Lung-Dependent Areas Collapse, Monitored by Electrical Impedance Tomography, May Predict the Oxygenation Response to Prone Ventilation in COVID-19 Acute Respiratory Distress Syndrome

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OBJECTIVES: ICUs have had to deal with a large number of patients with acute respiratory distress syndrome COVID-19, a significant number of whom received prone ventilation, which is a substantial consumer of care time. The selection of patients that we have to ventilate in prone position seems interesting. We evaluate the correlation between the percentage of collapsed dependent lung areas in the supine position, monitoring by electrical impedance tomography and the oxygenation response (change in Pao_2/Fio_2 ratio) to prone position.

DESIGN: An observational prospective study.

SETTING: From October 21, 2020, to 30 March 30, 2021. At the Sainte Anne military teaching Hospital and the Timone University Hospital.

PATIENTS: Fifty consecutive patients admitted in our ICUs, with COVID-19 acute respiratory distress syndrome and required mechanical, were included. Twenty-four (48%) received prone ventilation. Fifty-eight prone sessions were investigated.

INTERVENTIONS: An electrical impedance tomography recording was made in supine position, daily and repeated just before and just after the prone session. The daily dependent area collapse was calculated in relation to the previous electrical impedance tomography recording. Prone ventilation response was defined as a Pao_2/Fio_2 ratio improvement greater than 20%.

MEASUREMENT AND MAIN RESULTS: The main outcome was the correlation between dependent area collapse and the oxygenation response to prone ventilation. Dependent area collapse was correlated with oxygenation response to prone ventilation ($R^2 = 0.49$) and had a satisfactory prediction accuracy of prone response with an area under the curve of 0.94 (95% CI, 0.87–1.00; $p < 0.001$). Best Youden index was obtained for a dependent area collapse greater than 13.5 %. Sensitivity of 92% (95% CI, 78–97), a specificity of 91% (95% CI, 72–97), a positive predictive value of 94% (95% CI, 88–100), a negative predictive value of 87% (95% CI, 78–96), and a diagnostic accuracy of 91% (95% CI, 84–98).

CONCLUSIONS: Dependent lung areas collapse (> 13.5%), monitored by electrical impedance tomography, has an excellent positive predictive value (94%) of improved oxygenation during prone ventilation.

KEY WORDS: acute respiratory distress syndrome; COVID-19; electrical impedance tomography; mechanical ventilation; oxygenation; prone position

Since March 2020, France has been massively affected by the COVID-19 outbreak. The number of COVID-19 patients hospitalized in French ICUs has experienced several peaks during this period. A significant proportion of these patients presented acute respiratory distress syndrome (ARDS),

required invasive mechanical ventilation, and received prone ventilation (PV). The COVID-ICU group, in a large European cohort, found that 63% of these patients were intubated, and 70% recoursed to PV (1).

This context of ICUs saturated by many patients requiring PV represents a significant workload for the nursing staff. Thus, to put a patient presenting an ARDS COVID-19 in a prone position requires five nursing staff for approximately 30 minutes. This time is multiplied by the number of patients requiring this positioning therapy. In this context of saturation, it seems interesting to be able to select the patients who will benefit the most from PV. First, in nonresponders in terms of oxygenation to PV, it could allow to consider other methods such as extracorporeal membrane oxygenation (ECMO). One recent prospective, multicenter cohort study reported that a longer delay from intubation to initiation of ECMO was an independent risk factor for 6-month mortality (2). Second, because improved oxygenation during PV in moderate to severe ARDS may be associated with survival, as was recently reported by Lee et al (3).

Third, the recent literature has opened the debate that COVID 19-related ARDS is an atypical ARDS. Gattinoni et al (4) described two phenotypes: type L (low values of elastance, pulmonary ventilation/perfusion ratio, lung weight, and recruitability) and type H (high values of elastance, right-to-left shunt, lung weight, and recruitability), with the latter being more consistent with what they describe as typical severe ARDS. These phenotypes could have a different response to PV.

Electrical impedance tomography (EIT) is a noninvasive, radiation-free, real-time imaging modality, which has proved to correlate well with CT, according to the assessment of changes in gas volume and tidal volume (Vt) (5–7). EIT has largely been studied in ARDS: Scaramuzzo et al (8) demonstrated that variables derived from EIT were correlated with transpulmonary driving pressure, pleural pressure, and lung elastance. EIT has also been widely studied to evaluate the regional distribution of pulmonary volumes, notably in the open lung approach (9), but also to assess alveolar recruitment and hyperinflation (10, 11).

To date, no study, to our knowledge, has focused on the selection of patients who may be most susceptible to respond to PV in terms of oxygenation.

The main mechanisms of PV in oxygenation improvement of ARDS patients are affecting recruitment in dorsal lung regions, increasing end-expiratory lung volume, increasing chest wall elastance, decreasing ventilation/perfusion mismatch, and improving Vt (12). Because one mechanism for improved oxygenation is related to the amount of dorsal tissue recruited during the PV session if dorsal lung recruitment exceeds derecruitment of ventral sectors and because perfusion distribution is essentially unchanged, oxygenation should improve (13). We hypothesized that the collapse of the dependent lung area in supine position could be correlated to the oxygenation response during PV. The objective of our study was to evaluate the correlation of the daily percentage of lung dependent areas (DAs) collapse in the supine position, monitoring by EIT, and the oxygenation response (change in Pao_2/Fio_2 ratio) during PV.

MATERIALS AND METHODS

From October 21, 2020, to March 30, 2021, we conduct a bicentric prospective study at the Sainte Anne military teaching Hospital in Toulon and at the Timone University Hospital, Marseille, France.

Ethics Statement

According to the French law (14), Ethical approval for the study (N°ID RCB: 2020-A02823-36) was provided by the Protection to Persons Committee of Robert Ballanger hospital, GHT Grand Paris Nord-Est, Aulney-sous-Bois, France (Chairperson Prof Philippe Casassus) *Ile de France*, on October 20, 2020, and by the ethic committee of the Sainte Anne Military teaching Hospital, Toulon, France (N° IRB: 0011873-2020-21; Chairperson Prof Yves Auroy).

This study is registered on ClinicalTrials.gov, registration number NCT04603755.

Study Population

All patients admitted in our ICUs with COVID-19 pneumonia, fulfilling the Berlin criteria of ARDS (15) and needing invasive mechanical ventilation were prospectively investigated. The COVID-19 pneumonia diagnosis was made by reverse transcriptase polymerase chain reaction on nasopharyngeal or pulmonary samples. We included patients with COVID-19 ARDS who required mechanical ventilation and had been intubated for less than 7 days to reduce the risk

of bias related to the occurrence of other causes of hypoxemia and, in particular, the evolution toward pulmonary fibro-proliferation or the ICU complications such as bronchopulmonary superinfection. Exclusion criteria were as follows: refusal of the patient or his family to participate in the study, age less than 18 years, pregnant women, contraindications to EIT (chest malformation, active implantable device, unstable spinal injuries or fractures, skin lesion opposite the EIT monitoring area), presence of another cause of hypoxemia (pulmonary embolism, added bacterial superinfection, pleural effusion, cardiogenic cause), to avoid the bias related to the cause of hypoxemia because it is difficult, to define the contribution of each pathology to hypoxemia, and to analyze a homogeneous population. But also, because the presence of pulmonary embolism or significant pleural effusion may interfere with the interpretation of the data obtained from the EIT.

Study Protocol and Measurements

For the duration of the study, ventilator settings were set to volume-controlled mode with constant flow. All other ventilator variable settings were left to the physician's discretion but had to respect the recommendation for protective ventilation: fixed tidal volume (Vt) of 4–8 mL/kg of predicted body weight. Positive end-expiratory pressure (PEEP) was set after a recruitment maneuver and a decremental PEEP titration, plateau pressure less than 30 cm H_2O, and driving pressure less than 15 cm H_2O.

PV sessions were performed at the physician's discretion blind of EIT data. But PV was to be considered in the case of Pao_2/Fio_2 ratio less than 150 with a Fio_2 greater than or equal to 60% and PEEP greater than 5, use of a neuromuscular blocking agent and after optimization of ventilatory variables including recruitment maneuver, and titration of PEEP level (**PV protocol**, Supplemental Digital Content, http://links.lww.com/CCM/H73; **management protocol for ARDS Covid**, Supplemental Digital Content, http://links.lww.com/CCM/H74).

A 16-electrode silicon belt (Pulmovista500; Dräger, Lübeck, Germany) was placed around the patient's thoracic cage between the fifth and sixth intercostal spaces (16). EIT images were recorded at 20 Hz for 5 minutes and stored. Respiratory data from the ventilator were transferred to EIT via MEDIBUS connection. Vt, RR, inspiratory/expiratory ratio, and PEEP remained unchanged throughout the entire EIT recorded period. The

data were filtered using a Butterworth fourth-order low-pass filter with a cutoff frequency of 50/min to eliminate impedance changes synchronous with the heart rate.

EIT recordings were made once a day, in 45° semi-recumbent position and at least 1 hour apart from any procedure that could lead to lung derecruitment (nursing, endotracheal suctioning, modification of ventilator variables, patient transport) and from any recruitment maneuver. EIT recordings were continued as long as the patient was under controlled ventilation without active participation and for a maximum of 7 days. EIT recordings were stopped as soon as patients were on pressure support ventilation or in case of active respiratory efforts regardless of the ventilatory mode. For patients receiving PV, EIT recording was performed just before the prone position and immediately after the end of the prone session, in the supine position. For logistical reasons and because of the availability of the EIT monitor, we could not perform the EIT recordings during the PV session.

Arterial blood gas (ABG) analyses were performed every 4 hours. For patients who needed PV, ABG was performed 1 hour before, at 1, 4, 8, 12, and 16 hours after prone positioning (PP), and 1 hour after the patient was returned to the supine position.

Lung CT scan was performed at the ICU admission and repeated at the intubation day and then at the physician's discretions.

EIT Data Analysis

EIT data analysis was achieved offline with dedicated software (EITdiag; Dräger Medical). Global tidal impedance variation and end expiration lung impedance (EELI) in dependent and non-DAs were recorded for each EIT recorded. Percentage of lung collapse in dependant areas was calculated for each day (percentage of lung collapse = $\Delta EELI$ = [$EELI_{day}$ − $EELI_{day-1}$]/[$EELI_{day-1}$ × 100]) (**Fig. S1**, http://links.lww.com/CCM/H75; **legend**, http://links.lww.com/CCM/H80). A negative $\Delta EELI$ corresponds to lung collapse; conversely, a positive $\Delta EELI$ corresponds to lung recruitment.

Endpoints

The primary objective of our study was to evaluate the correlation of the daily percentage of lung DAs collapse in the supine position, monitoring by EIT, and the oxygenation response during PV. In agreement

with the literature (17), an increase in the Pao_2/Fio_2 ratio of 20% compared with the supine position before PV was chosen to define a responsive PV session in terms of oxygenation

Our secondary objectives were as follows:

- To determine a threshold for the pulmonary collapse in DAs to predict response to PV (because thresholds are most often used in clinical practice) and to assess its diagnostic performance.
- To determine the independent factors associated with the response to PV in terms of oxygenation.

Statistical Analysis

Statistical analysis was performed with SPSS 25 software (IBM Corp, Baden-Württemberg, Germany). All the results will be expressed as a median and interquartile range (25–75th percentile). Nonparametric variables were compared using a Mann-Whitney *U* test. Nominal variables are reported as numbers and proportions (%). Comparisons of proportions were made with Fisher exact test. We generated receiver operating characteristic (ROC) curves and estimated the area under the curve (AUC) to determine the predictive value of the percentage of lung collapse in DAs to predict PV response. AUCs were presented with 95% CI. The highest Youden index value determined the optimal diagnostic cutoff. We searched for predictors of PV response in term of oxygenation using a multidimensional analysis by linear regression. All variables were tested by univariate analysis. Only the Pao_2/Fio_2 ratio in supine position before PP and the variables with *p* value of less than 0.1 were included in the model. All comparisons were two tailed. *p* value of less than 0.05 was required to exclude the null hypothesis.

RESULTS

During the study period, 143 patients with COVID-19 pneumonia were admitted to our ICUs, 91 (63.6%) met the Berlin criteria for ARDS and required invasive mechanical ventilation; 50 patients were included. Forty-one were excluded: 37 due to the presence of another cause of hypoxemia (12 pulmonary embolisms, 3 pleural effusions, 10 pneumothoraxes, 12 bacterial superinfection), two due to skin lesions, one due to active implantable device, and one due to refusal to participate (**Fig. S2**, http://links.lww.com/CCM/H76; legend, http://links.lww.com/CCM/H80).

We performed 329 EIT recordings with a median of 6 (3–8) EIT recordings per patient.

Patient's Baseline Characteristics

Of the included 50 patients, 39 were (78%) with moderate ARDS and 11 (22%) with severe ARDS. All patients received an initial noninvasive strategy of high-flow oxygen and noninvasive ventilation between admission to the ICU and intubation. The median duration of this noninvasive strategy was 2 days (1–4 d). The median Pao_2/Fio_2 was 132 (118–153), and the median respiratory system compliance was 40 mL/cm H_2O (30–43.8 mL/cm H_2O) with a median driving pressure of 11 cm H_2O (10.5–13.5 cm H_2O).

Patients who were proning had a significantly greater daily DA collapse (–14.1% [–41.3% to –3%]) than those who were not (0.5 [–10.5 to 12.2]) (*p* < 0.001). There was no other significant difference between patients who were placed in prone position and those who were not (**Table S1**, http://links.lww.com/CCM/H77).

Twenty-four patients (48%) received PV sessions and completed a total of 58 sessions, with a median of 2 (1–3) PP per patient. All baseline patient characteristics are presented in **Table 1**.

Patients who responded in oxygenation term to the PV session had a significantly higher daily DA collapse (–14 [–3 to –41.5]) compared with patients who did not improve their oxygenation (0.6% [–10.2% to 12%]; *p* < 0.001). There was no other significant difference between patient responders and nonresponder. There was no cross-over; nonresponders at the first PV session were also nonresponders at the following sessions. Similarly, patients who were responders at the first PV session remained responders at the next sessions

PV Sessions Characteristics

The first PV session occurred at a median of 3 days (2–4 d) after intubation. Thirty-six PV sessions (62.1%) were followed by at least a 20% improvement in oxygenation. There was no significant difference between sessions with or without response in terms of duration of the noninvasive strategy before intubation, the timing of the first PV session ventilation variables, Pao_2/Fio_2 ratio, $Paco_2$, and physiologic dead space over Vt (VD/VT) before PV.

TABLE 1.
Characteristics Before the First Prone Session and Outcome of Patient's Responder and Nonresponder

Characteristics	All Patients Included, $N = 50$	Patients Nonresponder, $N = 12$	Patients Responder, $N = 12$	p
Age, yr, median (IQR)	63 (56–70.5)	60 (51–71)	60 (56–71)	0.808
Gender male, n (%)	38 (76)	11 (91.7)	9 (75)	0.590
Comorbidities				
Body mass index, kg/cm^2, median (IQR)	26.6 (24.6–29.3)	27 (25–29)	29 (26–33)	0.310
Sleep apnea, n (%)	3 (6)	1 (8.3)	1 (8.3)	1
Blood pressure, n (%)	24 (48)	7 (58.3)	5 (41.6)	0.684
Diabetes, n (%)	9 (18)	3 (25)	2 (16.6)	1
Chronic obstructive pulmonary disease, n (%)	4 (8)	2 (16.6)	1 (8.3)	1
CT scan lesions, n (%)				
Diffuse	36 (72)	9 (75)	6 (50)	0.400
Lobar	0 (0)	0 (0)	0 (0)	1
Posterior	21 (45)	2 (16.6)	5 (41.69)	0.370
Consolidation	7 (14)	2 (16.6)	1 (8.3)	1
Berlin classification, n (%)				0.653
Mild ARDS	39 (78)	9 (75)	8 (66.7)	
Severe ARDS	11 (22)	3 (25)	4 (33.3)	
Noninvasive strategy, n (%)				1
High-flow O$_2$	50 (100)	12 (100)	12 (100)	
Noninvasive ventilation	50 (100)	12 (100)	12 (100)	
Noninvasive strategy duration, d, median (IQR)	2 (1–4)	2 (1–2)	1 (1–4)	0.485
Ventilation variables, median (IQR)				
Tidal volume, mL/Kg of ideal body weight	6.2 (6–6.4)	6.4 (5.8–6.6)	6.4 (6–6.4)	0.764
F$_{IO_2}$, %	55 (45–70)	53 (48–70)	60 (45–70)	0.902
Positive end-expiratory pressure, cm H$_2$O	14 (12–16)	14 (12–16)	14 (13–15)	0.259
Driving pressure, cm H$_2$O	11 (10.5–13.5)	12 (11–13)	11 (11–13)	0.551
Dynamic compliance, mL/cm H$_2$O	40 (30–43.8)	40 (31–45)	41 (35–43)	0.809
Arterial blood gas, median (IQR)				
Pa$_{O_2}$/F$_{IO_2}$	132 (118–153)	131 (116–151)	121 (99–144)	0.450
Pa$_{CO_2}$, mm Hg	43 (38.1–46.9)	42.5 (40–47)	42 (38–46)	0.660
Ratio of physiologic dead space over tidal volume	0.15 (0.05–0.31)	0.23 (0.1 -0.36)	0.13 (0.05–0.34)	0.369
EIT monitoring, median (IQR)				
Number EIT per patient	6 (3–8)	3 (3–6)	8 (6–8)	< 0.001
Daily variation of end expiratory ling impedance	−10.1 (−26.8 to 5.7)	0.6 (−10.2 to 12)	−14 (−3 to −41.5)	< 0.001

(*Continued*)

TABLE 1. (*Continued*).
Characteristics Before the First Prone Session and Outcome of Patient's Responder and Nonresponder

Characteristics	All Patients Included, $N = 50$	Patients Nonresponder, $N = 12$	Patients Responder, $N = 12$	*p*
Prone ventilation, median (IQR)				
Number of prone session		2 (1–4)	3 (2–3)	0.324
First prone positioning after intubation, d		1 (1–1.5)	2.5 (1-3)	0.110
Use of muscular blocking agents, *n* (%)	34 (68)	12 (100)	12 (100)	1
Tracheotomy, *n* (%)	21 (42)	4 (33.3)	3 (25)	1
Outcome				
Ventilator-free day 30, d, median (IQR)	10 (0.5–19.5)	3 (0–15)	6 (0–21)	0.551
ICU length of stay, d, median (IQR)	20 (14–28)	23 (16–33)	16 (10–27)	0.190
Mortality, *n* (%)	13 (26)	5 (41.7)	2 (16.7)	0.370

ARDS = acute respiratory distress syndrome, EIT = electrical impedance tomography, IQR = interquartile range.
CT scan lesion definition: diffuse: presence of bilateral lesions affecting more than 50% of the lung parenchyma and not limited to a lung anatomical region (lobe, dorsal regions…); lobar: lesion limited to a lung lobe; posterior: lesions predominating in the dorsal lung regions behind the plane of the carina; consolidation: lesions with higher density than ground glass opacities and blurred margins of pulmonary blood vessels and bronchial tubes. We used the Enghoff dead space equation (18) (ratio of physiologic dead space over tidal volume = 1−end-tidal CO_2 concentration/$Paco_2$).

PV sessions were significantly more followed by improved oxygenation when lesions predominated in the posterior areas on CT scan (19 [52.8%] vs 4 [18.2%]) (*p* = 0.013). The responding sessions were preceded by a significantly greater DA collapse (–39.9% [–43.2% to –26%] vs –11.1% [–12.3% to –9.5%]) (*p* < 0.001). The PV sessions with oxygenation improvement had a lung DAs recruitment higher than session without oxygenation response (70.4% [45.7–102.2%] vs 1.7% [–8.6% to 11.6%]) (*p* < 0.001). All PV characteristics are summarized in **Table 2**.

Primary Endpoint

There was a linear correlation between the DA collapse, in the supine position, in the 24 hours before a prone session, and the oxygenation response to PV (R^2 = 0.49) (**Fig. S3**, http://links.lww.com/CCM/H78; legend, http://links.lww.com/CCM/H80).

Predictive Value of Percentage of DA Collapse

ROC curve showed that DA collapse had a satisfactory prediction accuracy of PV response in term of oxygenation with an AUC of 0.94 (95% CI, 0.87–1.00) (*p* < 0.001)

(**Fig. 1**). The maximum value of the Youden index was obtained for a percentage of DA collapse greater than 13.5%. The predictive performance of this threshold showed a sensitivity of 92% (95% CI, 78–97), a specificity of 91% (95% CI, 72–97), a positive predictive value of 94% (95% CI, 88–100), a negative predictive value of 87% (95% CI, 78–96), a positive likelihood ratio (LR) of 10.1 (95% CI, 2.7–37.9), a negative LR of 0.09 (95% CI, 0.03–0.27), and a diagnostic accuracy of 91% (95% CI, 84–98).

The determined DA collapse threshold of 13.5% kept a satisfactory prognostic performance to predict an improvement of oxygenation until 50% (**Table S2**, http://links.lww.com/CCM/H79).

Independent Factors Predicting Oxygenation Response to PV

In the multivariate linear regression (**Table 3**), DA collapse (coefficient beta 1.747 [95% CI, 0.998–2.313]; *p* < 0.001) was the only variable significantly associated with oxygenation response to PV.

DISCUSSION

Our study highlights a noninvasive means of selecting patients who will respond to PV. To our knowledge,

TABLE 2.
Characteristics of the Prone Ventilation Sessions

Characteristics	Prone Ventilation Without Response, N = 22	Prone Ventilation With Response, N = 36	p
CT scan lesions, n (%)			
Diffuse	15 (68.2)	28 (77.8)	0.418
Posterior	4 (18.2)	19 (52.8)	0.013
Consolidation	2 (9.1)	10 (27.8)	0.108
Ventilation variables			
Tidal Volume, mL/ Kg of ideal body weight, median (IQR)	6.4 (6.3–6.5)	6.4 (6–6.6)	0.884
Positive end-expiratory pressure, cm H_2O, median (IQR)	14 (14–16)	14 (14–16)	0.586
Driving pressure, cm H_2O, median (IQR)	12 (11.8–15)	12 (11–14)	0.867
Dynamic compliance, mL/cm H_2O, median (IQR)	35.4 (28–42.8)	40 (30–46.4)	0.526
Use of neuromuscular blocking, n (%)	22 (100)	36 (100)	1
Arterial blood gas before prone ventilation, median (IQR)			
Pao_2/Fio_2	125 (98–138.5)	117.5 (105.3–137.8)	0.948
$Paco_2$, mm Hg	46.4 (44.1–53.7)	47.7 (42.7–51)	0.962
VD/VT	0.26 (0.15–0.45)	0.27 (0.21–0.45)	0.269
Change in VD/VT during prone ventilation			
At H1	0 (−0.12 to 0.01)	0.17 (0–0.61)	0.069
At H4	0.01 (−0.03 to 0.04)	0.15 (0.08–0.52)	< 0.001
At H8	0 (−0.11 to 0.14)	0.22 (0.1–0.42)	0.009
At H12	0.02 (−0.1 to 0.08)	0.34 (0.19–0.54)	0.001
At H16	0.01 (−0.04 to 0.1)	0.34 (0.17–0.55)	< 0.001
Ventilation variables at the end of PP, median (IQR)			
Driving pressure, cm H_2O	13 (12–15)	11.5 (11–13)	0.004
Dynamic compliance, mL/ cm H_2O	35.6 (27.7–41.3)	40.6 (32.5–47)	0.154
Δ Driving pressure, %	0 (0–8.3)	−8.3 (−12.5 to 0)	< 0.001
Δ Dynamic compliance, %	−1.1 (−2.7 to 0)	4.8 (2.7–9)	< 0.001
Arterial blood gas at the end of PP, median (IQR)			
Pao_2/Fio_2	136.5 (107–150)	194 (149.8–233.8)	< 0.001
Δ Pao_2/Fio_2	11.7 (1.7–13.3)	71.1 (27.8–106.7)	< 0.001
$Paco_2$, mm Hg	46 (40.7–48.8)	44.7 (42–48)	0.441
Change in $Paco_2$, mm Hg	−0.3 (−3.4 to 2.5)	2.5 (−0.2 to 7.5)	0.033
VD/VT	0.33 (0.25–0.37)	0.18 (0.13–0.23)	< 0.001
Dependent area electrical impedance tomography monitoring on 24 hr			
Daily ΔEELI before PP, %, median (IQR)	−11.1 (−12.3 to −9.5)	−39.9 (−43.2 to −26)	< 0.001
Daily ΔEELI > 13.5% before PP, n (%)	2 (9.1)	33 (91.7)	< 0.001
ΔEELI after PP sessions, median (IQR)	1.7 (−8.6 to 11.6)	70.4 (45.7–102.2)	< 0.001

ΔEELI = variation of end expiratory ling impedance, IQR = interquartile range, PP = prone positioning, VD/VT = ratio of physiologic dead space over tidal volume.

CT scan lesion definition: diffuse: presence of bilateral lesions affecting more than 50% of the lung parenchyma and not limited to a lung anatomical region (lobe, dorsal regions…); posterior: lesions predominating in the dorsal lung regions behind the plane of the carina; consolidation: lesions with higher density than ground glass opacities and blurred margins of pulmonary blood vessels and bronchial tubes. We used the Enghoff dead space equation (18) (ratio of physiologic dead space over tidal volume = 1−end-tidal CO_2 concentration/$Paco_2$).
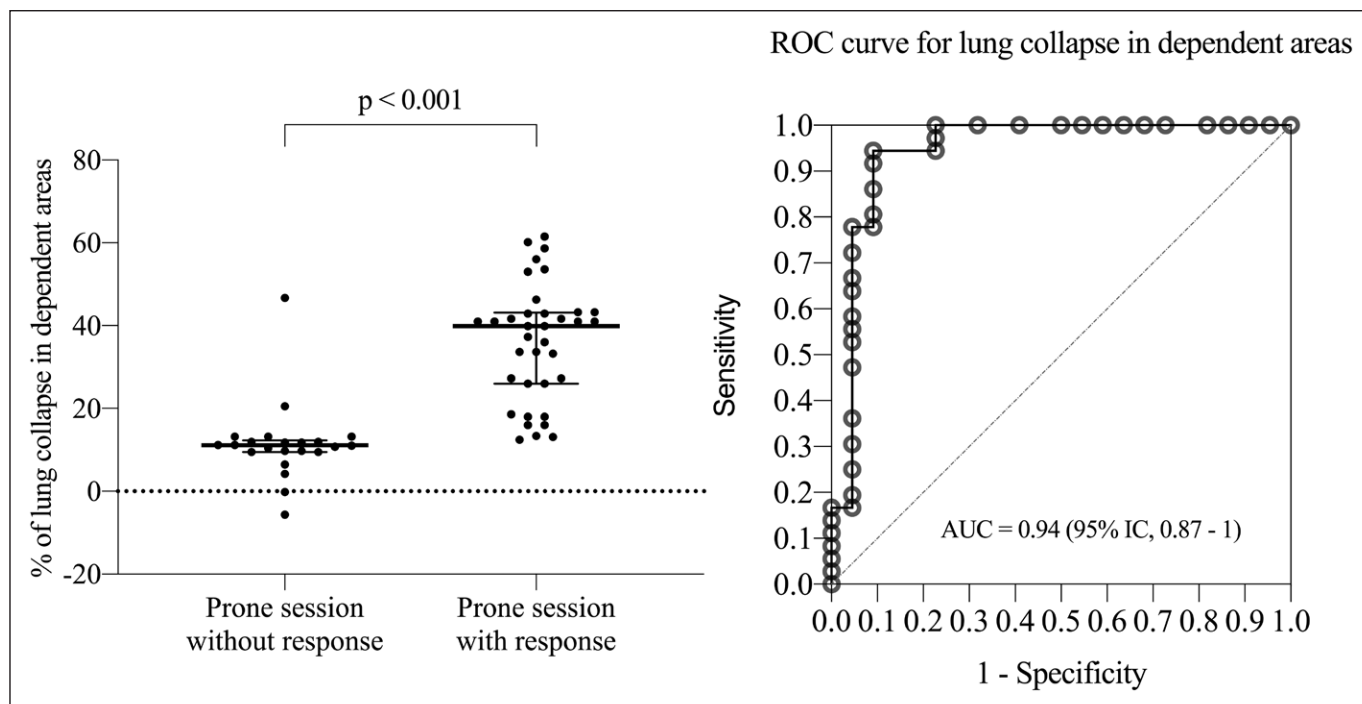
Figure 1. Abilities of lung collapse in dependent areas to predict prone ventilation response. AUC = area under the curve, ROC = receiver operating characteristic.

this is the first study to address the selection of patients who will show improved oxygenation during PV.

Although EIT is not yet widespread, it allows a personalized treatment, as underlined by our study, especially in difficult situations like the severe acute respiratory syndrome coronavirus 2 pandemic, which saturates our ICUs with ARDS patients.

Pesenti et al (19) already advanced in 2016 that this kind of technique would probably represent the future of ARDS imaging with imaging accessible at the bedside to help diagnose and complex management.

In our study, the levels of PEEP used may seem high, but they are still within the criteria of protective ventilation as evidenced by the driving pressures. Furthermore, the levels of PEEP are in agreement with the largest series in the literature (1, 20).

Few authors have focused on the prediction of improved oxygenation after PV. Haddam et al (21), in a multicenter study in 51 ARDS patients with the aim to predict the oxygenation response to the PV from using lung ultrasonography (LUS) aeration score, found no correlation. This may be explained by the fact that the LUS Aeration Score does not accurately measure reaeration because the LUS aeration score also tracks hyperinflation and not only lung recruitment. This is not the case with the EIT, which can assess lung recruitment,

TABLE 3.
Multivariate Linear Regression of Independents Factors Predicting Oxygenation Response to Prone Ventilation

Factors Included in the Model	Coefficients B	95% CI for B	p	Colinearity Statistics	
				Tolerance	Variance Inflexion Factor
Daily collapse in dependent areas	1.747	0.998–2.313	< 0.001	0.999	1.001
Posterior lesions on CT scan	16.157	−9.507 to 41.821	0.212	0.792	1.263
Consolidation on CT scan	10.840	−20.169 to 41.850	0.486	0.791	1.264

We used the Enghoff dead space equation (18) (ratio of physiologic dead space over tidal volume = $1 - $end-tidal CO_2 concentration/$Paco_2$).

collapse, and hyperinflation. Beda et al (22) showed that EIT-derived pressure-volume curves could identify presumed tidal recruitment and overdistension regions. Changes in pressure-volume curve shape-derived tidal recruitment were correlated with changes in poorly aerated regions. Changes in pressure-volume curve shape-derived overdistension were highly correlated with changes in the hyperaerated areas for higher PEEPs ($r = 0.73$).

The improvement in oxygenation depends not only on ventilation but also on pulmonary perfusion, which we did not assess in our study. But, the pulmonary blood flow is more uniformly distributed and follows less of a gravitational hydrostatic gradient during prone position, as observed in many animal studies (18). This agrees with the correlation between the improvement in oxygenation and the recruitment of the DAs found in our study. It is also consistent with the reduction in VD/VT, which indicates a decrease in pulmonary overdistension.

We may ask whether it is essential to predict oxygenation response to PV. Some authors might answer probably not. First, trials that have found benefits for patients, such as the Proseva study (23) or the meta-analysis by Gattinoni et al (24), have included patients without considering the oxygenation response to PV. Second, the objective of ventilation in ARDS patients is to ensure viable gas exchange while avoiding excessive stress on the lungs. It could be seen as positive that PV can maintain this protective ventilation, which is difficult to achieve in the supine position, even if there is little or no improvement in oxygenation.

In our opinion, the answer can be positive. In fact, in a cohort of 116 patients, Lee et al (3) found an association between increased Pao_2/Fio_2 ratio and survival in the ICU in moderate to severe ARDS. This is the first study to establish this relationship. This is a conceptually important result because it has two implications. First, in nonresponders in terms of oxygenation to PV, not to continue PP and consider other methods such as ECMO. A long delay between intubation and venovenous ECMO implantation is associated with excess mortality at 6 months (2). On the other hand, in responders to PV to continue this procedure beyond this first session. Thus, the results of our study provide a noninvasive means of predicting response to PV that could allow the selection of responder patients.

There is a proven benefit of PV on overall mortality in moderate to severe ARDS in one trial (23), a result reinforced by a recent network meta-analysis showing that the combination of low Vt (< 8 mL/kg weight predicted by height) and PV is closely associated with reduced mortality in moderate to severe ARDS (25). Gattinoni et al (26) had also demonstrated an association between oxygenation response and PV, but the strength of this association was weak. Furthermore, in the latter study (26), the link between the reduction in $Paco_2$ during the PV session and reduction in mortality was the strongest. We also find in our study a significantly greater reduction in $Paco_2$ and VD/VT in our study. Furthermore, in the current context of saturation of ICUs by patients with ARDS COVID-19, the number of patients receiving PV sessions on the sole criterion of Pao_2/Fio_2 less than 150 after muscular blocking and ventilation optimization may rapidly become significant. This represents an increase in workload and considerable consumption of care time, to the detriment of other necessary care. Our results provide a simple way to select COVID-19 ARDS patients who will benefit most from PV.

Finally, we are aware of the limitations of our study: first, it is carried out on a small cohort of patients. Second, it concerns only patients with ARDS COVID-19 in the first week of invasive mechanical ventilation. It can, therefore, hardly be extrapolated to other causes of ARDS, but also after the first week of ventilation where pneumopathy acquired under mechanical ventilation is added. Nevertheless, the pathophysiology of the response to PV remains unchanged, and we may find a concordant result in these patients.

In conclusion, our study showed that the lung DAs collapse, monitored by EIT, is a predictive variable of improved oxygenation during PV. This study and the collapsing threshold of the lung DAs highlighted need to be confirmed by a study on a larger cohort of patients with ARDS.

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