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NOVEL APPLICATIONS OF ULTRASOUND IN PATIENTS WITH COVID-19 INFECTIONS

Simplified Lung Ultrasound Examination and Telehealth Feasibility in Early SARS-CoV-2 Infection



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Background: In COVID-19, inpatient studies have demonstrated that lung ultrasound B-lines relate to disease severity and mortality and can occur in apical regions that can be imaged by patients themselves. However, as illness begins in an ambulatory setting, the aim of this study was to determine the prevalence of apical B-lines in early outpatient infection and then test the accuracy of their detection using telehealth and automated methods.

Methods: Consecutive adult patients (N = 201) with positive results for SARS-CoV-2, at least one clinical risk factor, and mild to moderate disease were prospectively enrolled at a monoclonal antibody infusion clinic. Physician imaging of the lung apices for three B-lines (ultrasound lung comet [ULC]) using 3-MHz ultrasound was performed on all patients for prevalence data and served as the standard for a nested subset (n = 50) to test the accuracy of telehealth methods, including patient self-imaging and automated B-line detection. Patient characteristics, vaccination data, and hospitalizations were analyzed for associations with the presence of ULC.

Results: Patients' mean age was 54 ± 15 years, and all lacked hypoxemia or fever. ULC was present in 55 of 201 patients (27%) at a median of 7 symptomatic days (interquartile range, 5-8 days) and in four of five patients who were later hospitalized (P = .03). Presence of ULC was associated with unvaccinated status (odds ratio [OR], 4.11; 95% CI, 1.85-9.33; P = .001), diabetes (OR, 2.56; 95% CI, 1.08-6.05; P = .03), male sex (OR, 2.14; 95% CI, 1.07-4.37; P = .03), and hypertension or cardiovascular disease (OR, 2.06; 95% CI, 1.02-4.23; P = .04), while adjusting for body mass index > 25 kg/m². Telehealth and automated B-line detection had 84% and 82% accuracy, respectively.

Conclusions: In high-risk outpatients, B-lines in the upper lungs were common in early SARS-CoV-2 infection, were related to subsequent hospitalization, and could be detected by telehealth and automated methods. (J Am Soc Echocardiogr 2022;35:1047-54.)

Keywords: COVID-19, Pneumonia, Point-of-care ultrasound, Lung ultrasound, Telehealth

Since its rapid spread in early 2020 and during every surge since, the COVID-19 pandemic has caused repeated concern regarding its potential to overwhelm a health care system, from hospital capacity to the distribution of outpatient services. Most individuals who test positive for SARS-CoV-2 are outpatients and have mild, nonspecific upper respiratory symptoms, but a sizable number, particularly those with clinical risk factors, may progress to hypoxic respiratory failure.¹

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Statistical analysis was supported by National Center for Advancing Translational Sciences grant UL1TR002550.

Conflicts of interest: None.

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0894-7317/\$36.00

Copyright 2022 by the American Society of Echocardiography. https://doi.org/10.1016/j.echo.2022.05.015 Involvement of the lung has been the driving force for COVID-19 hospitalization and mortality² and can be easily detected by ultrasound.³⁻⁵ Prior hospital-based point-of-care ultrasound studies of the lung have shown prevalence and prognostic value to the finding of B-lines,⁶⁻¹⁴ a sign of interstitial edema, by using extensive bilateral lung imaging.

Although prevalent in inpatients, B-lines were also reported by infected health care providers who imaged themselves during their own home isolation.¹⁵⁻¹⁷ The presence of three B-lines in the lung apex alone, a site specifically shown to be feasible for patient self-imaging,¹⁸ was observed by our group in a significant proportion, 33%, of hospitalized patients, who remarkably had only mild to moderate disease and lacked hypoxemia.¹⁹ Given these observations, the concept of incorporating simplified lung self-imaging into a telehealth appointment was envisioned to help identify and allocate resources to those outpatients who may develop worsening disease while in isolation. Therefore, as few imaging data exist on early SARS-CoV-2 infection in those at increased risk for hospitalization, we first sought to determine the prevalence and associations of B-lines in the

Abbreviations			
BMI = Body mass index			
OR = Odds ratio			
ULC = Ultrasound lung comet			

METHODS

lung apices in high-risk outpatients and then test the diagnostic accuracy of simplified imaging telehealth methods, including patient self-imaging and automated B-line detection protocols.

This prospective cohort study enrolled outpatients from October 2021 through January 2022 and was approved by the Scripps Health institutional review board (#21-7761). Adult outpatients who (1) had tested positive for SARS-CoV-2 by polymerase chain reaction or antigen testing, (2) were eligible for monoclonal antibody treatment with casirivimab/imdevimab or sotrovimab and (3) had been referred by a physician were directed to a dedicated COVID-19 infusion clinic. The monoclonal antibody infusions were authorized for patients who were within 10 days of symptom onset or exposure to SARS-CoV-2 and met "high-risk criteria," defined as the presence of at least one of the following risk factors^{20,21}: age > or equal to 65 years, body mass index (BMI) > 25 kg/m², pregnancy, chronic kidney disease, diabetes, immunosuppressive disease or immunosuppressive treatment, cardiovascular disease (including congenital heart disease) or hypertension, chronic lung diseases, sickle-cell disease, neurodevelopmental disorders, or medicalrelated technological dependence (tracheostomy, gastrostomy, or positive pressure ventilation). Indications and eligibility for infusion were confirmed before final scheduling. Of 208 consecutive clinic patients, six were unable to consent in English, and one refused to participate, resulting in N = 201 consenting participants.

Upon arrival to the clinic, patients underwent an intake interview and initial assessment of their vital signs, forehead skin temperature by noncontact infrared thermometer, and pulse oximetry by photoplethysmography by a registered nurse. Unstable patients or those with oximetry saturation < 94% were referred to the emergency department. All patients met the definition of asymptomatic, mild, or moderate COVID-19 severity.²² Consenting patients underwent a simplified lung ultrasound examination using a pocket-sized Lumify ultrasound system (S4-1 MHz transducer; Philips Healthcare) attached to a Samsung Galaxy S8 smartphone and using the Philips Lumify Ultrasound app version 3.0. One of four physicians, blinded to the patient's vaccination and clinical status, performed the apical lung imaging for the ultrasound lung comet (ULC) sign, defined as the presence or coalescence of three or more vertical ring-down linear B-line artifacts in a single image in the region of the second intercostal space in the midclavicular line (Figure 1).^{18,19,23,24} All imaging physicians had previously completed an established point-of-care ultrasound training program²⁵ and had used the Lumify device in clinical practice. Patients were considered ULC+ if either lung showed a comet sign as just defined. Findings were classified as unilateral or bilateral and confirmed by a second blinded physician reviewer.

Patient clinical data were obtained from the nurse intake interview and the electronic medical records (Epic Systems). The presence of fully vaccinated status, vaccine manufacturer, most recent injection date (including the date of any booster), and date of a positive result for COVID-19 were recorded from patient interview, vaccination card if available, or the electronic health record. The time since onset of symptoms to ultrasound imaging (symptom duration) and the type of symptoms, categorized as (1) asymptomatic, (2) viral upper respiratory illness (pharyngitis, myalgias, malaise, headache, cough), (3) dyspnea, (4) loss of taste or smell, and (5) gastrointestinal (nausea, vomiting, diarrhea), were recorded. Subsequent COVID-19-related patient hospitalization was sought by a separate COVID-19 clinical care team, blinded to the ultrasound findings, through patient phone interview and search of the electronic medical record ≥ 2 weeks after the last patient was enrolled and was confirmed by the study investigators.

Telehealth and Automated B-Line Assessment Imaging Study

A study of telehealth and automated B-line detection diagnostic accuracy was nested within the latter fourth (n = 50) of the study's consecutive enrollment and required the simultaneous availability of two physician investigators, one available by telehealth and the other at the infusion clinic. In these cases, each patient underwent three imaging protocols to detect ULC as follows. First, the patient was connected to the telehealth physician through secure, Health Insurance Portability and Accountability Act/Health Information Technology for Economic and Clinical Health Act-compliant telemedicine software, Doxy.me (https://doxy.me/en/), running on an Apple iPad 9 tablet at the patient's chair. The brief, 5-min telehealth appointment consisted of the telehealth physician guiding the patient to obtain and display the upper lobe images (Figure 1) to determine if ULC was present. Next, the clinic physician, blinded to the telehealth results, was summoned into the room to perform the reference standard examination, as previously described, and determined if ULC was present. Afterward, the same clinic physician used the Lumify device's built-in guided B-line quantification software during a third scan and noted if three or more B-lines were counted by the software in either apex in a 5-sec recording. The Lumify automated B-line detection software, approved by the US Food and Drug Administration and released in 2021, detects and counts the presence of B-lines during imaging, superimposing a line over the finding (Figure 2), while tabulating and displaying the maximum number of B-lines counted in any one zone. Images in which the software reported three or greater B-lines were considered ULC+.

Statistical Analysis

Continuous raw data are expressed as a mean \pm SD, and durations are expressed as median (interquartile range). Baseline clinical characteristics and symptoms were compared between patients who were and those who were not fully vaccinated using Student's t test or the Mann-Whitney U test for continuous variables and the Fisher exact test for categorical variables. Clinical risk factors, vaccination data, symptom type, and time from symptom onset were analyzed for univariable associations with the presence of ULC by logistic regression, reported as odds ratios (ORs) with 95% Cls. Multivariable associations with the presence of ULC were determined using a backward stepwise reduction approach. In a subset of patients (n = 50), diagnostic accuracy (sensitivity, specificity, accuracy, and positive and negative predictive value) were analyzed for any ULC and bilateral ULC for telehealth and automated diagnosis imaging, both relative to physician imaging as reference standard. P values were considered to indicate statistical significance when <.05. All data were analyzed using R version 4.0.3 (R Foundation for Statistical Computing).

HIGHLIGHTS

- Lung apical B-lines can be found in outpatients early in SARS-CoV-2 infection.
- Lung apical B-lines were associated with subsequent hospitalization.
- Telehealth and automated detection methods detect B-lines with 84% to 92% accuracy.
- Guided self-imaging could risk-stratify outpatients from within isolation.

RESULTS

Patients' mean age was 54 ± 15 years, 54% were women, and the mean BMI was 29.7 ± 6.4 kg/m². Patient characteristics, the most common being BMI > 25 kg/m² in 78%, are listed in Table 1 with their univariable associations with the presence of ULC. Of 55 ULC+ patients, 39 (19%) had unilateral ULC, without a significant difference between the right and left lungs, and 16 (8%) had bilateral ULC. Unilateral ULC was detected as early as day 3 of symptoms and occurred in one patient who was asymptomatic. Although only gastrointestinal symptoms were more common in unvaccinated versus vaccinated (16 of 43 [37%] vs 28 of 158 [18%], P=.01), no symptom type was significantly

related to the presence of ULC. Among vaccinated patients, there was no significant difference in the presence of ULC between those vaccinated <6 months versus >6 months previously (16 of 52 [31%] vs 21 of 106 [20%], respectively, P=.13). No relationship was seen between vaccine type and presence of ULC.

Older age, male sex, unvaccinated status, and the presence of hypertension or cardiovascular disease or type 2 diabetes were associated with the presence of ULC. In the multivariable model, presence of ULC was related to male sex (OR, 2.14; 95% CI, 1.07-4.37; P = .033), unvaccinated status (OR, 4.11; 95% CI, 1.85-9.33; P = .001), hypertension or cardiovascular disease (OR, 2.06; 95% CI, 1.02-4.23; P = .04), diabetes (OR, 2.56; 95% CI, 1.08-6.05; P = .03), and BMI > 25 kg/m² (OR, 0.46; 95% CI, 0.21-1.04; P = .06).

No patient had a forehead skin temperature > 101.5° F or finger oxygen saturation < 94% on initial assessment. Subsequent COVID-19-related hospitalizations occurred in five of 201 patients (2.5%), all of whom were admitted for hypoxemia and pneumonia (Table 2), and were related to the presence of ULC (four of 55 [7.3%] vs one of 146 [0.6%]; OR, 11.4; 95% CI, 1.64-225.3; *P*=.03). The two patients (patients 1 and 4) presenting with bilateral disease deteriorated and were admitted in <2 days, while the patient without ULC (patient 5) was admitted 12 days later.

Although the majority of patients were enrolled from October through December 2021, temporally during the delta-variant surge, the telehealth and automated diagnostic accuracy assessment (n = 50) was performed in mid-December and January, amid reports of the



Figure 1 Composite picture of imaging findings and telehealth setup. (A) Placement of the ultrasound transducer probe in the upper lung zones bilaterally (*black markers*). (B) A physician-obtained normal lung examination, without ULC, in an 80-year-old vaccinated man with hypertension. (C) A physician-obtained abnormal lung examination, with ULC, in a 40-year-old unvaccinated man with a BMI of 38 kg/m², demonstrating three B-lines (*asterisks*). (D) Telehealth appointment setup with the patient performing self-imaging and showing the result to the physician in the hospital.



Figure 2 Telehealth and artificial intelligence methods. Telehealth screenshot of the patient's hand holding the phone, showing four or five B-lines (*left*). The same patient's image as recorded using the automated method (*right*), which has detected only two of the five B-lines (*asterisks*) evident on the physician-obtained image.

emergence of the omicron variant. In this latter subset, the mean patient age was 56.0 \pm 14.2 years, and the prevalence of ULC was 24% (8% bilateral): 24.4% (10 of 41) in vaccinated patients versus 22.2% (two of nine) in unvaccinated patients (P > .99). This nested terminal quartile of the entire cohort was under the same entry criteria as the previous patients, and these patients were consecutively enrolled. Compared with the other 151 patients, these 50 patients had more baseline chronic cardiovascular disease or hypertension (56% vs 35%, P = .01), kidney disease (26% vs 6%, P < .01), lung disease (22% vs 7%, P < .01), and immune disease (26% vs 6%, P < .01); less loss of taste and smell (20% vs 40%, P=.01); and had been more recently vaccinated (median, 126 vs 221 days; P = .04). With regard to telehealth, no patient had previous imaging experience, and yet all 50 patients were able to perform self-imaging under the guidance of the telehealth physician. The diagnostic accuracy for the presence of ULC is reported in Table 3. Both the telehealth physician and automated B-line detection showed high specificity and lesser sensitivity, particularly when findings were unilateral, nonuniform, or patchy in distribution.

In this subset, of the 11 patients in whom telehealth or automated B-line detection errors occurred, no significant differences were found among the clinical variables, except for male gender (eight of 11 vs 12 of 39, P = .02). For telehealth diagnosis, two false positives and six false negatives occurred. For automated B-line detection, one false positive and eight false negatives occurred. Of the 12 patients who were ULC+, four of four patients (100%) who had bilateral disease were identified as having any lung involvement by the telehealth physician, but only two of the remaining eight patients who had unilateral ULC were identified. Automated B-line detection identified only two of the four patients with bilateral disease and only two of the eight patients with unilateral ULC.

DISCUSSION

This prospective cohort study shows a substantial prevalence of an abnormal lung ultrasound finding in high-risk outpatients with mild to moderate COVID-19 and shows the feasibility of these patients' performing a telehealth ultrasound examination to detect their own lung involvement. Within 1 week of symptoms and while lacking fever, hypoxemia, or specific symptoms, 27% of patients had B-lines in their lung apices, and 8% of patients had bilateral disease. Apical B-lines, previously shown to relate to disease severity and mortality in hospitalized patients,¹⁹ were associated with male sex, unvaccinated status, hypertension, cardiovascular disease, diabetes, and subsequent COVID-19 hospitalization in this cohort. Telehealth and automated methods demonstrated accuracy ranging from 84% to 92% for detecting patients with B-lines and were better for the detection of bilateral disease. These findings can potentially help in risk stratification and treatment allocation during the recurrent outpatient surges that are characteristic of this pandemic and support the feasibility of using a simplified examination suitable for a novel, patientapplied, telehealth ultrasound method.

Ultrasound ring-down artifacts called B-lines, or the ULC as defined in this study, have been described in COVID-19 and relate to prognosis.^{3-14,19} ULC is highly sensitive for an abnormal interstitium³, and can be present when radiographic findings are normal.^{26,27} When found in the easily accessed lung anteroapical location, B-lines are unlikely to be due to gravity-dependent edema or aspiration and may be more specific for direct infection and the immune response, as the apices may be particularly prone to inhaled pathogens, formation of oxygen-free radicals, and poor lymphatic drainage.²⁸⁻³⁰ Data from our center¹⁹ and others⁴⁻⁶ have demonstrated that B-lines occur in the apical zones in 27% to 33% of patients of varying disease severity presenting to emergency departments or admitted to hospitals. Few ultrasound studies have focused solely on the outpatient population, in which >80% of the disease resides and infection typically presents as a mild upper respiratory illness³¹ and is not expected to have lung B-lines. In an earlier outpatient study of symptomatic health care workers who were outpatients with COVID-19 (n = 722), a slightly higher prevalence, 41%, of three or more B-lines in a lung zone was found, but that study included a more ill cohort with at least one respiratory symptom, fever, and/or pulse oximetry

Table 1 Patient characteristics, symptoms, vaccine status and associations with the presence of ULC

	All patients	ULC	No ULC		P *
Characteristic	(N = 201)	(<i>n</i> = 55)	(<i>n</i> = 146)	OR (95% CI)	
Age, y	54 ± 15	60 ± 13	52 ± 15	1.04 (1.01-1.06)	<.01
BMI, kg/m ²	30 ± 6	31 ± 7	29 ± 6	1.04 (0.99-1.09)	.13
Clinical variables					
Age \ge 65 y	54 (27)	20 (36)	34 (23)	1.88 (0.96-3.67)	.06
Sex, male	93 (46)	33 (60)	60 (41)	2.15 (1.15-4.09)	.02
Diabetes	32 (16)	14 (25)	18 (12)	2.43 (1.10-5.30)	.03
Hypertension/CVD	81 (40)	30 (55)	51 (35)	2.24 (1.19-4.23)	.01
$BMI > 25 \text{ kg/m}^2$	156 (78)	39 (71)	117 (80)	0.60 (0.30-1.25)	.16
Chronic lung disease	21 (10)	6 (11)	15 (10)	1.06 (0.36-2.80)	.17
Chronic kidney disease	13 (6)	4 (7)	9 (6)	1.19 (0.31-3.84)	.78
Immunosuppressed	22 (11)	8 (14)	14 (10)	1.6 (0.61-4.00)	.32
Symptoms					
Viral URI	187 (93)	53 (96)	134 (92)	2.37 (0.62-15.58)	.27
Loss of taste/smell	71 (35)	14 (25)	57 (39)	0.53 (0.26-1.04)	.07
Dyspnea	22 (11)	8 (15)	14 (10)	1.6 (0.61-4.00)	.32
Gastrointestinal	44 (22)	16 (29)	28 (19)	1.73 (0.84-3.50)	.13
Symptom duration, d	6 (5-8)	7 (5-8)	6 (5-8)	1.09 (0.96-1.25)	.18
Vaccine status				0.45 (0.21-0.87)	.02
Unvaccinated	43 (21)	18 (33)	25 (17)		
Vaccinated	158 (79)	37 (67)	121 (83)		
Vaccine type					.06
Pfizer-BioNTech	85 (42)	21 (38)	64 (44)		
Moderna	63 (31)	12 (22)	51 (35)		
Johnson & Johnson/Janssen	14 (7)	8 (5)	6 (11)		
Days since last vaccination/booster	216 (125-257)	208 (91-258)	217 (144-256)	0.99 (0.99-1.00)	.2
COVID-19-related hospitalization	5 (2.5)	4 (7)	1 (0.6)	11.4 (1.64-225.3)	.03

Data are expressed as mean \pm SD, number (percentage), or median (interquartile range).

CVD, Cardiovascular disease; URI, upper respiratory illness.

*Univariable.

< 95% and a more extensive 12-zone lung imaging protocol.³² The present study, using a simple two-zone protocol, revealed a 27% apical ULC prevalence among outpatients who are at high risk but low

hospitalization and mortality rates of 2.5% and 0.5%, respectively, consistent with the reported benefits of vaccination³³ and the monoclonal antibody infusion.^{20,21}

Table 2 Characteristics of hospitalized patients (n = 5)

Patient	Age,* sex	ULC finding	Vaccine status (time since last injection)	Risk factor(s) present as indication for infusion	Symptom days before imaging	Symptom days before admission
1	40, M	Bilateral	Unvaccinated	BMI 38 kg/m ²	8	8
2	50, M	Right	Unvaccinated	BMI 33 kg/m ²	6	8
3	70, M	Right	Vaccinated (258 d ago)	BMI 58 kg/m ² , diabetes, chronic lung disease	8	17
4 [†]	60, F	Bilateral	Unvaccinated	BMI 29 kg/m ²	5	7
5	40, F	None	Vaccinated (153 d ago)	immunocompromise	6	18

F, Female; M, male.

*In years rounded to nearest decade.

[†]Died.

Finding	Sensitivity, %	Specificity, %	Accuracy, %	PPV, %	NPV, %
Any ULC (<i>n</i> = 12)					
Telehealth	50	95	84	75	86
Automated B-line	33	97	82	80	82
Bilateral ULC ($n = 4$)					
Telehealth	100	91	92	50	100
Automated B-line	50	93	90	40	96

Table 3 Test characteristics of ULC by telehealth versus automated B-line detection, using physician imaging as the reference standard (n = 50)

NPV, Negative predictive value; PPV, positive predictive value.

Our observations provide a unique snapshot of burgeoning infection and vaccine effectiveness³⁴⁻³⁶ in COVID-19 from an ultrasound perspective. Apical ULC appeared within the first week of an otherwise benign-appearing upper respiratory infection and may be an early immunologic phenomenon of SARS-CoV-2. Similarly, ULC has also been described during the initial febrile stage of dengue viral infection.³⁷ Apical ULC development, particularly when bilateral, could perhaps herald a clinically important disease stage signifying lower respiratory tract involvement that may presage hypoxemia and hospitalization in some patients. Although our data provide evidence of vaccine effectiveness, the substantial 23% prevalence of ULCs in the vaccinated and 42% prevalence in the unvaccinated group likely reflects the increased virulence of the delta variant coupled with waning immunity³⁶ or the effects of immune evasion by the omicron variant³⁸ in high-risk hosts. With vaccination and repeated variant surges posited to increase widespread SARS-CoV-2 immunity over time,³⁹ future health care efforts may encounter a larger burden of recurrent outbreaks of mild to moderate disease. In that scenario, the presence of ULC could be cost effective in identifying those outpatients showing vulnerability and in need of resources to prevent hospitalization, such as monoclonal antibody or antiviral therapy. Our study shows that the frequently used temperature or oximetry screening may lack sensitivity for the early identification of vulnerable patients, whereas the use of only clinical characteristics may be too encompassing and could include up to half of the population infected.⁴⁰ The high sensitivity of clinical characteristics to identify risk even after vaccination is underscored by outcomes in a large national database that reported severe vaccine breakthrough infections requiring hospitalization in 8% (189 of 2,246) of those infected, all of whom had at least one risk factor. Notably, no severe outcomes were seen in the patients (n = 446)who had received monoclonal antibody therapy.⁴¹ In the present study we enrolled predominantly vaccinated patients, all of whom had at least one risk factor and received monoclonal antibody therapy, and found that extensive bilateral lung disease occurred in 8% (16 of 201) and was noted in two of the five patients who were subsequently hospitalized. Both patients were unvaccinated, quickly deteriorated, and were hospitalized within 2 days, and one of these patients died. In contrast, the two vaccinated patients who were hospitalized had only unilateral or no initial ULC findings and a more delayed presentation requiring admission 9 to 12 days later, suggesting perhaps partial protection from vaccination and the infusion. Provision of monoclonal antibody and antiviral therapies to every outpatient with one qualifying risk factor and mild to moderate COVID-19 may be constrained by cost and availability worldwide. It may be possible that the addition of a pathologic ultrasound sign

such as ULC may help in the thoughtful allocation of treatments for those at highest risk and showing progressive disease, regardless of vaccination status or prevailing variant. More data are needed on the prevalence, airborne contagiousness, progression, and outcome of ULC in the general outpatient population when infected by SARS-CoV-2.

Telehealth communication has increased during the pandemic,⁴² primarily to provide health care while limiting in-person visits and disease transmission. Physical examination during telehealth is dependent largely upon visual findings on camera and lacks lung auscultation.⁴³ This study sought a simple diagnostic scan that could find widespread telehealth application in outpatients by untrained users, unlike prior studies that used complex expert imaging protocols and the scoring of B-lines in more acutely ill populations. The present investigation confirms the feasibility of outpatients' imaging their own upper lung zones to obtain a prevalent pathologic sign, ULC, a finding with known interobserver reproducibility.⁴⁴ Telehealth and artificial intelligence methods demonstrated 84% to 92% accuracy using currently available smartphone and Internet technologies, which was similar to the 88% accuracy found in our prior study of patient self-imaging.¹⁸ These observations underscore the potential of a simple imaging technique, which does not require undressing, to be applied by patients, household members, or individuals in the community using a smartphone. But despite telehealth accuracy, we noted that even the simplest of point-of-care ultrasound techniques is still best when applied by a physician. Particularly during early disease when B-lines are borderline, unilateral, or in a patchy distribution, the examining physician can use image interpretation and probe manipulation skills to actively search for findings. With visual cues but not tactile feedback, telehealth physician methods on average were less sensitive but, importantly, improved when the disease became more extensive and bilateral. In automated detection, the current first-generation artificial intelligence methods also appeared to have less sensitivity because of difficulty in separating confluent, transient, or fast-moving B-lines (Figure 2), a phenomenon the human eye can readily recognize. Spatial and temporal resolution and deep learning algorithms have demonstrated variable effects in early studies, having the potential for greater or lesser sensitivity, and are likely bounded by the subjective image search and acquisition process.⁴⁵⁻⁴⁷ Nonetheless, this study has demonstrated that a specific ultrasound examination can be performed during telehealth by patients without any prior training and has future implications for this methodology in other disease states. In COVID-19, the simplified lung examination could be performed not only from home isolation by patients but also in emergency departments, urgent care facilities, or COVID-19 testing centers for outpatients with minimal symptoms.

In less affluent or remote regions, simplified lung ultrasound may be better than screening temperature or oximetry for early detection or to demonstrate disease progression. In other diseases, simplified patient examinations can be used during telehealth visits to follow patients after hospital discharge with congestive heart failure or pericardial and pleural effusions, particularly in those without easy access to outpatient care.

Our study had several limitations. The observation that 79% of consecutive patients with COVID-19 in the clinic were vaccinated was not unlike the 78% concurrent vaccination rate in the community,⁴⁸ which could be consistent with both a waning vaccine effect on viral transmission^{36,38,49} and a bias in the self-referral for COVID-19 testing by the vaccinated. Although several ultrasound manufacturers have in-device telemedicine software that can directly transmit higher quality images, we decided to use independent, common telemedicine software and have the patient hold up the phone screen to the camera, as this represents the simplest practical method to show all the various medical device displays during a telehealth appointment. This practice may have reduced image quality and telehealth sensitivity. The higher proportion of men among the 11 patients in whom both telehealth and artificial intelligence made errors remains unexplained, as neither gender nor BMI differences have been previously described in B-line appearance. In the multivariable analysis, most of the predictors were also indications for monoclonal antibody infusion, possibly exposing a "frailty" bias whereby low BMI (<25 kg/m²) trended toward the presence of ULC, perhaps because of its association with other risk factors mandatory for study entry or not accounted for in the present study. Finally, the analyses of ULC prevalence, symptoms, and outcomes were confounded by multiple temporal factors, including the virulence of the predominant coronavirus variant, the efficacy of the monoclonal antibody formulation, prior unrecognized SARS-CoV-2 infection, and waning immunity in a high-risk population.

CONCLUSION

This study demonstrated that an ultrasound lung finding of apical B-lines was common within 1 week of mild to moderate SARS-CoV-2 infection in high-risk outpatients and that patients can perform a simplified lung ultrasound examination on themselves over telehealth. Future outcome studies are needed to address the utility and public health implications of telehealth-guided delivery of outpatient COVID-19 therapies.

ACKNOWLEDGMENTS

We acknowledge Karen V. Patel, RN, MSN, ACNP-BC, Christian A. Devera, RN, and the Scripps COVID Care Companion team for their assistance in this project.

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