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Case report

Usefulness of serial lung ultrasound for a severe COVID-19 patient on extracorporeal membrane oxygenation

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ABSTRACT

Computed tomography (CT) is the most reliable method to evaluate the progression of COVID-19 pneumonitis. However, in a pandemic, transportation of critically ill invasively ventilated patients to radiology facilities is challenging, especially for those on extracorporeal membrane oxygenation (ECMO). Notably, lung ultrasound (LUS) is a favored alternative imaging modality due to its ease of use at the point of care, which reduces the infectious risk of exposure and transmission; repeatability; absence of radiation exposure; and low cost. We demonstrated that serial LUS compares favorably with other imaging modalities in terms of usefulness for evaluating lung aeration and recovery in an ECMO-managed COVID-19 patient.

1. Introduction

Computed tomography (CT) is the most reliable method to evaluate the progression of COVID-19 pneumonitis [1,2]. However, in a pandemic, transportation of critically ill invasively ventilated patients to radiology facilities is challenging, especially for those on extracorporeal membrane oxygenation (ECMO) [3,4]. Notably, lung ultrasound (LUS) is an alternative favored imaging modality due to its utility for identifying and evaluating the serial progression of lung pathology, especially in COVID-19 patients in whom lung pathology is a key characteristic[5,6]. LUS also has other advantages, including ease of use at the point of care, which reduces the infectious risk of exposure and transmission; repeatability; absence of radiation exposure; and low cost [5,6].

2. Case presentation

A 57-year-old male office worker presented to his local hospital with a 3-day history of malaise and fever. He later developed shortness of breath that led to his hospitalization. Furthermore, a polymerase chain reaction–based test for severe acute respiratory syndrome coronavirus 2 in a nasopharyngeal swab sample returned positive results (Cobas SARS-CoV-2 Test; Roche Diagnostics, Rotkreuz, Switzerland). The patient was a heavy smoker, and his medical history included diabetes (HbA1c, 6.6; on insulin). After two days in the local hospital, he was transported to our emergency room (ER) due to worsening symptoms.

Upon admission to the ER, his vital signs were as follows: respiratory rate, 30 breaths/min; oxygen saturation, 97% on an oxygen mask at 6 L/min; heart rate, 135 beats/min; and blood pressure, 153/103 mmHg. A physical examination showed an alert man with no rashes or swelling. On auscultation, he had significant bilateral wheezing. He was therefore intubated and ventilated in the intensive care unit. After intubation, static lung compliance and airway occlusion pressure at 100 ms (P0.1) were measured (Table 1) [7].

The laboratory finding on admission are shown in Table 1. Chest radiography and CT findings showed pale, bilateral, ground-glass opacities (day 1; Fig. 1). LUS was performed at 6 points per hemithorax (superior and inferior regions anteriorly, laterally, and posteriorly) bilaterally (day 1; Fig. 1) [8]. A linear probe was placed in the intercostal muscles to evaluate the lungs. LUS was performed and graded by three emergency physicians who were experienced in performing LUS. The LUS Score (LUSS) was evaluated at the bedside as previously described [9]. Briefly, 0–3 points were allocated for each of the 12 pre-determined anatomical regions according to the ultrasound pattern: normal = 0, well-defined B-lines = 1, coalescent B-lines = 2, and consolidation = 3 (total score ranges from 0 to 36). Lung consolidations (scoring 3) were noted only when the thickness (measured perpendicular from the pleura) was greater than 15 mm. Sub-pleural thickening and sub-pleural consolidations (thickness: 15 mm or thinner) were graded as a score of 2. Each score with the detail of each zone was recorded day by day in a table and kept in the patient medical

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Table 1
Clinical parameters.

Measure	Day 1	Day 3	Day 5	Day 7	Day 9	Day 13	Day 14	Day 26
Laboratory findings			During ECMO management					
White blood cell count (/μL)	7,900	3,200	6,400	4,600	7,000	7,200	11,000	6,200
Absolute lymphocyte count (/μL)	979	714	761	961	1,379	1,044		
C-reactive protein (mg/dL)	7.09	15.8	31.5	17.8	20.4	8.25	4.2	4.4
Lactate Dehydrogenase (U/L)	500	820	845	705	634	533	407	294
Krebs von den Lungen-6 (ng/mL)	287	–	1,070	842	792	588	–	672
Respiratory parameter								
Respiratory rate (/min)	24	26	6	6	6	15	16	12
Minute volume (L/min)	10.5	13.3	1.9	1.9	1.9	3.6	8.5	6.2
PaO_2/FIO_2 ratio	224	118	69	223	170	242	285	280
P0.1 (cmH_2O)	0.8	6.4	–	0.6	0.8	1.6	0.8	0.8
Static Lung Compliance (mL/cmH_2O)	60	50	46	–	–	68	–	–
Lung Ultrasound Score	9	21	25	25	23	18	13	15

FiO_2, fraction of inspired oxygen; P0.1, airway occlusion pressure at 100 ms; PaO_2, partial pressure of oxygen.

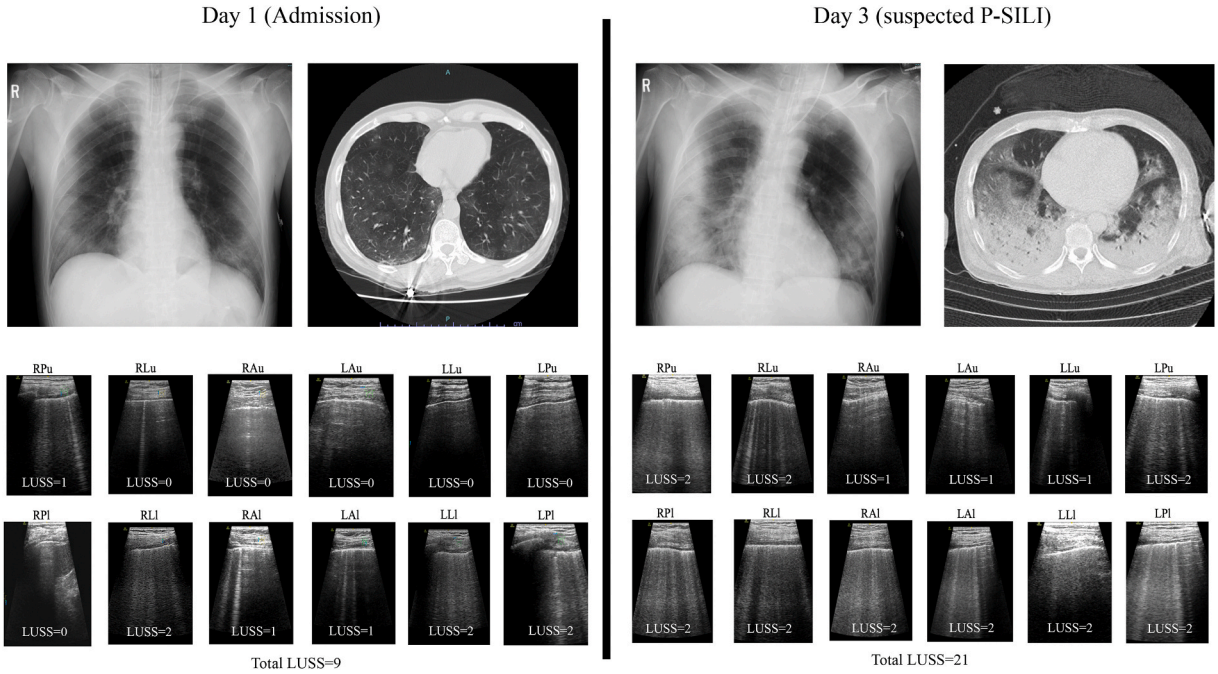

Fig. 1. Chest X-ray, CT, and LUS findings on days 1 and 3.
Day 1: Chest radiography and CT scan: pale bilateral ground-glass opacities.
LUSS: total 9 points. A-lines or <3 B-lines appeared in the bilateral upper lobes, and multiple B-lines appeared in the bilateral lower lobes.
Day 3: Chest radiography and CT scan: pulmonary consolidation appeared in the bilateral lower lobes, and bilateral ground-glass opacities were prominent in the right upper lobe.
LUSS: total 21 points. Multiple B-lines appeared in the upper bilateral lobes, and coalescent B-lines appeared in the bilateral lower lobes.
CT: computed tomography; LUS, lung ultrasound; LUSS: Lung ultrasound Score.

record.

After admission, bacterial pneumonia was considered; hence, ceftriaxone (1 g) and azithromycin (500 mg) were administered. To treat COVID-19, favipiravir (1,200 mg) and ciclesonide (800 μg) were also administered (Fig. 2). On day 2, although his C-reactive protein level had increased and his chest radiography findings remained unchange, his oxygenation improved (P/F ratio > 300 mmHg). Therefore, the ventilator settings were changed from pressure control ventilation (PCV; driving pressure).

10 cmH_2O; positive end-expiratory pressure [PEEP], 10 cmH_2O) to pressure support ventilation (PSV; fraction of inspired oxygen, 30%; PEEP, 5 cmH_2O; pressure support, 5 cmH_2O).

On day 3, his breathing pattern worsened, and he was in distress (Additional file 1). We evaluated the patient with a P0.1 measurement and an LUSS-based evaluation. His P0.1 was high at 6.4 cmH_2O (Table 1), and the LUSS results had worsened (day 3; Fig. 1) [10]. The P/F ratio and chest radiography findings continued to worsen; thus, the ventilator setting was changed back from PSV to PCV because a higher PEEP and driving pressure were needed to maintain oxygenation. We then performed a CT scan to evaluate his lungs (day 3; Fig. 1). Patient self-inflicted lung injury (P-SILI) was diagnosed because the CT images showed acute respiratory distress syndrome (ARDS) [11]. Accordingly, continuous infusion of muscle relaxants was administered to prevent excessive spontaneous breathing.

On day 5, all parameters worsened (Table 1 and Fig. 3). Therefore, we decided to initiate veno-venous extracorporeal membrane oxygenation (VV-ECMO). The right internal jugular vein was cannulated with a 25-Fr heparin-coated cannula for blood access, and the right femoral vein was cannulated with a 21-Fr heparin-coated cannula for blood return. The procedure was performed safely, and no complications occurred.

After the initiation of VV-ECMO, the patient's breathing pattern

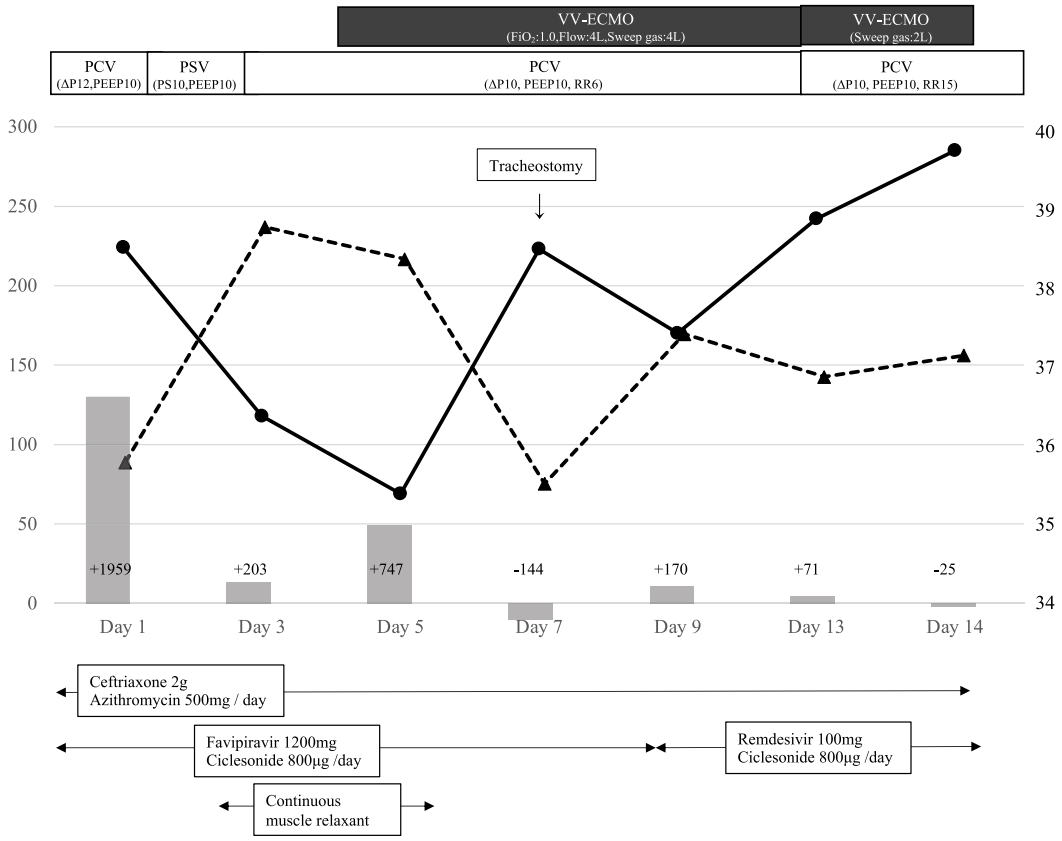

Fig. 2. Time course of physical conditions, therapeutic interventions, and ECMO status of this patient.
ECMO: extracorporeal membrane oxygenation; PCV: pressure control ventilation; PSV: pressure support ventilation; PEEP: positive end-expiratory pressure; VV-ECMO: veno-venous ECMO.

stabilized. The continuous infusion of muscle relaxants was stopped, and his lung function was reevaluated every day (P0.1 measurement, physical assessment, LUSS, chest radiography, and laboratory testing; Table 1). We performed a tracheostomy on day 7. Remdesivir (200 mg on the first day, 100 mg/day thereafter) was administered as a replacement for favipiravir on day 9. On day 13, his chest radiography findings, static lung compliance, and LUSS improved. VV-ECMO was eventually discontinued on day 14 (Fig. 3). The chest radiography and CT findings after weaning of VV-ECMO showed consistent daily improvements. On day 26, he was transferred to the hospital where he was previously admitted. Two months later, he was discharged home.

3. Discussion

3.1. Strategy for managing patients with severe COVID-19

Currently, VV-ECMO has been established as a standard step in managing ARDS when other treatments fail [12]. Although an effective treatment for COVID-19 has not been established, VV-ECMO has been used as the ultimate symptomatic treatment for COVID-19 [13–15]. Gattinoni et al. reported variations in the respiratory mechanics profiles of invasively ventilated patients with COVID-19 pneumonitis [16], and the following two clinical phenotypes were identified: (1) type L, which was characterized by low elastance, a low ventilation-to-perfusion ratio, a low lung weight, and low recruitability, and (2) type H, which was characterized by high elastance, a pronounced right-to-left shunt, high lung weight, and high recruitability. The transition from Type L to Type H may be due to the worsening of COVID-19 severity or due to an injury caused by high-stress ventilation.

Besides the severity of the disease itself, the depth of negative intrathoracic pressure may also play a possible key role in the phenotype shift from Type L to Type H [17]. Transpulmonary pressure (TPP), which is the distending force applied to the lungs, is the difference between the alveolar and intrathoracic pressures. TPP will increase with strong spontaneous breathing. Higher TPP and lung permeability due to inflammation result in interstitial lung edema. This phenomenon has recently been recognized as P-SILI [11].

Effective treatment for severe COVID-19 pneumonitis may prevent the occurrence of P-SILI and its progression from Type L to Type H. Systemic steroid administration, which was not used in this study, has been thought to reduce inflammation, thereby suppressing strong spontaneous breathing and improving the prognosis of patients on mechanical ventilation [18]. However, if the lungs are severely damaged, ECMO is the only way to gain time with lung-protective ventilation until recovery. In fact, we have previously reported successful treatment of a COVID-19 pneumonitis patient with VV-ECMO in 7 days [14].

3.2. Evaluation of lung condition during ECMO

Although VV-ECMO is one way to save lives, it is risky and associated with some complications, primarily including bleeding and infection [1]. Therefore, clinicians perform daily lung evaluations to determine when VV-ECMO should be induced and when a patient should be weaned off it.

It has been reported that CT scans provide the most reliable assessment of lung condition in COVID-19 pneumonitis patients [1,20]. However, during a pandemic, the transportation of critically ill ventilated patients to radiology facilities is challenging, especially for ECMO-managed patients[3,4]. Although increased levels of D-dimer, C-reactive protein, ferritin, and lactate dehydrogenase have also been reported as markers of severity for COVID-19, they are not specific to the lungs [21]. The serum Krebs von den Lungen-6 (KL-6) concentration is a

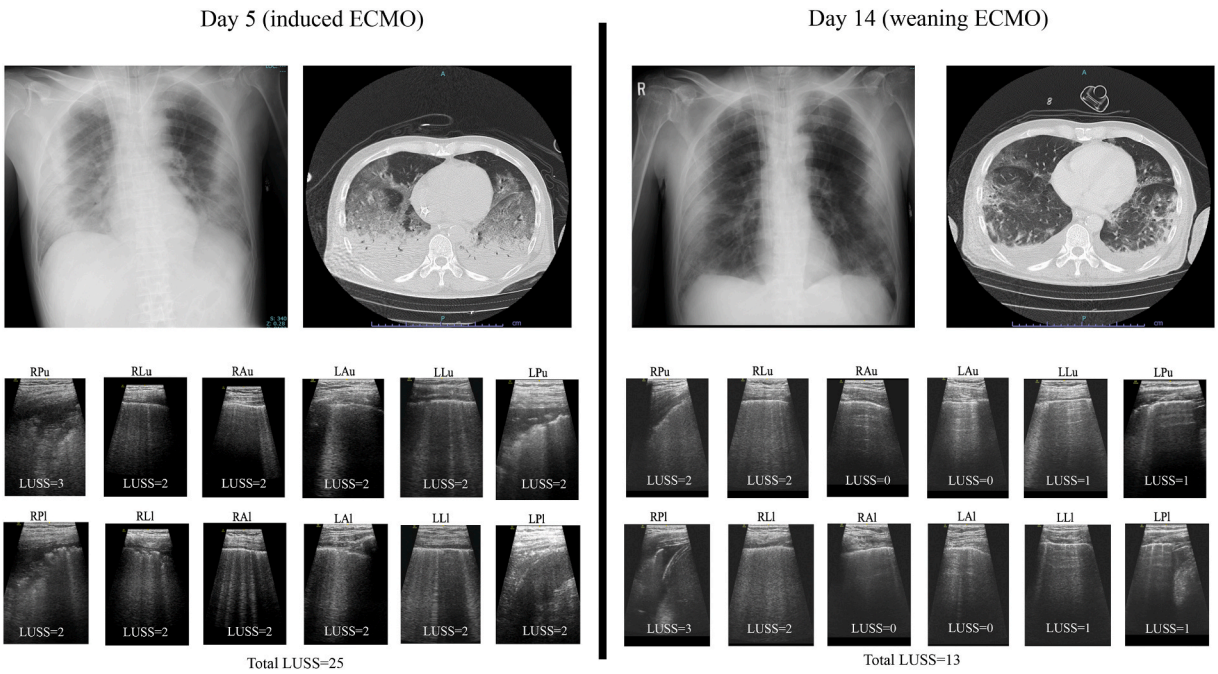

Fig. 3. Chest X-ray, CT, and LUS findings on days 5 and 14.
Day 5: Chest radiography and CT: pulmonary consolidation worsened in the bilateral lower lobes, and bilateral ground-glass opacities also worsened in the bilateral upper lobes.
LUSS: total 25 points. Coalescent B-lines were prominent in the bilateral anterior and lateral lobes. Subpleural consolidation appeared in the bilateral posterior lobe.
Day 14: Chest radiography and CT: pulmonary consolidation improved in the bilateral lower lobes, and bilateral ground-glass opacities decreased in the bilateral upper lobes.
LUSS: total 13 points. Multiple B-lines and subpleural consolidation decreased, and A-lines reemerged in the anterior lobe.
CT: computed tomography; LUS, lung ultrasound; LUSS: Lung ultrasound Score.

lung-specific biomarker, and its usefulness in COVID-19 has been reported [22]. However, the measurement of KL-6 levels is time-consuming and cannot be done at all facilities. Notably, LUS is the preferred imaging modality because of its utility for identifying and evaluating the serial progression of lung pathology, especially in COVID-19 pneumonitis cases where lung pathology is a characteristic feature [5,6]. LUS provides results that are similar to chest CT findings, and it is superior to chest radiography for the evaluation of COVID-19 [23–25]. However, the existing literature contains only a few case reports supporting the usefulness of serial LUS in ECMO-managed severe COVID-19 patients [26].

3.3. Usefulness of serial LUS in an ECMO-managed patient with severe COVID-19

We believe that serial LUS was very useful in our patient's case. First, the LUSS was associated with the progression and improvement of the patient's lung condition, as observed in CT images (Figs. 1 and 3) and laboratory findings (Table 1). The longer the ECMO management, the more complications patients have [19]. However, it is uncertain how long we should protect the lungs with ECMO. Because the condition of the lungs varies from case to case, laboratory findings like P/F ratios do not directly correlate with the improvement of lung condition during ECMO. LUS can be evaluated individually and specifically for the lungs, and the reemergence of A-lines suggests an improvement in lung condition [3–6,8]. Although serial LUS evaluation is also considered appropriate for patients on ECMO, few studies have examined its appropriateness for COVID-19 patients [27].

Second, LUS can be performed quickly by one clinician without displacing the patient or requiring radiation exposure [22]. Accordingly, LUS is faster, easier, and safer than other imaging modalities, with significant advantages during a pandemic [5,6].

Third, in this case, the LUSS increased sharply from day 1 to day 3 (score: from 9 to 21). We believe that P-SILI occurred on day 3 because the patient's P0.1 value increased and his respiratory patterns appeared distressed (Additional file 1). Given that there was an improvement in oxygenation, but not yet in inflammation, changing the ventilator setting from PCV to PSV probably led to increased respiratory efforts, increased transpulmonary pressure, and P-SILI. It has been reported that P-SILI increases transmural pulmonary vascular pressure, thereby resulting in increased vascular permeability and pulmonary edema [11]. Therefore, we suspect that the appearance of multiple B-lines, especially those in the lateral and posterior regions, might have been due to negative intrathoracic pressure generated by strong spontaneous breathing. Although no studies have demonstrated a relationship between P-SILI and LUS, we thought that the rapid increase of the LUSS suggested the occurrence of P-SILI.

This case study has several limitations. One limitation is that the inter-rater reliability was not evaluated, although three experienced emergency physicians performed LUS. The other limitation is that the pandemic is ongoing, and the existing knowledge about COVID-19 might be modified by future findings.

4. Conclusion

This case report demonstrated that serial LUS was useful for evaluating lung condition in a COVID-19 patient requiring ECMO. The present findings suggest that LUS may be useful for the detection of P-SILI. However, further prospective studies are needed to test this hypothesis.

Declaration of competing interest

The authors have no conflicts of interest directly relevant to the content of this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2021.101383.

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