

# Ultrasound Assessment of Lung Aeration in Subjects Supported by Venovenous Extracorporeal Membrane Oxygenation

Xiao Lu, Charlotte Arbelot, Annia Schreiber, Olivier Langeron, Antoine Monsel, and Qin Lu

**BACKGROUND:** The value of ultrasound in assessing lung aeration of patients with ARDS who require venovenous extracorporeal membrane oxygenation (ECMO) has, to our knowledge, never been studied. The objective of the study was to evaluate by using ultrasound lung aeration at ECMO initiation and withdrawal in subjects with severe ARDS supported by venovenous ECMO. **METHODS:** Fifty subjects were included in this pilot retrospective study. The lung ultrasound aeration score (LUS) and respiratory variables were collected at ECMO initiation (T0) and ECMO withdrawal (T1). The LUS at T0 between the subjects who survived to ICU discharge and those who died in ICU was compared. The relationship between changes in LUS and changes in  $P_{aO_2}/F_{IO_2}$  from T0 to T1 was assessed. **RESULTS:** The ICU mortality was 34%. The LUS at T0 did not differ between survivors and non-survivors (median 22 [interquartile range] {IQR} 19–26 vs median 24 [IQR, 19–28];  $P = .60$ ). From T0 to T1, the LUS decreased significantly in survivors (median 22 [IQR, 19–26] vs median 16 [IQR, 13–19];  $P < .001$ ), it decreased moderately in non-survivors who were weaned off ECMO (median 26 [24–29] vs median 22 [IQR, 17–24],  $P = .031$ ), and remained stable in those who died during ECMO (median 25 [IQR, 19–29] vs median 25 [IQR, 23–31];  $P = .22$ ). Changes in  $P_{aO_2}/F_{IO_2}$  were not related to changes in the LUS between T0 and T1. **CONCLUSIONS:** At the time of ECMO placement, the subjects who survived ARDS had aeration loss close to that observed in the subjects who did not survive. At the time of ECMO withdrawal, there was a significant improvement in lung aeration in the survivors, whereas a severe loss of lung aeration persisted in the non-survivors, although some were weaned off ECMO. Lung ultrasound provided a valuable tool for bedside assessment of lung aeration in subjects supported by ECMO. *Key words:* ARDS; ultrasound; VV ECMO; lung aeration; oxygenation; survivors; non-survivors. [Respir Care 2019;64(12):1478–1487. © 2019 Daedalus Enterprises]

## Introduction

Venovenous extracorporeal membrane oxygenation (VV ECMO) is a treatment option for patients with ARDS re-

fractory to conventional therapies.<sup>1,2</sup> Despite the increasing use of VV ECMO, in-hospital or 60-d patient mortality remains high.<sup>1,3,4</sup> Many factors have been demonstrated as being independently associated with mortality during ECMO: age,<sup>5</sup> duration of mechanical ventilation before ECMO, pulmonary compliance, driving pressure, and ARDS associated with extrapulmonary organ dysfunction.<sup>6–8</sup> In ARDS, it has been reported that the initial degree of lung aeration loss as well as the changes in lung

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aeration after applying a new ventilatory strategy could affect the mortality of patients with ARDS.<sup>9,10</sup> In patients with severe ARDS and who require ECMO support, it is still unknown whether the severity of lung aeration loss at the onset of ECMO could influence the outcome in these patients. In addition, among the criteria commonly used for ECMO weaning, the recovery of lung function attested by pulmonary re-aeration is not necessarily considered.

Lung transthoracic ultrasound is increasingly used in the ICU for bedside assessment of PEEP-induced alveolar recruitment,<sup>11</sup> antibiotic-induced lung re-aeration in ventilator-associated pneumonia,<sup>12</sup> and lung aeration changes during a spontaneous breathing trial.<sup>13</sup> Lung aeration assessed by ultrasound is correlated with lung volume assessed by computed tomography.<sup>11,12</sup> To date, lung aeration changes in patients with ARDS who require VV ECMO have only been reported in a few patients.<sup>14</sup> Thus, the primary objective of the present study was to evaluate lung aeration by ultrasound at the beginning of the ECMO in the subjects who survived to ICU discharge and those who died in ICU. Secondary objectives were changes in lung aeration from ECMO initiation to ECMO withdrawal and the relationship between lung re-aeration and improvement of oxygenation in subjects who received VV ECMO.

## Methods

### Subjects and Study Protocol

This was a pilot retrospective cohort study. Subjects were recruited between April 2012 and March 2018 from 2 multidisciplinary ICUs of a university hospital. Inclusion criteria were patients with severe ARDS<sup>15</sup> supported by VV ECMO assistance. The indication for the establishment of VV ECMO was  $P_{aO_2}/F_{IO_2} < \text{of } 60 \text{ mm Hg for } \geq 3 \text{ h}$  or of  $< 90 \text{ mm Hg for } > 6 \text{ h}$ , and/or refractory respiratory acidosis ( $\text{pH} < 7.25$ ), with inspiratory plateau pressure of  $\geq 32 \text{ cm H}_2\text{O}$  despite optimization of conventional therapy. In our ICU, transthoracic lung ultrasound is routinely performed to monitor changes in lung aeration in patients with ARDS.

Each subject was assessed by transthoracic lung ultrasound from  $-24$  to  $24$  h after the initiation of ECMO (T0), and from  $-24$  to  $24$  h of ECMO withdrawal, or the last lung ultrasound assessment before ECMO removal if the subject died during ECMO support (T1). Exclusion criteria were patients without lung ultrasound assessment between  $-24$  h and  $24$  h after the onset of ECMO or patients in whom assessment by lung ultrasound did not include total lung regions due to the presence of subcutaneous emphysema or pleural drainages.

According to the French law on ethics on retrospective studies, written informed consent of subjects or their relatives was waived, but the information that concerned the study was explained to the subjects and consent to data collection was

## QUICK LOOK

### Current knowledge

The initial degree of lung aeration loss could affect the mortality of patients with ARDS. In patients who receive venovenous extracorporeal membrane oxygenation (ECMO), it is unknown whether the severity of lung aeration loss at onset and withdrawal of ECMO influences the outcome.

### What this paper contributes to our knowledge

At the time of ECMO placement, the subjects who survived ARDS had lung aeration loss close to that observed in the subjects who did not survive. At the time of ECMO withdrawal, a significant improvement in lung aeration was obtained in the survivors, whereas a severe loss of lung aeration persisted in non-survivors, although some were weaned off ECMO. Lung ultrasound provides a valuable tool for bedside assessment of lung aeration in subjects supported by ECMO.

requested from the subjects. The study was entered into the register of data protection of the study institution. The study was performed in the Multidisciplinary Intensive Care Unit, Department of Anesthesiology and Critical Care, La Pitié-Salpêtrière Hospital, Assistance Publique-Hôpitaux de Paris, Sorbonne Université, Paris, France.

### Lung Ultrasound Assessment

Transthoracic lung ultrasound was performed either by an experienced physician with level-3 certification<sup>16</sup> or by a resident or a senior physician who had completed lung ultrasound training.<sup>17</sup> A Siemens Acuson CV70 (Siemens Medical Solutions, Malvern, PA) or a Philips Sparq (Philips Ultrasound, Bothell, WA) ultrasound device equipped with a 2- to 5-MHz convex probe was used for the examination. In each subject, upper and lower lung areas of the right and left lungs were delineated by the parasternal, anterior axillary, and posterior axillary and paravertebral lines. Therefore, 12 lung regions that corresponded to antero-superior, antero-inferior, latero-superior, latero-inferior, postero-superior, and posterior-inferior lung areas were examined.<sup>13</sup> A numeric value was assigned to each area according to the most-severe lung ultrasound finding detected in the corresponding intercostal space as follows (Fig. 1): 0, normal aeration (defined by the presence of lung sliding with horizontal A lines or fewer than 2 isolated vertical B lines); 1, moderate loss of lung aeration (defined as the presence of either multiple well-defined and spaced B1 lines issued from the pleural line or from small juxtapleural consolidations and correspond to interstitial

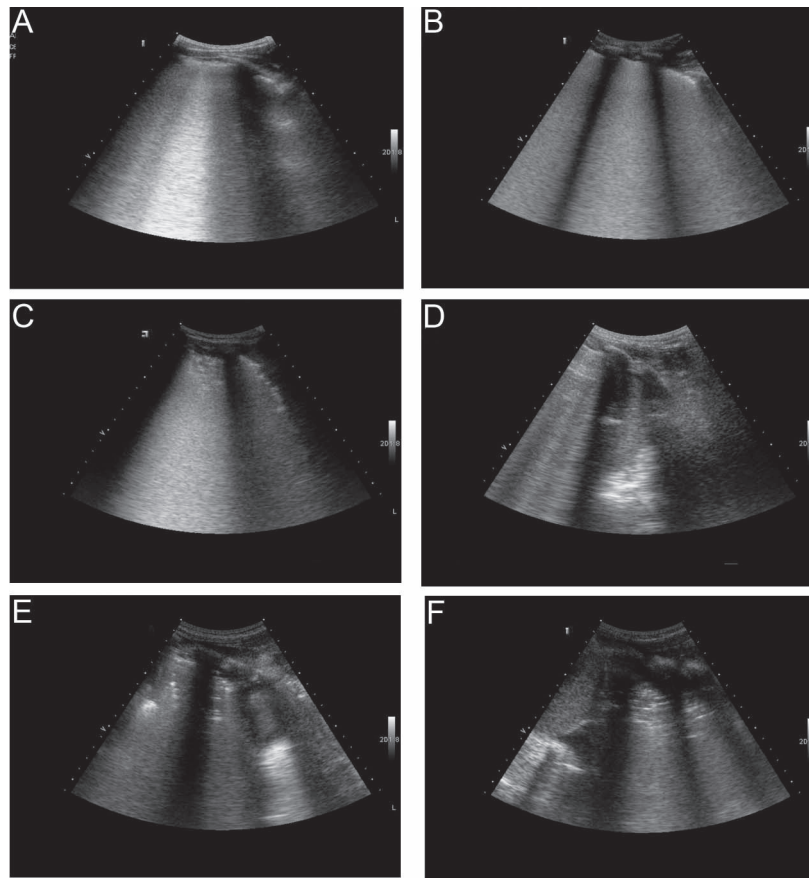


Fig. 1. Ultrasound assessment of lung aeration. A-F: Lung ultrasound images of 6 examined lung areas (antero-superior, antero-inferior, latero-superior, latero-inferior, postero-superior, and postero-inferior parts of the right lung) in a subject of the study. A numeric value was assigned to each area according to the most-severe lung ultrasound finding. A-C: Multiple coalescent vertical B2 lines issued from the pleural line. C-F: The presence of a tissue pattern that contains either hyperechoic punctiform or linear images.

edema, or coalescent B1 lines issued from the pleural line or from small juxtapleural consolidations, present in a limited portion of the intercostal space, which correspond to localized alveolar edema); 2, severe loss of lung aeration (multiple coalescent vertical B2 lines issued either from the pleural line or from juxtapleural consolidations, detected in the whole area of one or several intercostal spaces, which correspond to diffuse alveolar edema); and 3, lung consolidation (defined as the presence of a tissue pattern that contains either hyperechoic punctiform or linear images representative of static air bronchograms, or the same images with inspiratory centrifugal movement, representative of dynamic air bronchograms,<sup>18</sup> which correspond to complete loss of aeration).<sup>19</sup> The lung ultrasound aeration score (LUS) was calculated as the sum of the numeric values assigned to each lung zone, ranging from 0 to 36.<sup>13,20</sup>

### VV ECMO Technique

The cannulae were percutaneously inserted: a large venous drainage cannula was inserted into the femoral vein up to the

right atrium, and the return cannula carried oxygenated blood into the jugular vein to the superior vena cava. If this was not possible, then the opposite femoral vein was cannulated to the lower part of the inferior vena cava. Cannula insertion was always accompanied by transesophageal or transthoracic echocardiography to ensure correct placement. The VV ECMO technique consisted of Raumedic cannulas (Raumedic, Helmbrechts, Germany), a PLS-i membrane oxygenator with BIOLINE coating (Maquet, Rastatt, Germany), and a Rota-flow RF32 centrifugal pump and console (Maquet). In some cases, a CARDIOHELP device (Maquet) was used. Anticoagulation was achieved with unfractionated heparin with anti-Xa activity between 0.2 and 0.3 IU per mL unless contraindicated.<sup>1,21</sup>

An ECMO weaning test was performed by decreasing the membrane ventilation to 0 L/min for at least 1 h when clinical improvements were observed. The ECMO device could be withdrawn if  $P_{aO_2}$  was  $> 70$  mm Hg, with  $F_{IO_2} < 60\%$ , inspiratory plateau pressure  $< 30$  cm  $H_2O$  with tidal volume  $< 6$  mL/kg, and if echocardiography did not reveal evidence of acute cor pulmonale.<sup>1</sup>

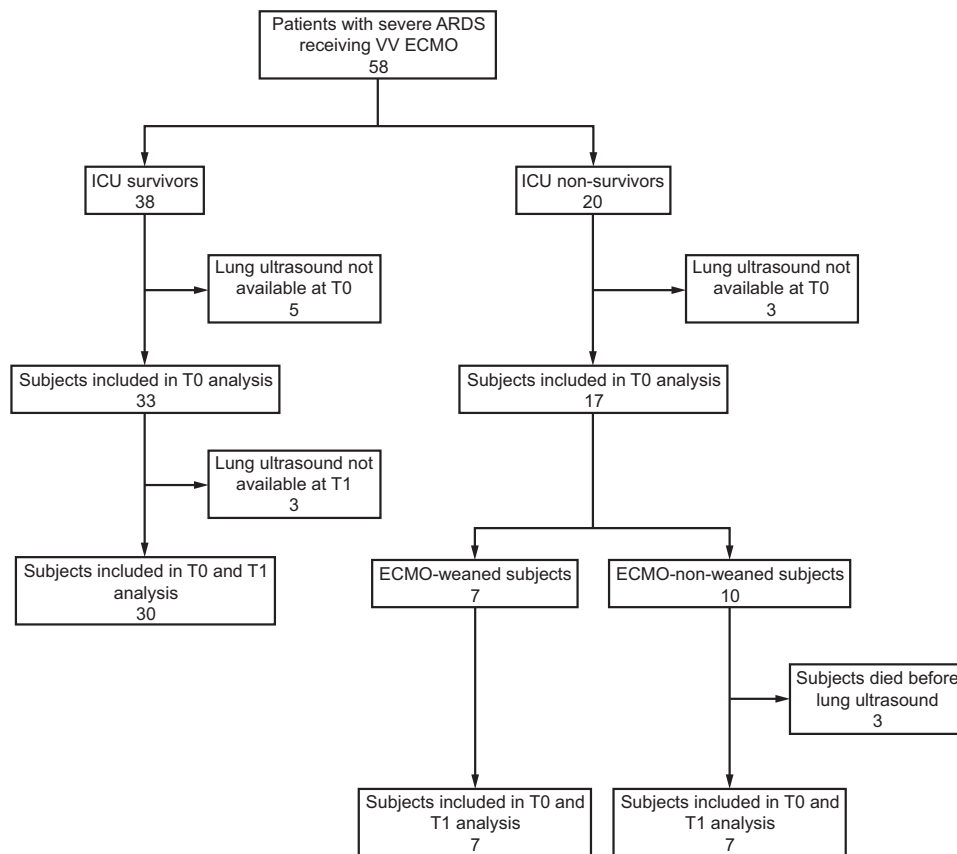


Fig. 2. Flow chart. VV ECMO = venovenous extracorporeal membrane oxygenation; T0 = ECMO initiation; T1 = ECMO withdrawal.

## Data Collection

The following data were collected for each subject: age, sex, body mass index, Sepsis-Related Organ Failure Assessment, Simplified Acute Physiology Score II at admission, and clinical and respiratory characteristics at the time of ECMO initiation. The duration of mechanical ventilation before ECMO placement, the duration of ECMO assistance, and treatment with neuromuscular blockade were also recorded. The total LUS, the LUS of each region of interest, and respiratory parameters were recorded at the same time points, at T0 and T1.

## Statistical Analysis

The primary end point was the assessment of the LUS at initiation of ECMO for survivors and non-survivors. The secondary end points were (1) changes in the LUS from T0 to T1, (2) the relationship between the changes in lung aeration and the changes in arterial oxygenation between T0 and T1, and (3) regional changes of lung aeration between T0 and T1 in the survivors. Quantitative variables between survivors and non-survivors were compared by using the Mann-Whitney U test and were expressed as median and 25–75% interquartile

range (IQR), unless otherwise specified. Categorical variables were compared by using the chi-square test or the Fisher exact test and were expressed as number and percentage. The changes of the LUS from T0 to T1 in survivors or non-survivors were compared by using the Wilcoxon signed rank tests. The relationship between changes in the LUS and  $P_{aO_2}/F_{IO_2}$  between T0 and T1 was analyzed by simple linear regression.

We did an exploratory post hoc analysis in the subjects who were weaned off ECMO to compare the LUS and respiratory variables at VV ECMO withdrawal between survivors and non-survivors by using the Mann-Whitney U test. All analyses were made by using SigmaStat 3.5 (Systat Software, Point Richmond, CA) or SPSS 13.0 for Windows (SPSS, Chicago, Illinois). The statistical significance level was fixed at 0.05.

## Results

### Clinical Characteristics

During the study period, a total of 58 patients with severe ARDS received VV ECMO support; 8 were excluded for lack of lung ultrasound evaluation at T0. The flow diagram is shown in Figure 2. Clinical character-

ULTRASOUND ASSESSMENT OF LUNG AERATION DURING ECMO

Table 1. Clinical Characteristics of the Subjects Who Received VV ECMO

| Characteristic  | Overall (N = 50) | ICU Survivors (n = 33) | ICU Non-Survivors (n = 17) | P    |
|---|------------------|------------------------|----------------------------|------|
| Age, median (IQR) y   | 44 (25–63)       | 37 (25–51)             | 63 (41–69)                 | .006 |
| Men, n (%)  | 39 (78)          | 26 (79)                | 13 (76)                    | >.99 |
| SOFA admission score, median (IQR)                          | 12 (8–14)        | 12 (9–13)              | 13 (8–15)                  | .48  |
| SAPS II admission, median (IQR)                             | 44 (37–55)       | 42 (36–56)             | 47 (42–56)                 | .27  |
| BMI, median (IQR) kg/m <sup>2</sup>                         | 24 (22–28)       | 24 (23–28)             | 25 (23–27)                 | .63  |
| Cause of admission, n (%)                                   |                  |                        |                            | .16  |
| Surgical  | 14 (28)          | 7 (21.2)               | 7 (41)                     |      |
| Medical   | 19 (38)          | 12 (36.4)              | 7 (41)                     |      |
| Multiple trauma   | 17 (34)          | 14 (42.4)              | 3 (18)                     |      |
| Cause of ARDS, n (%)  |                  |                        |                            | .29  |
| Pulmonary   | 41 (82)          | 28 (85)                | 13 (76)                    |      |
| CAP   | 9                | 4                      | 5                          |      |
| VAP   | 12               | 8                      | 4                          |      |
| Aspiration  | 4                | 4                      | 0                          |      |
| Lung contusion  | 16               | 12                     | 4                          |      |
| Extrapulmonary  | 9 (18)           | 5 (15)                 | 4 (24)                     |      |
| Shock, n (%)  | 33 (66)          | 21 (64)                | 12 (71)                    | .43  |
| Mechanical ventilation duration before ECMO, median (IQR) d | 2.9 (1.1–6.0)    | 2.0 (1.0–8.6)          | 3.8 (1.7–4.9)              | .64  |
| Pump flow (first 24 h), median (IQR) L/min                  | 4.7 (4.1–5.5)    | 4.8 (4.1–5.3)          | 4.7 (4.2–5.7)              | .73  |
| Membrane ventilation (first 24 h), median (IQR) L/min       | 4 (4–6)          | 4.0 (4.0–6.0)          | 5.0 (3.8–5.0)              | .77  |

VV ECMO = venovenous extracorporeal membrane oxygenation  
 IQR = interquartile range  
 SOFA = Sequential Organ Failure Assessment  
 SAPS II = Simplified Acute Physiology II Score  
 BMI = body mass index  
 CAP = community-acquired pneumonia  
 VAP = ventilator-associated pneumonia

Table 2. Respiratory Parameters at VV ECMO Initiation

| Parameter  | Overall (N = 50) | ICU Survivors (n = 33) | ICU Non-Survivors (n = 17) | P   |
|--|------------------|------------------------|----------------------------|-----|
| P <sub>aO<sub>2</sub></sub> /F <sub>IO<sub>2</sub></sub> , mm Hg | 71 (55–83)       | 70 (56–80)             | 61 (53–84)                 | .51 |
| P <sub>aCO<sub>2</sub></sub> , mm Hg                             | 47 (40–59)       | 48 (40–59)             | 44 (39–58)                 | .64 |
| pH   | 7.29 (7.17–7.37) | 7.32 (7.06–7.38)       | 7.26 (7.21–7.33)           | .86 |
| Frequency, breaths/min   | 29 (25–31)       | 28 (24–31)             | 30 (26–32)                 | .61 |
| V <sub>T</sub> , mL  | 400 (338–452)    | 430 (344–470)          | 391 (335–433)              | .41 |
| V <sub>T</sub> /IBW, mL/kg                                       | 5.8 (5.2–6.5)    | 6.1 (5.4–6.6)          | 5.4 (4.8–6.1)              | .15 |
| PEEP, cm H <sub>2</sub> O  | 10 (8–12)        | 12 (8–13)              | 10 (8–11)                  | .18 |
| P <sub>I<sub>max</sub></sub> , cm H <sub>2</sub> O               | 37 (33–44)       | 39 (32–44)             | 37 (35–42)                 | .98 |
| Inspiratory P <sub>plat</sub> , cm H <sub>2</sub> O*             | 33 (30–35)       | 33 (31–37)             | 32 (30–35)                 | .46 |

Data are presented as median (25–75% interquartile range).  
 \* For P<sub>plat</sub>, a comparison was made in 22 subjects with available data: 16 survivors and 6 non-survivors.  
 VV ECMO = venovenous extracorporeal membrane oxygenation  
 Frequency = breathing frequency  
 V<sub>T</sub> = tidal volume  
 V<sub>T</sub>/IBW = tidal volume based on ideal body weight  
 P<sub>I<sub>max</sub></sub> = maximum inspiratory pressure  
 P<sub>plat</sub> = plateau pressure

istics of the subjects are summarized in Table 1. Thirty-three subjects survived to ICU discharge, with an overall ICU survival rate of 66%. The non-survivors were older than the survivors. The severity scores, the

causes of admission and ARDS, the presence of shock that required norepinephrine at the beginning of ECMO, and the duration of mechanical ventilation before ECMO did not significantly differ between survivors



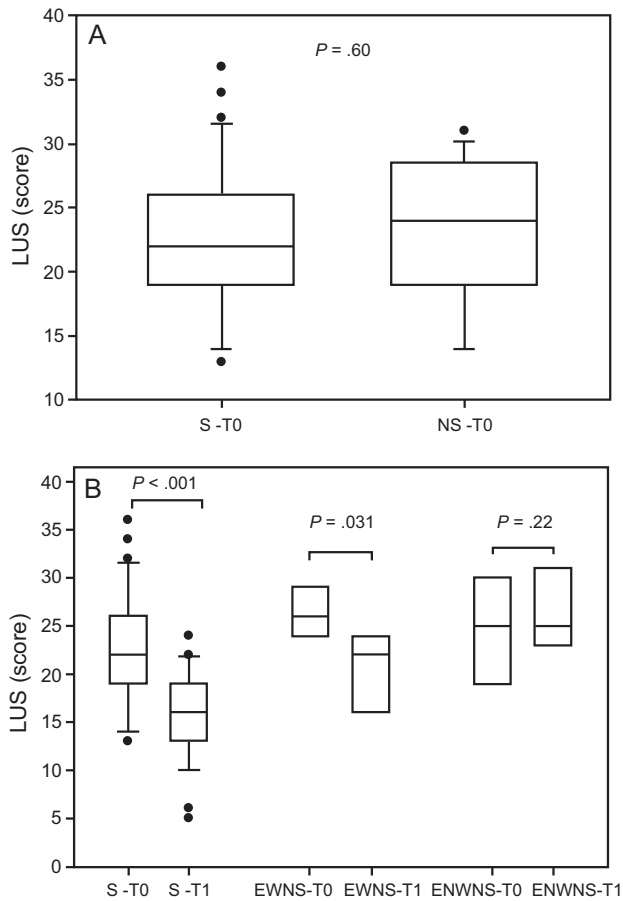


Fig. 3. A: The LUS at VV ECMO initiation (T0) in survivors and non-survivors. B: LUS at ECMO initiation and withdrawal in survivors and non-survivors who were weaned or not from ECMO. Data are expressed as median and 25–75% interquartile range (IQR). LUS = lung ultrasound aeration score; VV ECMO = venovenous extracorporeal membrane oxygenation; S-T0 = survivors-ECMO initiation; NS-T0 = non-survivors-ECMO initiation; S-T1 = survivors-ECMO withdrawal; EWNS = ECMO-weaned non-survivors; ENWNS = ECMO non-weaned non-survivors.

and non-survivors. At T0, all the subjects were in a half-sitting position, between 30° and 45°, and were paralyzed with atracurium. The treatment duration with neuromuscular blockade was longer in the non-survivors than in the survivors (median 7.0 [IQR, 3.0–13.8] d vs median 2.4 [IQR, 1.1–10.0] d;  $P = .032$ ). At T0, the respiratory parameters and ventilator settings were not different between the survivors and the non-survivors (Table 2).

**Lung Aeration At ECMO Initiation and Its Changes From T0 to T1**

The LUS at ECMO initiation did not significantly differ between the survivors and non-survivors (median 22 [IQR, 19–26] vs median 24 [IQR, 19–28];  $P = .60$ ) (Fig. 3A). A

significant decrease in the LUS from T0 to T1 was observed in the survivors (median 22 [IQR, 19–26] vs median 16 [13–19];  $P < .001$ ), which indicated an improvement in lung aeration at the time of ECMO withdrawal. In the non-survivors, the LUS decreased moderately in the subjects who were weaned off ECMO (median 26 [IQR, 24–29] vs median 22 [17–24];  $P = .031$ ) and remained stable in those who died during the ECMO time period (median 25 [IQR, 19–29] vs median 25 [IQR, 23–31];  $P = .22$ ) (Fig. 3B). The changes in  $P_{aO_2}/F_{IO_2}$  between T0 and T1 were not linearly related to the changes in the LUS (Fig. 4). The regional changes in the LUS between T0 and T1 in the survivors are shown in Figure 5. Regional lung re-aeration, as evidenced by a decrease in regional LUS occurred primarily in the anterior and upper lung areas.

**Post Hoc Analysis of Subjects Who Were Weaned Off ECMO**

ECMO assistance was successfully withdrawn from all survivors and 7 non-survivors. The median ECMO duration was 9 (IQR, 6–14) d. Of the 7 non-survivors, 6 were not weaned off mechanical ventilation. At ECMO withdrawal, the LUS,  $P_{aCO_2}$ , and maximum inspiratory pressure were significantly higher, and  $P_{aO_2}/F_{IO_2}$  was significantly lower in the non-survivors than in the survivors (Table 3).

**Discussion**

The results of this pilot study showed that the subjects who survived to the ICU discharge and those who died in the ICU did not differ significantly for lung aeration loss at the time of ECMO initiation. In the survivors, the success of ECMO withdrawal was associated with a significant improvement in lung aeration, whereas severe loss of lung aeration persisted at ECMO withdrawal in the subjects who did not survive, although some were weaned off ECMO support. Lung re-aeration occurred primarily in anterior and upper lung areas. The changes in arterial oxygenation were not related to the changes in lung aeration.

ARDS is characterized by low respiratory compliance and reduced aerated lung volume, which results in severe hypoxemia. Patient outcome could be influenced by the severity of lung aeration loss and pulmonary compliance.<sup>10,22</sup> It is known that the degree of hypoxemia is not always correlated with the severity of lung aeration loss due to ventilation–perfusion mismatch.<sup>23</sup> To date, however, decision making regarding initiating and weaning off ECMO remains challenging and is largely based on the blood gas findings.<sup>24</sup> To our knowledge, our study was the first to explore bedside assessment of lung aeration from

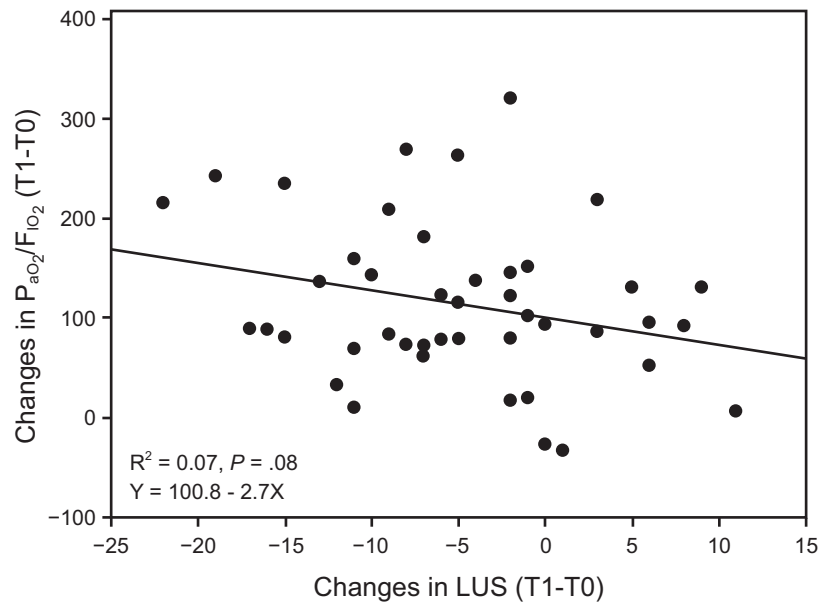


Fig. 4. Relationship between changes in the lung ultrasound aeration score and changes in  $P_{aO_2}/F_{iO_2}$  between VV ECMO initiation (T0) and withdrawal (T1). VV ECMO = venovenous extracorporeal membrane oxygenation.

the initiation to the withdrawal of ECMO and its relationship to patient outcomes by lung ultrasound.

At the ECMO onset, the loss of lung aeration and the impairment of gas exchange did not differ between the survivors and the non-survivors. In one subject who died during ECMO support, the LUS at ECMO initiation was only 14 due to the presence of diffuse interstitial edema in each lung area. These results indicated that the initial degree of lung aeration loss might not be predictive of patient outcome. At ECMO withdrawal, although it was not surprising to find a difference in severity of lung aeration between the subjects who survived ARDS and those who died during ECMO, to our knowledge, our study was the first to show these findings and to demonstrate that the LUS is a useful and valuable tool for bedside follow up on lung function in patients supported by ECMO. Of note, in the subjects who died during ECMO support, T1 corresponded to the last lung ultrasound before death; thus, this lack of improvement may suggest a poor prognosis. Interestingly, changes in the aeration score have been used to assess the effectiveness of prone positioning, and a relationship between prone-positioning response in terms of changes in lung aeration and patient prognosis was reported.<sup>25</sup> In addition, we found that the non-survivors were older than the survivors. Some prediction models showed that older age seemed to be one of the determinants of a poor outcome.<sup>5,6</sup>

Among the 7 subjects who were initially weaned off ECMO support but who did not survive ARDS, with the exception of one subject who died suddenly from pericardial tamponade, our exploratory post hoc analysis showed

a persistence of severe loss of lung aeration, with a median LUS as high as 22 during ECMO withdrawal, associated with impaired lung mechanics compared with the survivors. In addition, these subjects were not weaned off mechanical ventilation until death. Deciding when to wean off ECMO support remains highly challenging. Conventionally, ECMO is stopped according to blood gas results,<sup>1</sup> and the recovery of lung aeration is not necessarily taken into account. Unfortunately, our results did not show any relationship between lung re-aeration and oxygenation improvement. A lack of the correlation between lung aeration changes and oxygenation responses was also found in patients with severe ARDS who had undergone prone positioning.<sup>25,26</sup> Further prospective studies are needed to assess the clinical relevance of integrating lung aeration assessment into the ECMO weaning process and to determine whether this assessment can play a role in predicting patient outcome beyond a successful weaning off ECMO.<sup>13,27</sup>

Several limitations of the study should be discussed. First, due to the nature of the retrospective design, lung ultrasound was not systematically performed in all the subjects, which led to the exclusion of 8 subjects from the cohort for primary end point analysis. For the same reason, the LUS was not assessed at a specific time, and a range of 24 h around ECMO was allowed. It should be pointed out, however, in the subjects in whom LUS was assessed both before and 24 h after ECMO initiation, we did not find any significant difference in the LUS between these 2 time points. Second, ultrasound assessment is operator dependent. In our study, ~40% of the lung ultrasound

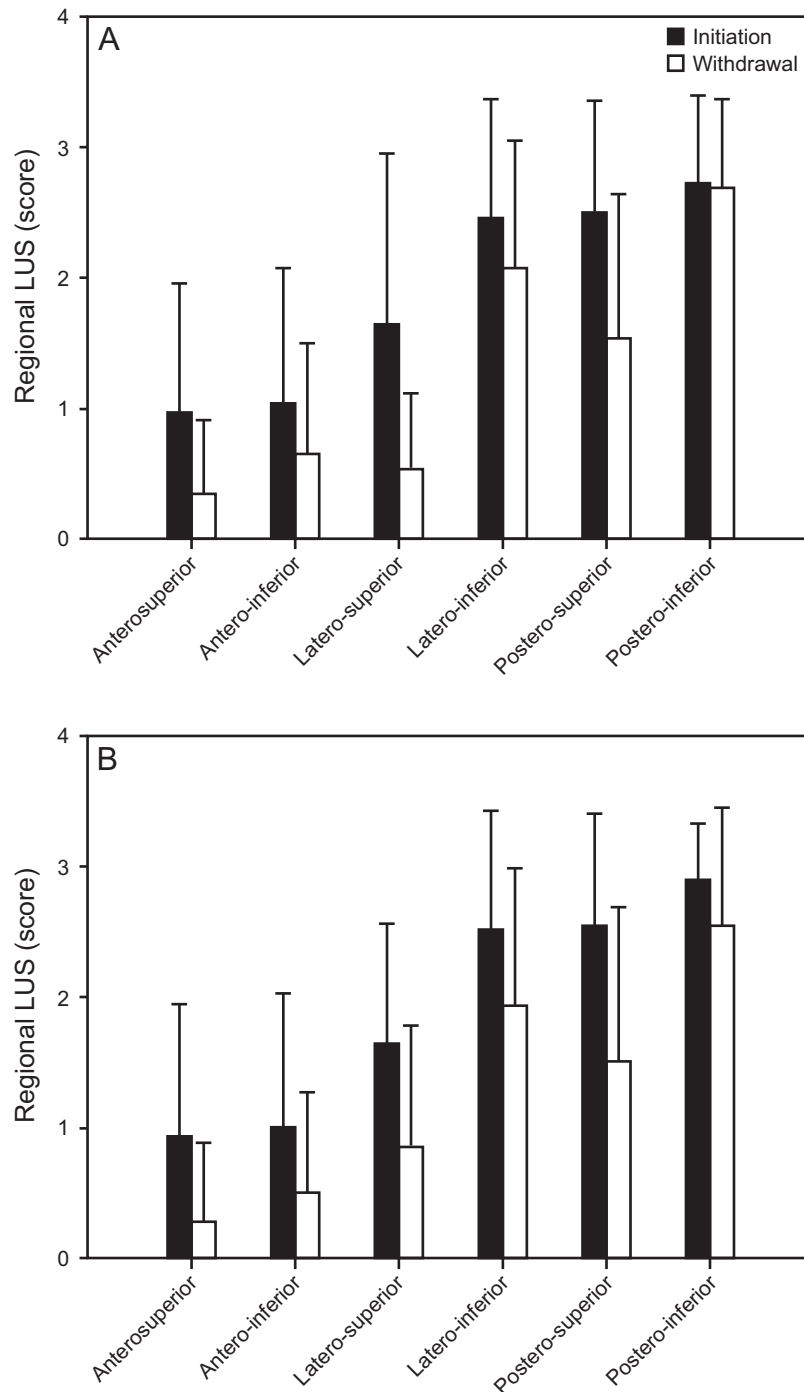


Fig. 5. Regional distribution of the lung ultrasound aeration (LUS) score assessed on 12 lung regions at the initiation and withdrawal of venovenous extracorporeal membrane oxygenation in survivors. A: Right lung. B: left lung. Data are shown as mean  $\pm$  SD.

examinations were performed by the residents who had completed lung ultrasound training, but inter-observer variability between experienced senior physicians and residents could not be assessed. It should be noted, however, a good inter-observer agreement for ultrasound assessment of lung aeration has been reported in previous studies.<sup>12,17</sup>

Furthermore, one of the limitations of lung ultrasound is a poor acoustic window in patients who are obese.<sup>28</sup> The incidence of technically difficult echocardiography has been reported to be 45% in subjects with an increased body mass index.<sup>29</sup> This incidence is still unknown for lung ultrasound assessment. In our study, 2 subjects had a



Table 3. Post Hoc Analysis of Subjects Weaned Off ECMO at VV ECMO Withdrawal

| Parameter  | ICU Survivors<br>(n = 33) | ICU Non-Survivors<br>(n = 7) | P    |
|--|---------------------------|------------------------------|------|
| LUS  | 16 (13–19)                | 22 (17–24)                   | .045 |
| P <sub>aO<sub>2</sub></sub> /F <sub>IO<sub>2</sub></sub> , mm Hg | 198 (156–262)             | 132 (113–182)                | .02  |
| P <sub>aCO<sub>2</sub></sub> , mm Hg                             | 38 (36–42)                | 44 (43–46)                   | .03  |
| pH   | 7.43 (7.39–7.47)          | 7.36 (7.31–7.42)             | .03  |
| Frequency, breaths/min   | 26 (22–29)                | 26 (23–29)                   | .92  |
| V <sub>T</sub> , mL  | 393 (364–442)             | 374 (352–408)                | .49  |
| V <sub>T</sub> /IBW, mL/kg                                       | 5.9 (5.1–6.2)             | 6.0 (5.5–6.3)                | .39  |
| PEEP, cm H <sub>2</sub> O  | 8 (7–10)                  | 8 (6–10)                     | .83  |
| P <sub>I</sub> max, cm H <sub>2</sub> O                          | 29 (25–33)                | 35 (32–40)                   | .02  |

Data are presented as median (25–75% interquartile range).  
 VV ECMO = venovenous extracorporeal membrane oxygenation  
 LUS = lung ultrasound aeration score  
 V<sub>T</sub> = tidal volume  
 V<sub>T</sub>/IBW = tidal volume based on ideal body weight  
 P<sub>I</sub>max = maximum inspiratory pressure

body mass index > 40 kg/m<sup>2</sup> in whom lung ultrasound assessments were successfully achieved. Also, a number of factors could affect lung aeration, such as end-expiratory positive pressure, recruitment maneuvers, use of neuromuscular blockade, upper-abdominal surgery, fluid balance, prone positioning, and patient positioning during ECMO. Unfortunately, our study was unable to discern how these factors influenced the LUS and correlated with clinical outcomes. The small sample size and lower power precluded any multivariate analyses for independent risk factors. Thus, this study can be only considered as a pilot exploratory one, and the results obtained from the present study deserve further prospective investigations.

**Conclusions**

Transthoracic lung ultrasound provides a valuable tool for bedside assessment of lung aeration in patients with severe ARDS who are receiving VV ECMO support. Although the LUS at ECMO initiation may not be discriminating in terms of patient’s severity, the assessment of its changes from ECMO onset to withdrawal may help physicians to better estimate the evolution of lung function. Further large-scale prospective studies are needed to evaluate the clinical relevance of assessing lung aeration by ultrasound in the daily management for patients with severe ARDS supported by VV ECMO.

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