The Impact of Lung Ultrasound on Coronavirus Disease 2019 Pneumonia Suspected Patients Admitted to Emergency Departments

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Objective: The aim of this study was to identify the sensitivity and specificity of lung ultrasound (LUS) and show its place in diagnosing patients with known coronavirus disease 2019 (COVID-19) pneumonia, according to chest computed tomography and the COVID-19 reporting and data system (CO-RADS).

Methods: Nineteen patients who admitted to a single university hospital emergency department between March 5, 2020, and April 27, 2020, describing dyspnea were included in the study and underwent LUS by a single emergency specialist. The patient population was divided into 2 groups, COVID-19 positive and negative, and the sensitivity and specificity of LUS according to chest computed tomography were calculated for COVID-19 pneumonia diagnosis. In the subgroup analysis, the patient group was divided into real-time reverse transcription–polymerase chain reaction positive (n = 7) and negative (n = 12), and sensitivity and specificity were calculated according to the CO-RADS.

Results: According to the CO-RADS, significant differences were detected between the LUS positive and negative groups in terms of COVID-19 pneumonia presence. Only 1 patient was evaluated as CO-RADS 2 in the LUS positive group, and 2 patients were evaluated as CO-RADS 4 in the LUS negative group ($P = 0.04$). The sensitivity of LUS according to the CO-RADS for COVID-19 pneumonia diagnosis was measured to be 77.78% (95% confidence interval [CI], 39.9%–97.1%), specificity was 90% (95% CI, 55.5%–99.75%), positive predictive value was 87.5% (95% CI, 51.35%–97.8%), and accuracy was 84.21% (95% CI, 60.4%–96.62%; $P = 0.004$).

Conclusions: In conclusion, LUS is easily used in the diagnosis of COVID-19 pneumonia because it has bedside application and is fast, easy to apply, reproducible, radiation free, safe for pregnant women, and cheap.

Key Words: COVID-19, pneumonia, lung ultrasound, chest computed tomography

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The disease caused by the severe acute respiratory syndrome coronavirus 2 (coronavirus disease 2019 [COVID-19]) virus first appeared in Wuhan, China, in December 2019 and spread globally until it was recognized as a pandemic by the World Health Organization on February 11, 2020.[1] For COVID-19, the importance of achievable, reliable, and bed-side assessments is highlighted because of the nonspecific symptoms and rapid progression of the clinical manifestation toward pneumonia. Coronavirus disease 2019 pneumonia is characterized by patchy interstitial thickening, alveolar edema, and damage in the subpleural area and centrifugal diffusion. Consolidations and acute respiratory distress syndrome patterns may also be detected in cases where the disease progresses.[2]

Lung ultrasound (LUS) is a reliable technique that is easily applied and portable, and does not contain ionizing radiation.[3–5] Michels et al[4] stated that pneumonia can be easily detected by LUS because of the infiltrates spreading peripherally in critically ill patients.

Lung ultrasound has become a frequently used pneumonia diagnosis tool in adults and children in recent years.[6,7] Also, in recent years, the use of LUS has been defined to differentiate bacterial pneumonia from viral infections.[8,9]

With LUS, the irregular pleural line and B lines, particularly the "white lung" and hypoechogenic areas in the pleural plane, in pleural effusion can be seen in the diagnosis of COVID-19 pneumonia.[10,11]

The purpose of this study was to identify the sensitivity and specificity of LUS and show its place in diagnosing patients with COVID-19 pneumonia, according to chest computed tomography (CCT) and the COVID-19 reporting and data system (CO-RADS).

METHODS

Before the study commenced, approval was obtained from the Ethics Committee of Ufuk University (number, 20200521/10). A total of 61 patients, who were suspected of COVID-19 according to the Turkish Republic Ministry of Health COVID-19 Guideline, who admitted with similar

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complaints to the university hospital's emergency department between March 5, 2020, and April 27, 2020, were examined. Of these patients, 19 who underwent LUS examination because of the complaint of shortness of breath were included in the study.[12] The demographic data, comorbidities, smoking habits, and admission complaints of the patients were recorded according to their anamnesis. Detailed physical examinations were performed after the vital findings of the patients were recorded. Complete blood count, including white blood cell (WBC), lymphocyte count, and neutrophil count; lactate dehydrogenase as a biochemical marker; C-reactive protein (CRP) and ferritin as acute phase reactants; and D-dimer tests in terms of thrombosis were performed on the patients suspected of COVID-19. The neutrophil/lymphocyte ratio (NLR) was also calculated. Nasopharynx swabs were taken for real-time reverse transcription–polymerase chain reaction (RT-PCR) analysis. A total of 19 patients, who described dyspnea, underwent LUS by a single emergency specialist.

LUS Examination

A total of 19 patients, who described dyspnea, underwent LUS before CCT. Lung ultrasound measurements were performed with a TerasonUsmart 3200 T Ultrasound System (Burlington, MA) and a 3.5-MHz curved probe. Both hemithoraces were divided into 3 regions, and LUS was performed. The anterior area was identified as the area between the parasternal and anterior axillary line, the lateral area was identified as the area between the anterior and posterior axillar lines, and the posterior area was identified as the area between the paravertebral and posterior axillary line. All areas were scanned with ultrasound as transverse and longitudinal, lateral-medial, and up and down. Lung ultrasound was performed by an experienced emergency specialist. The pneumonic fields were evaluated for consolidation, irregular thick pleural line, pleural effusion, confluent B lines, and glass rockets (Figs. 1, 2). Together with pleural line anomalies, without air bronchograms, small subpleural consolidations and single or confluent B lines were mostly considered to be related to viral pneumonia.[8,9,13]

As recommended in the guidelines, CCT was then performed on the patients, and the images were classified by a radiologist according to the CO-RADS as levels 1, 2, 3, 4, 5, and 6.[12,14] As identified in the literature, CO-RADS 1, 2, and 3 are evaluated as COVID-19 negative, and CO-RADS 4, 5, and 6 are evaluated as COVID-19 positive.[14] The patient population was divided into 2 groups: those with signs of COVID-19 pneumonia according to the LUS results (n = 8) and those who did not have any signs of COVID-19 pneumonia (n = 11). Clinical and laboratory parameters, CCT findings, and RT-PCR results were compared between the 2 groups. The sensitivity and specificity of LUS according to CCT were also calculated for the COVID-19 pneumonia diagnosis. In addition, in the subgroup analysis, the patient group was divided into RT-PCR positive (n = 7) and negative (n = 12) groups, and sensitivity and specificity were calculated according to the CO-RADS.

Exclusion Criteria

Patients who were diagnosed with lung infections other than COVID-19, patients with malignancies, patients younger

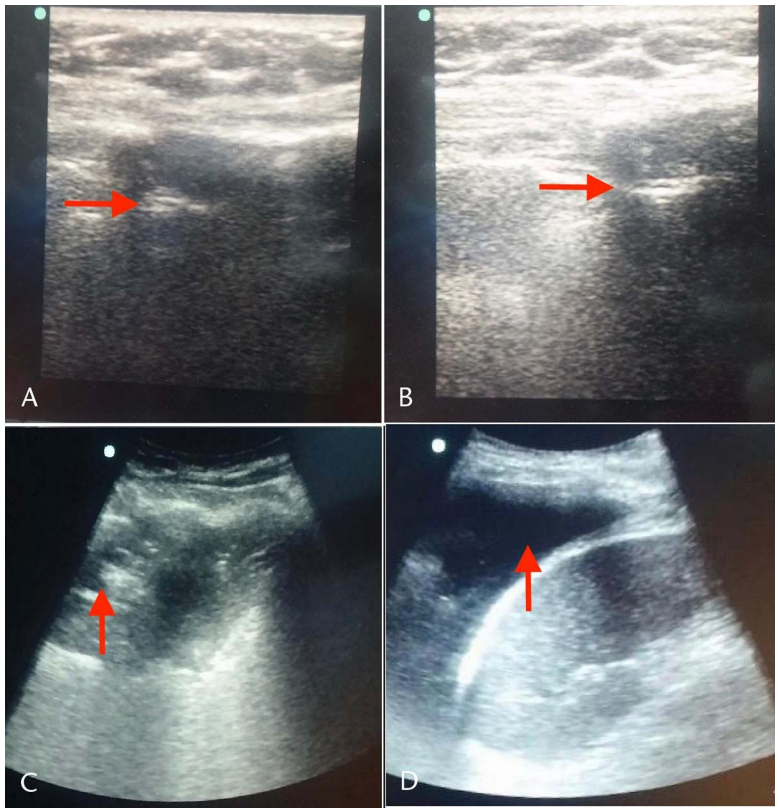

FIGURE 1. A, B, C, Arrow indicates subpleural consolidations; (D) arrow indicates pleural effusion.

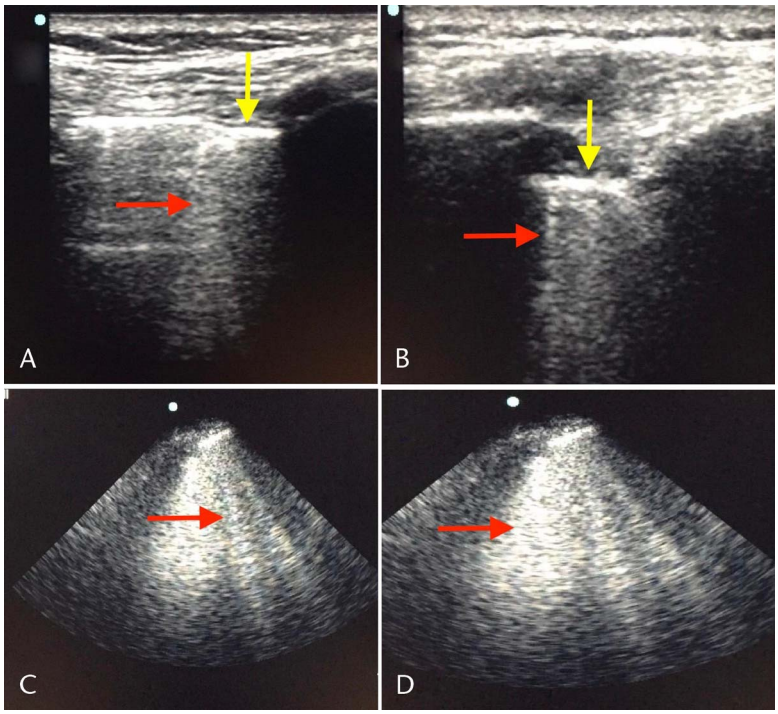

FIGURE 2. A, B, Yellow arrows indicate irregular thick pleural lines, and red arrows indicate confluent B lines; (C, D) arrow indicates glass rockets (coalescence of B lines).

than 18 years, and pregnant women were not included in the study.

Blood Sampling and Measurement of Laboratory Parameters

Peripheral venous blood samples (5 mL) were drawn into serum separator tubes (Vacuette; Greiner Bio-One, Kremsmuenster, Austria) at admission. Serum samples were left 30 to 60 minutes to form clots before centrifugation at 1500*g* for 10 minutes at room temperature. Routine biochemical and hematologic results were obtained by reviewing the patients' records. Hematologic analyses were performed using the CELL-DYNRuby Hematology analyzer (Abbott Laboratories, Diagnostics Division, Santa Clara, CA). All biochemical parameters were analyzed using the Architect c8000 Chemistry analyzer (Abbott Laboratories, Diagnostics Division, Santa Clara, CA). Reverse transcription–polymerase chain reaction results were performed using the CFX96 Touch Real-Time PCR Detection System (Bio-Rad, Hercules, CA). Routine biochemical, hematological, and RT-PCR test results were recorded.

Statistical Analysis

Statistical analysis was performed with SPSS, version 23.0 statistical software (SPSS, Inc., Chicago, IL). The categorical variables were described as frequencies and percentages. Continuous variables were presented as mean and SDs. χ^2 Tests were used to evaluate the relationship between the categorical variables of the study subgroups. The independent *t* test and Mann-Whitney *U* test were used for the comparison of 2 groups with continuous variables. The area under the curve was calculated by receiver operating characteristic regression analyses. We calculated sensitivity, specificity, positive predictive value (PPV), and negative predictive value (95% confidence intervals [CIs]) of LUS in diagnosing COVID-19 pneumonia to assess test performance. *P* values of <0.05 were considered statistically significant.[15]

RESULTS

No significant differences were detected between the LUS positive and negative groups in terms of age, sex, admission complaint, smoking habit, and comorbidity ($P > 0.05$). The most common admission complaints of patients were cough and dyspnea, and there was no significance between LUS

TABLE 1. Clinical and Inflammatory Parameters of Groups

Parameters	LUS+ (n = 8)	LUS− (n = 11)	*P*
Demographics			
Age, y	57.8 ± 19	48.8 ± 12.6	0.22
Sex, male, n (%)	5 (62.5)	7 (63.6)	0.96
Clinical parameters			
Body temperature, C°	36.96 ± 0.50	36.62 ± 0.49	0.17
SaO_2, %	89.75 ± 14.2	93.73 ± 9.9	0.48
Laboratory parameters			
WBC, $10^3/\mu L$	9.46 ± 6.97	9.75 ± 5	0.91
CRP, mg/L	70.69 ± 77.5	22.4 ± 38.6	0.09
D-dimer, µg/L	359 ± 270	641 ± 242	0.55
LDH, U/L	324.8 ± 345	217.8 ± 156.2	0.37
Neutrophil, $10^3/\mu L$	6.9 ± 6.5	7.13 ± 5.1	0.95
Lymphocyte, $10^3/\mu L$	1.5 ± 0.7	2 ± 1	0.28
NLR	7.26 ± 9	5.7 ± 6.2	0.68
Ferritin, µg/L	408.1 ± 673	400.3 ± 622.7	0.98

LDH, lactate dehydrogenase.

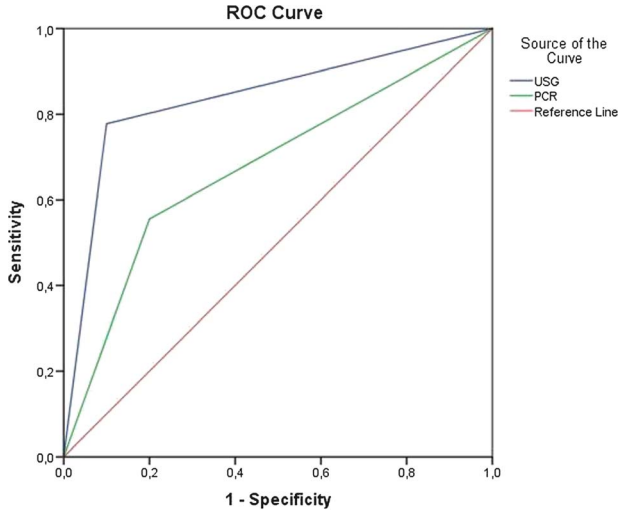

FIGURE 3. Receiver operating characteristic curve analysis of LUS (blue line), RT-PCR (green line), Reference line (red line).

positive and negative groups according to the χ^2 test ($P = 0.43$). In the LUS positive group, 3 (37.5%) of 8 patients were smokers, and 5 (45.5%) of 11 were smokers in the LUS negative group ($P = 0.72$). In the LUS positive group, 4 (50%) of 8 patients had comorbidities, and 4 (36.4%) of 11 had comorbidities in the LUS negative group ($P = 0.7$). The most common comorbidities were hypertension and diabetes mellitus, respectively.

No significant differences were detected between the LUS positive and negative groups in terms of the clinical parameters of peripheral oxygen saturation (SaO_2) and body temperature, or the laboratory parameters of CRP, NLR, neutrophil count, lymphocyte count, D-dimer, ferritin, or WBC (Table 1).

According to the CO-RADS, significant differences were detected between the LUS positive and negative groups in terms of COVID-19 pneumonia presence. Only 1 patient was evaluated as CO-RADS 2 in the LUS positive group, and 2 patients were evaluated as CO-RADS 4 in the LUS negative group ($P = 0.04$).

Significant differences were detected in terms of RT-PCR positivity between the LUS positive and negative groups. Reverse transcription–polymerase chain reaction positivity was detected in 5 (62.5%) of 8 patients in the LUS positive group and in 2 (28.6%) of 11 patients in the LUS negative group ($P = 0.04$).

The sensitivity of LUS according to the CO-RADS for COVID-19 pneumonia diagnosis was measured to be 77.78% (95% CI, 39.9%–97.1%), specificity was 90% (95% CI, 55.5%–99.75%), PPV was 87.5% (95% CI, 51.35%–97.8%), and accuracy was 84.21% (95% CI, 60.4%–96.62%; $P = 0.004$; Fig. 3). According to the CO-RADS, the sensitivity and specificity of the RT-PCR positive and negative groups for COVID-19 pneumonia diagnosis were calculated to be 55.56% and 80%, respectively; in addition, accuracy was 68.42% (95% CI, 43.45%–87.42%), and PPV was 71.43% (95% CI, 38.84%–90.78%; $P = 0.07$; Fig. 3). The parameters for sensitivity and specificity are detailed in Table 2.

DISCUSSION

Coronavirus disease 2019 pneumonia LUS findings included thickening in the pleural line; multifocal, discrete, or confluent B lines; small centromeric consolidations; and multilobe involvement.[16] Guan et al[17] reported that 86.2% of patients had various abnormalities in CCT, and 75% of these had diffuse and peripheral localizations with bilateral lung involvement. The B lines are hyperechoic vertical lines originating from the pleura to the edge of the screen.[18] The main LUS finding for ground glass opacity is B lines.[16,19]

One of the main results of our study was that the CCT result of only 1 patient in the LUS positive group was not compatible with a COVID-19 diagnosis, and only 2 of the patients in the LUS negative group were found to be compatible with COVID-19. This difference might have occurred because LUS is not adequate for detecting lesions that are located deep within the lung or because the disease is at an early stage according to the symptom start time; however, because COVID-19 pneumonia lesions already tend to settle peripherally, LUS will be largely sufficient for the detection of existing lesions.[10,20] The presence of a correlation with LUS and CCT will reduce the need for CCT in each patient. With LUS, which can be easily applied at the bedside, the number of medical staff that come into contact with the patient will decrease, and the CCT unit will be prevented from becoming contaminated. In addition, the discrimination of low-risk from high-risk patients in the triage field will also be made quickly.[21] Finally, LUS is cost-effective for developing countries because the cost is more advantageous compared with CCT.[22] Recently, the idea of using LUS instead of the stethoscope has arose with the emergence of studies demonstrating the superiority of LUS over x-rays and auscultation.[23] Cardiologists also experienced the idea of use of ultrasound over auscultation and x-rays, with echocardiography. There are studies reporting that LUS has limited the use of x-rays by 26% and CCT by 47%, although the effect of auscultation is not known in patients admitting with dyspnea.[24]

According to the results of our study, the RT-PCR positivity rate was 62.5% in the LUS positive group, and the RT-PCR negativity rate was 71.4% in the LUS negative group. In other words, LUS results and RT-PCR results were correlated. In a current study, it was reported that the sensitivity of CCT was higher than real-time RT-PCR (71%–98%) in the diagnosis of COVID-19 pneumonia.[25] Among the reasons why RT-PCR sensitivity was low in our study may be due to the inadequacy of the virus nucleic acid detection method, low viral load, false negativity due to the window period, or inappropriate sampling. For this reason, it is argued that, if a patient's clinical

TABLE 2. Sensitivity, Specificity, and PPVs of LUS and rRT-PCR Results for CO-RADS Positive COVID-19 Pneumonia

	Sensitivity, % (n)	Specificity, % (n)	PPV, % (n)	NPV, % (n)	Accuracy, % (n)	*P*
LUS results	77.7 (7/9)	90 (9/10)	87.5 (7/8)	81.8 (9/11)	84.2 (16/19)	0.004
RT-PCR results	55.56 (5/9)	80 (8/10)	71.43 (5/7)	66.67 (8/12)	68.42 (13/19)	0.07

NPV, negative predictive value; RT-PCR, real-time reverse transcription–polymerase chain reaction.

manifestation suggests COVID-19 pneumonia, CCT can be applied, especially for RT-PCR negative patients.[25] Peng et al[16] indicated in their study that lung abnormalities may develop faster than clinical manifestations and nucleic acid detection, so they recommend using CCT for screening patients suspected of COVID-19. However, COVID-19 is a highly contagious disease, and the need of transporting unstable patients with hypoxemia increases risk, making CCT a limited option for some patients. The results of LUS are similar to those of CCT and are superior to chest x-ray for evaluating pneumonia with or without acute respiratory distress syndrome.[16]

The criterion standard test for evaluating thoracic diseases is high-resolution CCT,[26] but in several studies, it is stated that the use of several diagnostic techniques together, such as CCT, RT-PCR, and antibodies, with clinical findings would be more useful for the accurate diagnosis of COVID-19 pneumonia specifically, because there is no generally accepted gold standard test to date.[27,28]

It was argued in another study that follow-up CCT can be performed to track changes for the stage of the disease and the response to treatment, and follow-up CCT was recommended to determine whether the lung progressed to the white lung level at the earliest stage.[29] However, considering that routine CCT has negative points, such as ionizing radiation exposure, the transportation of the patient could result in failure in monitoring and follow-up, contaminating the CCT room, and increasing the time needed for resterilization. Lung ultrasound can be used safely for the follow-up and can detect early-stage changes of the disease, especially in pregnant women with a generally stable condition, in which the fetus should be protected from ionizing radiation.[30]

According to the results of our study, the sensitivity of LUS was 77%, and the specificity was 90% in the diagnosis of COVID-19 pneumonia. These rates were 55.56% and 80%, respectively, in RT-PCR positivity. In another recent study, RT-PCR sensitivity was reported as 71%.[25] In our study, this rate was relatively low; however, the limited number of patients may be the reason for this difference. In this case, LUS appears to be a more useful method than RT-PCR.

Another result of our study that supported the use of LUS was that no differences were detected between LUS positive and LUS negative cases in terms of vital findings, such as fever and SaO_2, and laboratory parameters, such as WBC, CRP, D-dimer, lactate dehydrogenase, neutrophil count, lymphocyte count, NLR, and ferritin values. According to these results, patients cannot be diagnosed or suspected as COVID-19 positive or negative only by looking at their vital signs and laboratory values. We think that performing LUS until the RT-PCR results are finalized will save time for appropriate treatment and preserve clean areas and staff exposure in emergency departments.

CONCLUSION

In conclusion, LUS can be easily used in the diagnosis of COVID-19 pneumonia because it can be easily applied on the bedside and is fast, reproducible, radiation free, safe for pregnant women, and cheap. Because its use in the triage area is important in differentiating critical patients, its use in emergency clinics should be expanded. Multicenter studies are needed with large groups of patients to support these findings.

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