients [11, 12]. Despite the extensive literature describing the use of ultrasound in hospital settings, employment and utility in ambulatory settings have seldom been reported. Integrating thoracic ultrasound during evaluation may allow clinicians to identify the etiology of dyspnea in this complex population. We report on our experience of employing thoracic ultrasound to investigate post-acute lung injury with lung ultrasound, and respiratory muscle strength with diaphragm excursion measurement in a post-ICU population recovering from COVID-19 ARDS. We hypothesize that higher lung ultrasound score (LUS) and lower inspiratory diaphragm excursion (DE) will predict a higher severity of patient-reported dyspnea in this population.

Study Design and Methods

Data Source and Study Cohort

This is a single-center, prospective, cross-sectional study, conducted in an academic medical center in the Bronx, New York. The study population included adults ≥ 18 years old who survived critical illness from COVID-19 pneumonia, survived to hospital discharge and established care at our post-ICU clinic between January 2021 and January 2022 (Fig. 1).

Critically ill COVID-19 pneumonia was defined as acute hypoxemic respiratory failure with ARDS (per the Berlin definition [13]) requiring invasive or non-invasive mechanical ventilation (IMV, NIPPV), and/or high-flow nasal cannula (HFNC). The study was conducted following the Declaration of Helsinki and was approved by our Institutional Review Board (IRB# 2020–11869).

The primary outcome of the study investigated a correlation between lung ultrasound score and diaphragm excursion with patient-reported dyspnea (e-Fig. 1. Per the Modified Borg Dyspnea Scale, mMBD [14]) at rest and at end-exertion during 6-min walk test (6MWT). Secondary endpoints investigated correlations between lung ultrasound score or diaphragm excursion and 6-min walk test distance and exertional oxygen desaturation.

Equipment and Personnel

We used a Sonosite™ PX (FUJIFILM Sonosite Inc., Bothell, WA, USA) ultrasound machine equipped with a phased array transducer (frequency 5–3 MHz) and a linear array transducer (frequency 15–4 MHz). All patients underwent evaluation by an experienced pulmonary and critical care attending. Ultrasound recordings were stored in Q-Path (Telexy Healthcare Inc., Everett, WA, USA) and lung ultrasound scoring was reviewed for interpretation by a blinded independent reviewer trained in thoracic ultrasound.

Lung Ultrasound Protocol

For lung ultrasound scoring, subjects were scanned in the upright position. Twelve fields were assessed (six zones per hemithorax). Each zone was scanned based on predetermined anatomical landmarks to assess anterior, medial, and posterior lung areas per published protocols [15, 16] (e-Fig. 2).

Fig. 1 Consort diagram showing patient enrollment and Post-ICU clinic follow-up
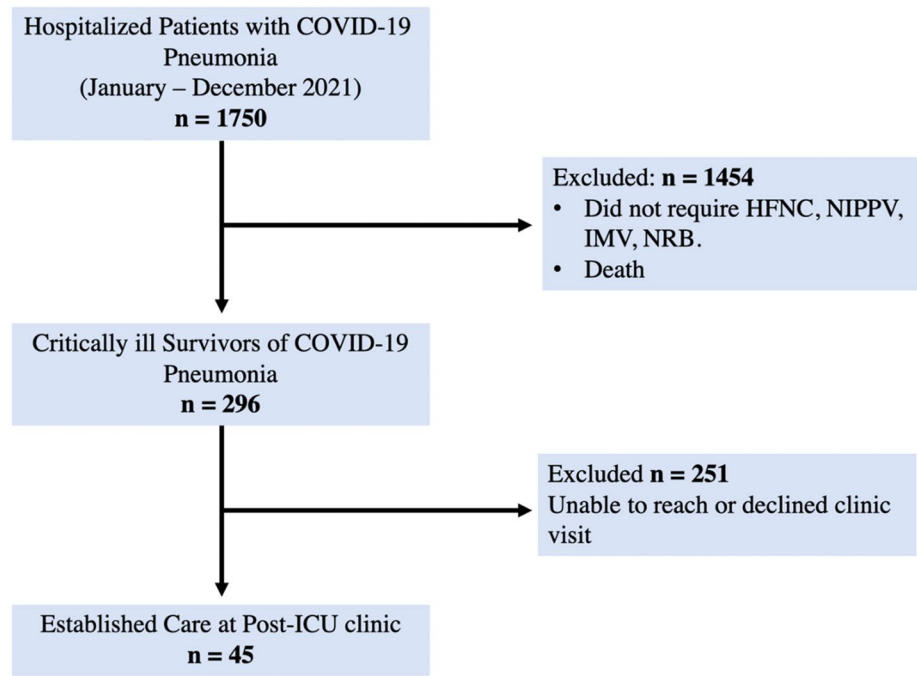
HFNC = High flow nasal canula; NIPPV = Non-invasive positive pressure ventilation; IMV = Invasive mechanical ventilation; CORE

Lung ultrasound score consisted in the identification of four sonographic patterns of lung ultrasound: normal lung by the presence of lung sliding with A-lines (score 0); presence of significant B-lines (score 1); confluent B-lines with or without small lung consolidations (score 2); and extensive lung consolidations with B-lines (score 3) (Fig. 2). The total lung ultrasound score was calculated by a composite of the sum of all individual zone scores, ranging between 0 and 36 [17].

Diaphragm Ultrasound Protocol

Subjects underwent scanning in a supine position of the right hemidiaphragm via a subcostal approach, using two-dimensional B-mode and M-mode ultrasound views [18]. Diaphragm excursion was measured during resting respiration (quiet breathing) and deep inspiration (deep breathing) [19, 20] (e-Fig. 3). We obtained three (3) consecutive measurements which were averaged into a final composite distance recorded in centimeters (cm).

Fig. 2 Lung ultrasound score system, based on the identification of four sonographic patterns
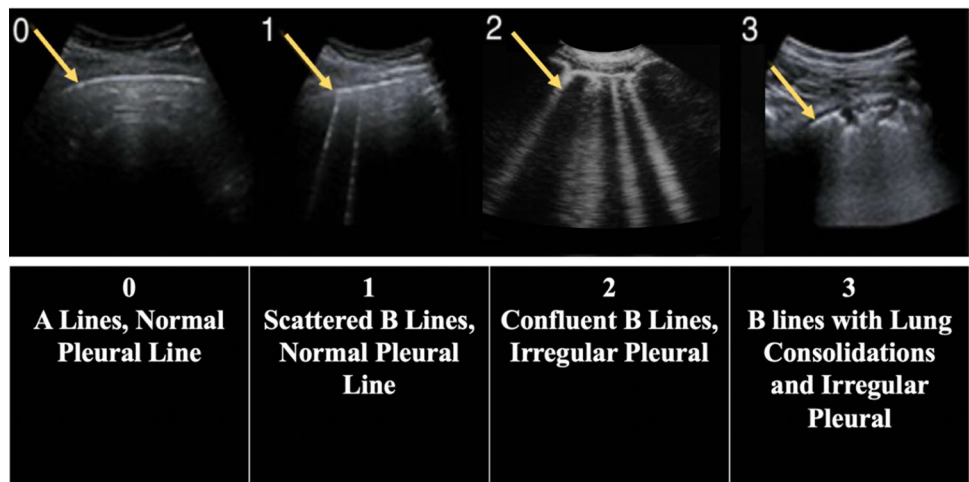

| 0 A Lines, Normal Pleural Line | 1 Scattered B Lines, Normal Pleural Line | 2 Confluent B Lines, Irregular Pleural | 3 B lines with Lung Consolidations and Irregular Pleural |

Table 1 Baseline Patient Characteristics and Hospitalization Variables

Hospitalization Characteristics			
Total Subjects, n	45		
Male Gender, n (%)	26 (57.7)		
Age in years, mean (SD)	61.5 (13.9)	Age in years, median (IQR)	60 (55–71)
Race, n (%)	Hispanic 25 (55.6)	White 9 (20)	Black 6 (13.33)
	Other 3 (7.3)	Asian 2 (4.4)	
Hospitalization Length of Stay (days)			
LOS, mean (SD)	22.3 (16.9)	LOS, median (IQR)	18 (10–29)
Past Medical History			
BMI, mean (SD)	32.3 (7.2)	COPD, n (%)	8 (17.7)
Obesity, n (%)	26 (57.7)	Asthma, n (%)	7 (15.5)
Hypertension, n (%)	23 (51.1)	OSA, n (%)	6 (13.3)
Diabetes, n (%)	13 (28.8)	ILD, n (%)	2 (4.4)
CKD, n (%)	3 (6.6)	Pulmonary HTN, n (%)	1 (2.2)
Cancer, n (%)	2 (4.4)	Home O2, n (%)	7 (15.5)
Heart Failure, n (%)	7 (15.5)	Immunocompromise, n (%)	4 (8.8)
Hospitalization Therapies			
Shock, n (%)	5 (11.1)	Positive BCx, n (%)	3 (6.6)
Paralyzed, n (%)	3 (6.6)	Positive RCx, n (%)	3 (6.6)
VTE, n (%)	9 (20)	Received Antibiotics, n (%)	26 (57.7)
Received Anticoagulant, n (%)	23 (51.1)	Received Dexamethasone, n (%)	37 (82.2)
Received Tocilizumab, n (%)	17 (37.7)	Received Plasma Trial, n (%)	6 (13.3)
Received Remdisivir, n (%)	36 (80)		
Oxygen Requirements			
HFNC, n (%)	39 (86.6)	Placed NRB, n (%)	34 (75.5)
NIV (BiPAP), n (%)	7 (15.5)	Placed NRB only, n (%)	3 (6.6)
IMV, n (%)	7 (15.5)		
Highest Fi02%, mean (SD)	84.7 (15.1)	Highest FiO2%, median (IQR)	90 (75–100)

CKD Chronic kidney disease, *COPD* Chronic obstructive pulmonary disease, *OSA* Obstructive sleep apnea; *ILD* Interstitial lung disease; *HTN* Hypertension; *VTE* Venous thromboembolism, *BCx* Blood culture, *RCx* Respiratory culture, *HFNC* High-flow nasal canula, *NIV* Non-invasive ventilation, *IMV* Invasive mechanical ventilation, *FiO2* Fraction of inspired oxygen, *NRB* Non-rebreather mask

Statistical Analysis

Baseline characteristics were expressed as means, standard deviations (SD), and interquartile ranges (IQR) for continuous variables. Categorical variables were summarized as counts and percentages. We used Pearson correlation coefficient (r) to estimate the linear unadjusted association between lung ultrasound scores or diaphragmatic excursion as the main predictor variables and the degree of dyspnea reported per the mBorg scale as the main dependent variable [21]. Using the Kolmogorov–Smirnov Test of Normality, we found to have a standard data distribution. We used multivariable linear regression models to assess for potential correlates between baseline characteristics, hospital treatment, and ambulatory visit variables versus dyspnea as the outcome variable. A sample size of 50 patients was determined to achieve 80% power and detect a minimum correlation of 0.3 and 0.4 between lung ultrasound score or diaphragm

excursion distance and dyspnea using a two-sided hypothesis test. A p-value < 0.05 was considered statistically significant and mean values were reported along with a 95% confidence interval. Stata version 17 (StataCorp., College Station, TX, USA) was used for all the statistical analyses.

Results

Baseline Characteristics

Between January and December 2021, we screened $n = 1750$ patients hospitalized with severe COVID-19 pneumonia. $N = 296$ patients were identified as critically ill with COVID-19 ARDS and survived to hospital discharge, and $n = 45$ patients established care in clinic and completed all study procedures (Fig. 1).

The mean (Standard Deviation: SD) age was 61.5 (13.9) years, consisting of 57.7% males, with a mean (SD) Body Mass Index (BMI) of 32.3 (7.2). The most common comorbidities were obesity (57.7%), hypertension (51.1%), and diabetes (28.8%). All patients required advanced respiratory support for hypoxemic respiratory failure due to COVID-19 pneumonia, with 86.6% ($n = 39$) requiring HFNC, 15.5% ($n = 7$) requiring NIPPV and 15.5% ($n = 7$) requiring IMV. The median (Inter Quartile Ratio: IQR) Fraction of inspired oxygen (FiO2) level required was 90% (75–100). The mean (SD) Sequential Organ Failure Assessment (SOFA) score was 3 (0.8) consisting with low probability of inpatient mortality. Table 1 shows detailed baseline characteristic and hospitalization treatment variables.

Post-ICU Clinic Visit Results

The median (IQR) interval of days between hospital discharge and ambulatory clinic assessment was 70 days (41–106). Within the first 6 months following hospital discharge, 86% of subjects were evaluated.

We performed thoracic ultrasound in all 45 patients. The mean (SD) lung ultrasound score composite was 8.3 (6.6) with a median (IQR) 8 (3–12). Diaphragm excursion assessment was performed in $n = 38$ patients during quiet breathing and $n = 37$ patients with deep inspiration. The mean (SD) diaphragm excursion distance during quiet breathing was 1.9 cm (0.6), and 4.8 cm (2.2) with deep inspiration.

The mean (SD) rated perception of dyspnea per mBorg scale was 1.17 (1.36) at rest signifying "very slight" breathlessness, and 2.98 (2.2) at end-exertion signifying "moderate" breathlessness. The mean (SD) 6-min walk test distance was 949 feet (402), which was 58.2 of percent predicted. During 6-min walk test, the mean (SD) nadir room air of saturation of arterial oxygen (SaO$_2$) was 88% (8.3) and zenith heart rate was 115 beats per minute (13.5) (Table 2).

We found that higher lung ultrasound score correlated positively and significantly with the severity of reported dyspnea, both at rest ($r = +0.41$, p < 0.01) and at end-exertion ($r = +0.40$, $p < 0.01$) (Table 3; Fig. 3 and 4).

Of n = 40 patients who completed the 6-min walk test, higher lung ultrasound score correlated negatively and

Table 2 Post-ICU Clinic Visit Characteristics and Results

Post-ICU clinic visit Characteristics			
Interval of days between hospital discharge and clinic visit. *N* = 45			
Interval days, mean (SD)	97 (80.4)	Interval days, median (IQR)	70 (41–106)
Seen within 30 days of hospital discharge, *n* (%)	6 (13.3)	Seen within 90 days of hospital discharge, *n* (%)	25 (55.5)
Seen within 180 days of hospital discharge, *n* (%)	39 (86.6)	Seen after 180 days of hospital discharge, *n* (%)	6 (13.3)
6-Minute Walk Test Assessment			
Borg Dyspnea Scale (0–10)			
Rest. *N* = 45		Exertion. *N* = 42	
Borg Rest, mean (SD)	1.17 (1.36)	Borg Exertion, mean (SD)	2.98 (2.2)
Borg Rest, median, (IQR)	1 (0–2)	Borg Exertion median (IQR)	3 (1–4)
6-Minute Walk Test distance (feet). *N* = 40			
6MWT, mean (SD)	949 (402)	6MWT, median (IQR)	937 (577–1,215)
%Predicted 6-Minute Walk Test. *N* = 40			
%6MWT		58.2	
Lowest 6-Minute Walk Test SaO2 (nadir, %). *N* = 39			
SpO2, mean (SD)	88.7 (8.3)	SpO2, median (IQR)	92 (85–95)
6-Minute Walk Test Max HR (zenith, beats per minute). *N* = 38			
6MWT HR, mean (SD)	115 (13.5)	6MWT HR, median (IQR)	115 (106–124)
Thoracic Ultrasound Assessment			
Lung Ultrasound Score (0–36). *N* = 45			
LUS, mean (SD)	8.3 (6.6)	LUS, median (IQR)	8 (3–12)
Diaphragm Excursion—Quiet Breathing (cm). *N* = 38			
Quiet breathing, mean (SD)	1.9 (0.6)	Quiet breathing median (IQR)	1.9 (1.5–2.3)
Diaphragm Excursion—Deep Inspiration (cm). *N* = 37			
Deep inspiration, mean (SD)	4.8 (2.2)	Deep inspiration, median (IQR)	4.5 (3.3–6)

6MWT 6-Minute Walk Test, *SaO2* Saturation of arterial oxygen, *HR* Heart rate, *LUS* Lung ultrasound score

Table 3 Thoracic Ultrasound, Dyspnea Score, and 6-min Walk Test Correlation Results

Thoracic Ultrasound and Borg Dyspnea Scale	Pearson Correlation Coefficient (r)	p-value
Lung Ultrasound Score vs Borg Dyspnea Scale (Rest). $N = 45$	**+ 0.4051**	**0.0058***
Lung Ultrasound Score vs Borg Dyspnea Scale (Exertion). $N = 42$	**+ 0.3969**	**0.0093***
Diaphragm Excursion, quiet breathing vs Borg Dyspnea Scale (Rest). $N = 38$	− 0.0631	0.7065
Diaphragm Excursion, deep inspiration vs Borg Dyspnea Scale (Rest). $N = 37$	+ 0.0258	0.8794
Diaphragm Excursion, quiet breathing vs Borg Dyspnea Scale (Exertion) $N = 36$	+ 0.0081	0.9628
Diaphragm Excursion, deep inspiration vs Borg Dyspnea Scale (Exertion) $N = 35$	+ 0.0858	0.6240
Thoracic Ultrasound and 6-Minute Walk	Pearson Correlation Coefficient (r)	p-value
Lung Ultrasound Score vs. 6-Minute Walk Distance (feet) $N = 40$	**− 0.4380**	**0.0047***
Lung Ultrasound Score vs. 6-Minute Walk Distance (% Predicted). $N = 40$	− 0.2689	0.0934
Lung Ultrasound Score vs. 6-Minute Walk SaO2 (nadir). $N = 39$	**− 0.5506**	**0.0003***
Lung Ultrasound Score vs. 6-Minute Walk Distance Max HR	+ 0.0044	0.9792
Diaphragm Excursion, quiet breathing vs 6-Minute Walk Distance (feet). $N = 35$	**+ 0.3255**	**0.0564****
Diaphragm Excursion, quiet breathing vs. 6-Minute Walk Distance (% Predicted). $N = 35$	**+ 0.3425**	**0.0440***
Diaphragm Excursion, quiet breathing vs. 6-Minute Walk SaO2 (nadir). $N = 34$	+ 0.1173	0.5089
Diaphragm Excursion, quiet breathing vs. 6-Minute Walk Distance Max HR (bpm). $N = 33$	+ 0.0394	0.8277
Diaphragm Excursion, deep inspiration vs 6-Minute Walk Distance (feet). $N = 34$	**+ 0.3676**	**0.0325***
Diaphragm Excursion, deep inspiration vs. 6-Minute Walk Distance (% Predicted). $N = 34$	+ 0.2656	0.1290
Diaphragm Excursion, deep inspiration vs. 6-Minute Walk SaO2 (nadir). $N = 33$	+ 0.2529	0.1557
Diaphragm Excursion, deep inspiration vs. 6-Minute Walk Distance Max HR	+ 0.0256	0.8874

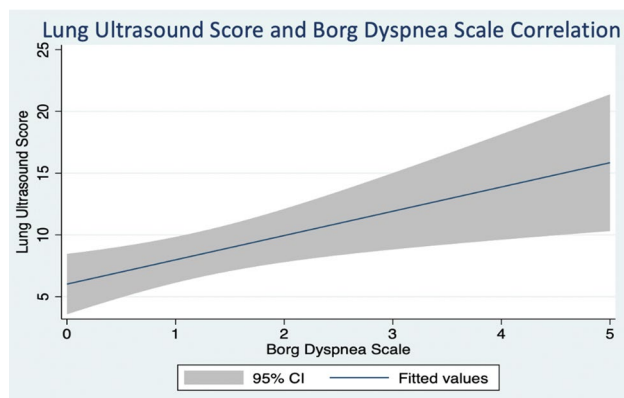Bold and asterisks are represents statistically significant $p < 0.05$

HR Heart rate

Fig. 3 Lung ultrasound score and Borg dyspnea scale correlation at rest. Results from Pearson coefficient calculation

Fig. 4 Lung ultrasound score and Borg dyspnea scale correlation after Exertion. Results from Pearson coefficient calculation

significantly with lower oxygen saturation during the 6-min walk test ($r = − 0.55$, $p < 0.01$) and lower 6-min walk test distance ($r = − 0.44$, p < 0.01) (Table 3; Fig. 5). Diaphragm excursion, during both quiet and deep inspiration, correlated significantly with the 6-min walk test distance ($r = + 0.33$, $p = 0.05$; $r = + 0.37$, $p = 0.03$), but did not correlate with dyspnea at rest or during exertion.
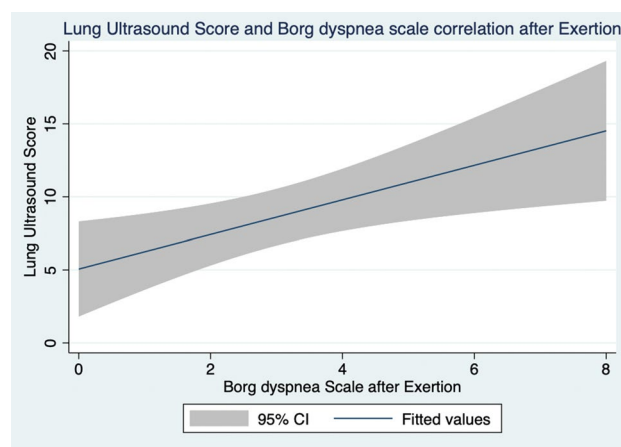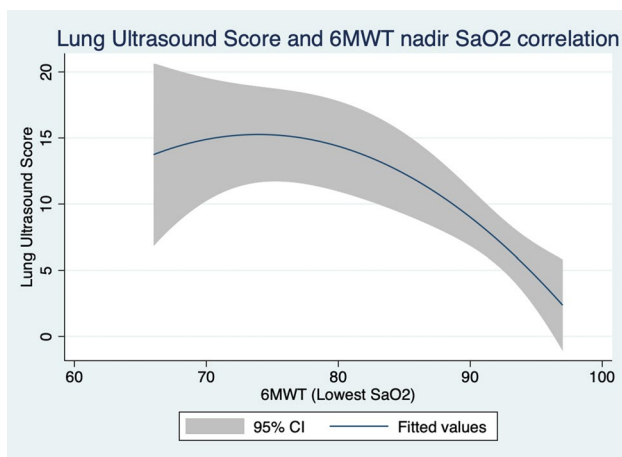
Discussion

In the current study using thoracic ultrasound to evaluate dyspnea in adult survivors of COVID-19 ARDS, we found higher lung ultrasound score to significantly correlate with

Fig. 5 Lung ultrasound score and saturation of arterial oxygen correlation after 6-min walk test. Results from Pearson coefficient calculation. *6MWT* 6-min walk test; *SaO2* Saturation of arterial oxygen

patient-reported dyspnea both at rest and with exertion. Higher lung ultrasound score also significantly correlated with the severity of exertional oxygen desaturation, and exercise tolerance as reflected by lower 6-min walk test. While diaphragm excursion did not correlate with dyspnea, higher degree of diaphragm excursion did correlate with the 6-min walk test distance.

Lung ultrasound score has been employed in ICU settings to evaluate the degree of loss of aeration of the lungs in patients with acute respiratory failure secondary to ARDS [22]. We used the lung ultrasound score to quantify the degree of lung injury in patients recovering from ARDS. In early ARDS, the B-lines identified represent widening of interlobular septa from fluid accumulation from non-cardiogenic pulmonary edema [23]. In this post-acute phase, B-lines identified in our patient population likely signify widening of interlobular septa from inflammation and/or deposition of fibrotic material [24]. Indeed, B-lines, pleural line irregularities, and subpleural consolidations have all been characterized as notable lung ultrasound findings present in interstitial lung disease [25].

In dyspnea evaluation, our findings suggest lung ultrasound can quantify the degree of post-ARDS injury within the lungs, which impacts the severity of dyspnea and exercise limitation. Interstitial lung disease can reduce diffusion capacity [26], thus high lung ultrasound score and its correlated exertional hypoxemia likely denote a degree of interstitial lung disease following COVID-19 ARDS in this patient population. While we identified an inverse correlation between lung ultrasound score and diffusion capacity of carbon monoxide (DL_{CO}), this finding was not statistically significant likely due to low power with a low

number of completed DL_{CO} studies ($n = 15$). Clinically, lung ultrasound score can predict which patients may desaturate with exertion and guide requirements for prolonged oxygen support during recovery.

We found diaphragm excursion to correlate significantly with exercise capacity as determined by the 6-min walk test distance. Additionally, thoracic ultrasound with diaphragm excursion may provide a measure of neuromuscular strength and respiratory fitness as it relates to patient exercise tolerance. Poor diaphragm excursion, along with high lung ultrasound score, may both be markers of greater physical impairment in the continuum of post-intensive care syndrome, and thus may guide clinicians to advocate for physical and pulmonary rehabilitation as therapies to support recovery.

Our study is not without limitations. While the study cohort is multiracial and reflects that of an urban academic medical center, it is a single-center analysis. Although we identified statistically significant findings, our patient population was small. In addition, there was heterogeneity in interval times between hospital discharge and follow-up in the Post-ICU clinic. However, given that dyspnea and lung ultrasound evaluations were performed concurrently, the non-uniformity in follow-up times did not affect the primary outcome of our study. Finally, while complete pulmonary function testing with lung volumes and DL_{CO} measurements would allow for further correlation analyses with thoracic ultrasound, given the limited number of patients who completed this assessment, this could not be evaluated.

Conclusion and Implications for Clinical Practice

Our investigation shows that point-of-care ultrasound in the ambulatory setting is feasible and can provide meaningful information when evaluating dyspnea in a complex patient population, where the etiology of breathlessness can be challenging to elucidate. While dyspnea may be multifactorial, higher lung ultrasound scores when present likely denote a more severe post-viral lung injury and are likely to be contributory. Given the complex nature of dyspnea in the post-COVID-19 population, further studies investigating changes in lung ultrasound score longitudinally and this relationship with pulmonary function testing may allow for better characterization of post-ARDS recovery trajectory in survivors of critically ill COVID-19.

Declarations

Conflict of interest Any conflict of interest has been disclosed as required by the editorial panel.

Guarantor Statement G.E. and M.I. are the authors responsible for all content of this manuscript.

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