BNS University
Critical Care Departement

The Egyptian Journal Of Intensive Care And Emergency Medicine (JICEM)

Prediction of (Covid-19) Patients Outcomes byLung Ultrasound Score

Mohamed B. El Kholy, David Neseam, Hamdy Saber, Mohamed A. Hamila

Critical care department, Faculty of medicine, Beni Suef University, Egypt

Abstract:

Background: Lung ultrasound (LUS) imaging is a quick, non-invasive, accurate and quantitative method. Its prognostic value in those with Coronavirus disease 2019 (COVID-19) is still unknown. **Aim:** To know if poor outcomes in COVID-19 patients could be predicted on the basis of LUS score at admission. **Patients and methods:** A prospective cohort study involved 40 patients diagnosed with COVID-19 according to Egyptian protocol for management of COVID-19 patients. All patients subjected to full history taking, clinical assessment, laboratory investigation (routine labs, serum ferritin, C-reactive protein, LDH and D-dimer) and imaging (chest X-ray, ultrasound and CT without contrast). **Results:** The baseline LUS score of patients was significantly higher among patients who neededmechanical ventilation and patients who died at admission (p=0.012 and 0.015 at admission, respectively) and at 4thday (0.026 and 0.024 at 4th day, respectively). Baseline LUS score could predict the need of MV at cutoff value >17 with sensitivity 73.68%, specificity 66.67%, PPV 66.7% and NPV 73.7% andcould predict the mortality at cut off value 17 with sensitivity 70%, specificity 65%, PPV 66.7%, NPV 68.4%. **Conclusion:** Lung ultrasound score was a strong predictor of mortality, ICU admission, and the need for mechanical ventilation in patients with critical condition.

Keywords: COVID-19 Lung Ultrasound Score, SARS-CoV-2

1. Introduction:

Coronavirus disease 2019 (COVID-19) is a worldwide hazard caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) lead to severe acute respiratory distress syndrome (ARDS), multi-organ dysfunction syndrome [1]. The primary therapy during hospitalization is supportive therapy, as there is no specific therapy to treat COVID-19 [2]. Mildcases may be cured by close monitoring and pain medication, while severe cases need extensive treatment and admission in an intensive care unit (ICU) [3]. As a result, early detection of COVID-19 patients' illness deterioration may be critical to providing proper health treatment. Recent research has demonstrated a number of demographic and clinical variables may be used to predict disease progression [4–7]. COVID-19, on the other hand, is a respiratory illness, that mostly affects the lung [8]. Because of this, admitted patients needed imaging of lung lesionsto help detect patients who need more extensive care and support. When it comes to diagnosinga wide range of respiratory problems as pulmonary edema, pneumonia and interstitial lung disease [9–11]. Lung ultrasound (LUS) imaging is a quick, non-invasive, accurate and quantitative method. Patients with COVID-19 particularly under the age of 18 and pregnant women, have begun using LUS to diagnose and monitor lung affection and alterations in the disease. [12, 13]. Ultrasound has the advantage of being bedside imaging tool, allowing for early detection of respiratory and other organ issues, therefore minimizing is the danger of contagiousness [13]. Though, LUS has been linked to poor outcomes in individuals with lungillness [14, 15]; its prognostic value in in those with COVID-19 is still unknown. Accordingly,the study's goal was to see if poor outcomes in COVID-19 patients could be predicted on the basis of LUS at admission.

2. Patients and methods:

This was prospective cohort study carried out at Critical Care Department, Beni-Suef University Hospitals during the period from February 2021 to July 2021. Patients was admittedin critical care according to Egyptian protocol for management of COVID-19 patients.[16] Prior to being included in the research, all individuals provided written informed permission. Approval No: **FMBSUREC/09052021/Hindi**

This study involved 40 Egyptian patients diagnosed with COVID-19 were include in this work, which followed the interim guidance of the World Health Organization [17]. Patients with cardiac failure, interstitial pneumonia, tuberculosis, bronchiectasis, chronic obstructive pulmonary disease (COPD), other pulmonary disease hampering image acquisition (significant pleural effusion, previous pneumonectomy, breast prosthesis, pneumothorax) or suboptimal ultrasound window and chest trauma were excluded from this work.

***Methods*:**

All participants underwent to full history taking, clinical assessment, laboratory investigation (routine labs, serum ferritin, C-reactive protein, LDH and D-dimer) and imaging (chest X-ray, ultrasound and CT without contrast), scoring according to CoRad.

CORADS assesses the suspicion for pulmonary involvement of COVID-19 on a scale from 1 (very low) to 5 (very high) score.

- Corad 1 CT is normal
- Corad 2 Findings consistent with other

infections like typical bronchiolitis

- CoRad 3 CT abnormalities indicating infection, but unsure whether COVID-19 is involved, like widespread bronchopneumonia, lobar pneumonia, septic emboli with ground glass opacities.
- CoRad 4 suspicious CT findings but not extremely typical
- Unilateral ground glass
- Multifocal consolidations without any other typical finding
- Findings suspicious of COVID-19 in underlying pulmonary disease.
- coRad 5 bilateral multifocal GGO, vascular thickening , subpleural bands.
- coRad 6 Patient with positive PCR and bilateral GGO.[18]

lung ultrasound protocol:

Lung ultrasound examination was done at the day of admission for all patients and was repeatedafter 72 hours for critically ill patients using Vivid S5 General Electric (5.5MHz) convex probe. Each lung was divided into anterior, lateral and posterior fields using anterior and posterior axillary lines, and each field was divided into superior and inferior areas using two axial lines (one above the diaphragm and the other 1 cm above the nipples).

A total of 12 regions was assessed using a two-dimensional view with the probe placed perpendicular to the chest wall and evaluated for the following signs: pleural line (a horizontalhyperechoic line between the ribs), A-lines (horizontal reverberation artefacts repeated at a constant distance equal to the distance between pleural line and probe surface), B-lines (vertical hyperechoic reverberation artefacts deriving from the pleural line) and consolidation (presenceof a tissue-like pattern) [19,20]. In each region, LUS signs including B-lines/consolidation and pleural line abnormalities had been assessed, and the worst ultrasound pattern had been recorded. B-lines/consolidation had been quantitatively scored according to a previous study.

(1) score 0: well-spaced B-lines<3; (2) score1: well-spaced B-lines>3 (3) score 2: multiple coalescent B-lines. (4) score3: lung consolidation. The pleural line was quantitatively scored as follows: (1) score 0: normal; (2) score 1: irregular pleural line; (3) score 2: blurred pleural line. A composite score of each region was calculated by summing the individual scores for B-lines/consolidation (score 0–3) and pleural abnormalities (score 0–2). The sum of the scores inall twelve zones yielded a final score of the COVID-19 patient (ranging from 0 to 60), definedas the LUS score.

Statistical analysis:

Data analyzed using SPSS v. 25 (Statistical Package for Social science) for Windows. Description of quantitative variables was in the form of mean, standard deviation (SD) and/ormedian. ROC curve analysis was used to predict mortality and need to mechanical ventilation from Baseline and follow up LUS score. Pearson correlation was done to assess the association between scale variables. P-value was considered significant when P-value ≤ 0.05.

3. Results:

A total of 40 critically ill covid-19 patients enrolled in this work, their age ranged from 29 to 85 with a mean 60.2 ± 12.9 years. There were 25 females (62.5%) and 15 males (37.5%). Theassociated comorbidities of the studied population were 16 diabetic patients (40%), 12 hypertensive (30%), 5 were asthmatic (12.5%), and 3 were smokers (7.5%).

Regarding scoring system, APACHE score of the studied population ranged from 10 to 32 with a mean 19.1±5.8, CoRad score of the studied population ranged from 3 to 5 with a mean 4±1 and lung ultrasound score of the studied population ranged from 8 to 38 with a mean 21.8±8.3 (Table 1).

Our patient's mean ICU stay ranged from 5 to 35 days with a mean 15.9±9.4, 19 (47%) patients of them needed mechanical ventilation with a mean 12±7.6. Also, there were 20 (50%) survivors and 20 (50%) non survivors among patients (Table 2).

The baseline LUS score of patients at admission was significantly higher among patients who needed mechanical ventilation and patients who died (p=0.012 and 0.015, respectively) and at 4th day (0.026 and 0.024 at 4th day, respectively) (Table 3).

There was a significant positive linear moderate correlation between the baseline LUS and the CoRad score (r=0.521 and p=0.001) and there was moderate linear negative correlation between the LUS after 4 days and baseline PO2/Fio2 ratio (r=0.426 and p=0.006) (Figure 1 & 2).

Baseline lung ultrasound score could predict the need of MV at cutoff value >17 with sensitivity 73.68%, specificity 66.67%, PPV 66.7% and NPV 73.7% and could predict the mortality at cut off value 17 with sensitivity 70%, specificity 65%, PPV 66.7%, NPV 68.4% (Figure 3&4).

Table (1): Scoring systems of the study populations:

Scoring systems	Mean	Standard deviation
APACHE	19	5.8
CoRad score	4	1
Lung ultrasound score	21.8	8.3

Table (2): Lengths of ICU stay (LOS) and mechanical ventilation Days.

	Range	mean	SD
ICU stay	5-35	15.9	9.4
MV days	4-32	12	7.6

Table (3): relation between baseline LUS score at admission and at 4th day and need to mechanical ventilation, dialysis and in-hospital, 30-day mortality

Outcomes		**Mean ± SD**	**P-value**
At admission			
Need to mechanical ventilation	**No**	17.76±6.26	**0.012***
	Yes	23.05±8.17	
Need dialysis	**No**	20.31±7.45	0.933
	Yes	20.00±9.69	
30-day Mortality	**Alive**	17.60±6.021	**0.015***
	Died	22.95±8.24	
At 4th day			
Need to mechanical ventilation	**No**	18.7±6.46	**0.026***
	Yes	25.2±9.05	
Need dialysis	**No**	22.17±7.94	0.465
	Yes	19.20±11.71	
30-day Mortality	**Alive**	18.65±6.38	**0.024***
	Died	24.95±9.06	

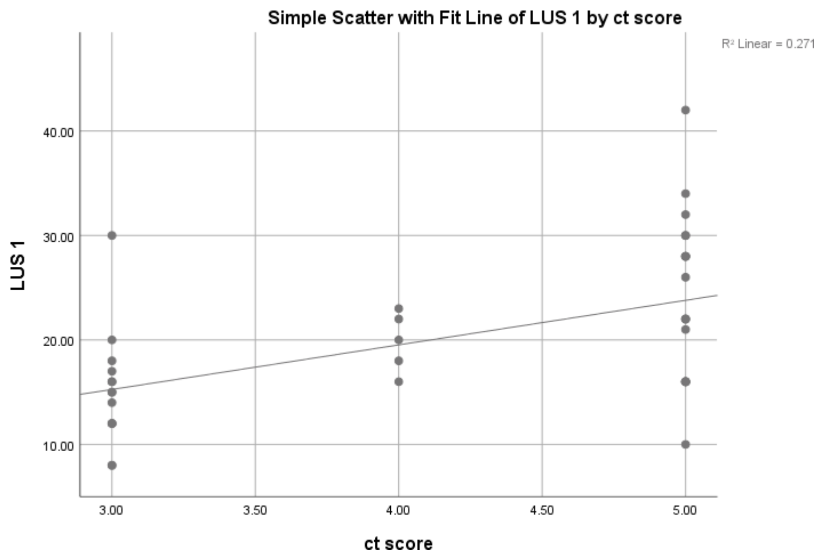

Figure (1): Correlation between baseline LUS and CoRad score

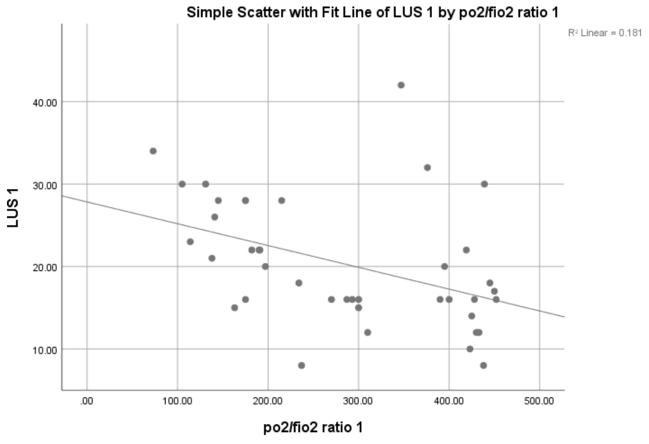

Figure (2): Correlation between baseline LUS and PO2/FIO2 ratio

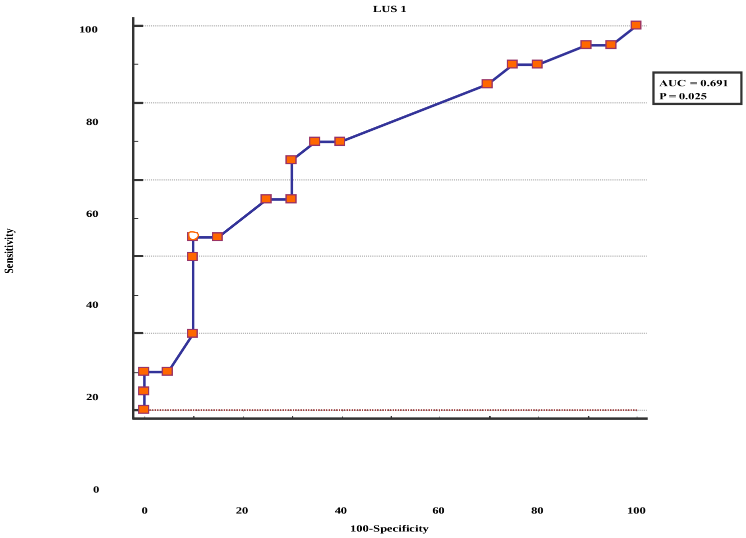

Figure (3) Receiver operating characteristics curve for prediction of need to MV using baseline LUS score

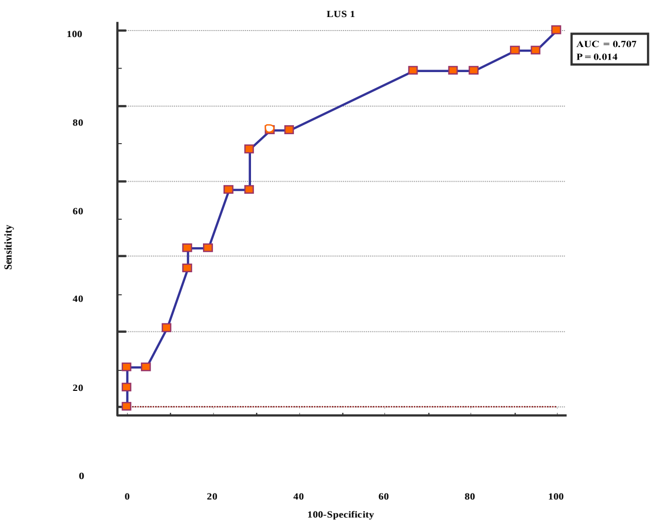

Figure (4): Receiver operating characteristics curve for prediction of 30-day mortality usingbaseline LUS score.

4. Discussion:

Children and pregnant women with COVID-19 have benefitted from the use of LUS in recent years to diagnose lung invasion and evaluate the progress of the disease [12, 13]. In fact, ultrasound is the only imaging tool that can be used bedside of patients to detect respiratory and other organ issues in real time, lowering the risk of infection and decreasing the number ofunstable patients who need to be moved [14].

The results of this study which was done on 40 COVID-19 showed that baseline lung ultrasound score was higher among 30 day mortality patients and need for MV with p-value 0.025 and 0.014 respectively and AUC 0.691 and 0.707 respectively. Furthermore, there was correlationbetween day4 LUS and both14 day mortality and need of MV with p-value 0.024 and 0.026 respectively. It also represented that LUS with a cut off value 17 predicts 14 day mortality withsensitivity 70 % and specificity 65% and need of mechanical ventilation with sensitivity 73% specificity 66%.

This was in accordance with study of de Alencar *et al.* [21] which was done on 180 patients concluded when using hospitalized (including those who are intubated or already dead) using LUS, it was shown higher LUS levels were related with deteriorating illness.. LUS predicts mortality with AUC 0.72, and score≥26 had 90% accurate in predicting death during hospitalization. Lung ultrasound can dynamically check the ventilation condition and early identify the worsening of respiratory ventilation status and the illness [22]. De Alencar et al study found that LUS increased with increasing clinical severity, the intubated group had a significantly greater LUS.

LUS ≥25 on admission showed a 90% specificity for intubation, and may be a warning for intubation or exacerbations in critical patients.

Furthermore, another study by Ji *et al.* [23] that included 280 consecutive patients, patients with higher LUS had a larger percentage of these consequences, which included respiratory failure, 49; ARDS, 37; sepsis, 14; acute heart injury, 40; acute kidney injury, 26. 267 patients were discharged from the hospital, 13 of them had a high LUS at time of discharge. During hospitalization, patients with low and intermediate LUS did not die. As a result, the research found that A cut-off value of 12 for the LUS score at admission predicted unfavorable in COVID-19 patients with sensitivity of 91.9% and a specificity of 90.5%.

In our study we correlated between LUS and different parameters like CoRad chest score, po2/fio2 ratio, CRP, LDH, lymphocytes, d-dimer, ferritin, MV days and TLC. There was no correlationbetween these parameters and LUS except for CoRad score and po2/fio2 ratio which showed a positive moderate linear correlation between LUS and CoRad score with p value 0.001 and r=0.521and a negative moderate linear correlation with po2/fio2 ratio with p value 0.006 and r=-0.426.

Similarly, study of Nouvenne *et al.* [24] which involved 62 patients who underwent chest CT and bedside LUS at admission and were urgently admitted to hospital due to COVID-19. All of them were enrolled in an observational study to correlate between them. It suggested that there was positive correlation between CT score and lung ultrasound score with p value <0.001andr = 0.65. It also showed a negative correlation with po2/fio2 ratio with p value<0.001 and r=-0.66. It is now possible to take a step ahead in the clinical follow-up of COVID-19 according to a link between ultrasound and CT scores that is statistically significant.

The study's result validate the use of bedside LUS in the assessment of patients with suspected COVID-19; however, lung ultrasound should not be regraded an alternative for chest CT. A meta-analysis by Barssoum *et al.* [25] found a sensitivity of 68–93.3% and of NPV of 52– 94.1% for lung ultrasound as a screening tool for COVID-19 pneumonia, indicating the efficacy of LUS. When it comes to specificity and PPV there is a wide range of data published with one research showing 92.9% and 84.6%, while another reported 21.3% and 19.2%, respectively.

Overall, when comparing marked lung ultrasound changes to CT visual scores, a poor association despite statistical significance. Based on this finding, LUS may be less reliable thanCT for the stratifying of the degree of lung condition in COVID-19. It has been also not possible to compare the false-negative and false-positive rates of LUS results in COVID-19 pneumonia to those of the CT scans until now. Although, it has been shown to be good to excellent in many other pulmonary diseases. LUS in COVID-19 pneumonia is still controversial [26]. Isolated patients were considered a limitation for using LUS in COVID-19 infection [27].

5. Conclusion:

Ultrasound on the lung is a simple useful method that can be performed bedside. Lung ultrasound score was a strong predictor of mortality, and the need for mechanical ventilation in patients with critical care condition. The findings of this study highlight the need future research, preferably using combination clinical, laboratory, and imaging variables, to assess the probability of bad outcomes from COVID-19 infection.

6. References:

1. Liang WH, Guan WJ, Li CC, et al. Clinical characteristics and outcomes of hospitalized patients with COVID-19 treated in Hubei (epicentre) and outside Hubei (non-epicentre): a nationwide analysis of China. EurRespir J. 2020;55 (6):2000562. https://doi.org/10.1183/13993003.00562-

2020.

2. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patientswith SARS- CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8 (5):475–81.
3. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of2019 novel coronavirus pneumonia in Wuhan, China: adescriptive study. Lancet. 2020;395 (10223):507–13.
4. Wu C, Chen X, Cai Y, Associated RF, with Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease Pneumonia in Wuhan, China. JAMA. Intern Med. 2019; https://doi.org/10.1001/jamainternmed.2020.0994.
5. Huang G, Kovalic AJ, Graber CJ. Prognostic value of leukocytosis and lymphopenia for coronavirus disease severity.Emerg Infect Dis. 2020. https://doi.org/10.3201/eid2608.201160.
6. Luo X, Zhou W, Yan X, et al. Prognostic value of C-reactive protein in patients with COVID-19. Clin Infect Dis. 2020. https://doi.org/10.1093/cid/ciaa641.
7. Kuderer NM, Choueiri TK, Shah DP, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. Lancet. 2020;395 (10241):1907–18.
8. Carsana L, Sonzogni A, Nasr A, et al. Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: a two-centre descriptive study. Lancet Infect Dis. 2020. https://doi.org/10.1016/S1473-3099(20)30434-5.
9. Ferré A, Guillot M, Lichtenstein D, et al. Lung ultrasound allows thediagnosis of weaning- induced pulmonary oedema. Intensive Care Med.2019;45 (5):601–8.
10. Wang G, Ji X, Xu Y, Xiang X. Lung ultrasound: a promising tool to monitorventilator- associated pneumonia in critically ill patients. Critical Care. 2016;20(1):320.
11. Barskova T, Gargani L, Guiducci S, et al. Lung ultrasound for the screeningof interstitial lung disease in very early systemic sclerosis. Ann Rheum Dis.2013;72 (3):390–5.
12. Denina M, Scolfaro C, Silvestro E, et al. Lung Ultrasound in Children withCOVID-19. Pediatrics.2020. https://doi.org/10.1542/peds.2020-1157.13. Youssef A, Serra C, Pilu G. Lung ultrasound in the COVID-19 pandemic: apractical guide for obstetricians and gynecologists. Am J Obstetric Gynecol.2020;223 (1):128–31.
13. Wang B, Zhang L, Zhang D, et al. Bedside

ultrasound in assessment of 510severe and critical patients with COVID-19 pneumonia in Wuhan, China.Adv Ultras Diagn Therapy. 2020;4 (2):60–6.

14. Platz E, Merz AA, Jhund PS, Vazir A, Campbell R, McMurray JJ. Dynamicchanges and prognostic value of pulmonary congestion by lungultrasound in acute and chronic heart failure: a systematic review. Eur JHeart Fail. 2017;19 (9):1154–63.
15. Gargani L, Bruni C, Romei C, et al. Prognostic value of lung ultrasoundB-lines in systemic sclerosis. Chest.2020. https://doi.org/10.1016/j.chest2020.03.075.
16. Management Protocol for COVID-19 Patients Version 1.4/30th May 2020 Ministry of health and population (MOHP), Egypt.. Ministry of Health and Population.
17. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected.Published March 13, 2020.AccessedJanuary 28, 2020: 20.
18. An JY, Unsdorfer KML, Weinreb JC. BI-RADS, C-RADS, CAD-RADS, LI-RADS, Lung- RADS, NI-RADS, O-RADS, PI-RADS, TI-RADS: Reporting and Data Systems. RadioGraphics. 2019;39(5):1435–1436.
19. Volpicelli G, Elbarbary M, Blaivas M, Lichtenstein DA, Mathis G, Kirkpatrick AW, et al. International Liaison Committee on Lung Ultrasound (ILC-LUS) for International Consensus Conference on Lung Ultrasound (ICC-LUS). International evidence-based recommendations for point-of-care lung ultrasound. Intensive Care Med. 2012 Apr;38(4):577-91. doi: 10.1007/s00134-012-2513-4. Epub 2012 Mar 6.
20. Mojoli F, Bouhemad B, Mongodi S, Lichtenstein D. Lung ultrasound forcritically ill patients. Am J RespirCrit Care Med. 2019;199 (6):701–14.
21. de Alencar JC, Marchini JF, Marino LO, da Costa Ribeiro SC, Bueno CG, da Cunha VP, Neto FL, Neto RA, Souza HP. Lung ultrasound score predicts outcomes in COVID-19 patients admitted to the emergency department. Annals of intensive care. 2021 Dec;11(1):1-8.
22. Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front Med.2020; 14(2):185192. doi:10.1007/s11684-020-0754-0
23. Ji L, Cao C, Gao Y, Zhang W, Xie Y, Duan Y, Kong S, You M, Ma R, Jiang L, Liu J. Prognostic value of bedside lung ultrasound score in patients with COVID-19. Critical Care. 2020 Dec;24(1):1-2.

24. Nouvenne A, Zani MD, Milanese G, Parise A, Baciarello M, Bignami EG, et al.. Lung ultrasound in COVID-19 pneumonia: correlations with chest CT on hospital admission. Respiration. 2020;99(7):617-24.

25. Barssoum K, Victor V, Salem A, Kumar A, Mubasher M, Hassib M, et al. Echocardiography, lung ultrasound, and cardiac magnetic resonance findings in COVID- 19: A systematic review. Echocardiography. 2021 Aug;38(8):1365-404.

26. Gullett J, Donnelly JP, Sinert R, Hosek B, Fuller D, Hill H, et al. Interobserver agreement in the evaluation of B-lines using bedside ultrasound. J Crit Care. 2015 Dec;30((6)):1395–9.

27. Sungnak W, Huang N, Bécavin C, Berg M, Queen R, Litvinukova M, et al. HCA Lung Biological Network. SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. Nat. Med. 2020;26:681-7.