Effects of Prone Position on Lung Recruitment and Ventilation-Perfusion Matching in Patients With COVID-19 Acute Respiratory Distress Syndrome: A Combined CT Scan/Electrical Impedance Tomography Study*

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OBJECTIVES: Prone positioning allows to improve oxygenation and decrease mortality rate in COVID-19–associated acute respiratory distress syndrome (C-ARDS). However, the mechanisms leading to these effects are not fully understood. The aim of this study is to assess the physiologic effects of pronation by the means of CT scan and electrical impedance tomography (EIT).

DESIGN: Experimental, physiologic study.

SETTING: Patients were enrolled from October 2020 to March 2021 in an Italian dedicated COVID-19 ICU.

PATIENTS: Twenty-one intubated patients with moderate or severe C-ARDS.

INTERVENTIONS: First, patients were transported to the CT scan facility, and image acquisition was performed in prone, then supine position. Back to the ICU, gas exchange, respiratory mechanics, and ventilation and perfusion EIT-based analysis were provided toward the end of two 30 minutes steps (e.g., in supine, then prone position).

MEASUREMENTS AND MAIN RESULTS: Prone position induced recruitment in the dorsal part of the lungs (12.5% ± 8.0%; $p < 0.001$ from baseline) and derecruitment in the ventral regions (−6.9% ± 5.2%; $p < 0.001$). These changes led to a global increase in recruitment (6.0% ± 6.7%; $p < 0.001$). Respiratory system compliance did not change with prone position (45 ± 15 vs 45 ± 18 mL/cm H_2O in supine and prone position, respectively; $p = 0.957$) suggesting a decrease in atelectrauma. This hypothesis was supported by the decrease of a time-impedance curve concavity index designed as a surrogate for atelectrauma (1.41 ± 0.16 vs 1.30 ± 0.16; $p = 0.001$). Dead space measured by EIT was reduced in the ventral regions of the lungs, and the dead-space/shunt ratio decreased significantly (5.1 [2.3–23.4] vs 4.3 [0.7–6.8]; $p = 0.035$), showing an improvement in ventilation-perfusion matching.

CONCLUSIONS: Several changes are associated with prone position in C-ARDS: increased lung recruitment, decreased atelectrauma, and improved ventilation-perfusion matching. These physiologic effects may be associated with more protective ventilation.

KEY WORDS: atelectrauma; electrical impedance tomography; prone position; pulmonary perfusion; recruitment

T he COVID-19 pandemic has already caused the death of more than 4 million people. In most severe cases, the acute respiratory infection leads to severe pneumonia. In around 20% of hospitalized patients, pneumonia worsens to progressive hypoxemia and acute respiratory distress

syndrome (ARDS) (1), which mortality rate is higher than 50% (2). The overwhelming number of intubated patients with ARDS associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (COVID-19–associated ARDS [C-ARDS]) and the severity of their disease warrant urgent implementation of simple and effective therapies to decrease mortality.

Prolonged sessions in the prone position represent a simple and effective intervention to decrease mortality in patients with ARDS (3). Prone position has been widely adopted for the treatment of C-ARDS, both before intubation and during invasive ventilation (4, 5). Interestingly, despite time and staff constraints due to the pandemic, the proportion of patients with C-ARDS turned prone is significantly higher than patients with ARDS from other etiologies (6, 7), and the prone position is now indicated as a cornerstone for the ventilatory management of C-ARDS (8).

Pilot observational studies showed that the prone position in intubated patients with C-ARDS may decrease hospital mortality (9). From a physiologic standpoint, prone position improves oxygenation in patients with C-ARDS, while respiratory mechanics appear unaffected (10). Thus, the physiologic pathway leading to decreased mortality in patients with C-ARDS undergoing pronation needs further exploration, especially since there is no correlation with oxygenation (11) or respiratory mechanics (7).

In "classical ARDS," lung recruitment with nearly constant airway pressure is a key mechanism of lung protection associated with pronation. However, this feature may be unlikely in C-ARDS, as a large proportion of patients presents quasi-normal respiratory system compliance, which may indicate preserved lung inflation and limited recruitability (12). A pilot study suggested a dead space reduction in patients with C-ARDS turned prone (13), which may decrease the risk of deleterious regional hypocapnia (14). Finally, the potential effect of prone position on atelectrauma has, at our knowledge, never been investigated in C-ARDS.

Aim of this study was to further characterize the physiologic effects of prone position on key mechanisms of regional lung protection, namely: recruitment, reduced atelectrauma, and improved ventilation-perfusion matching, by CT scan and electrical impedance tomography (EIT).

METHODS

Study Population

We conducted a prospective physiologic study in patients admitted to the dedicated COVID-19 ICU of Luigi Sacco Hospital (ASST Fatebenefratelli Sacco), Milan, Italy.

We enrolled intubated patients admitted to the ICU with confirmed infection by novel COVID-19 (SARS-CoV-2) and moderate or severe ARDS according to the Berlin definition. Decision for pronation was reached if the Pao_2/Fio_2 ratio was measured below 150 mm Hg or as an emergent rescue therapy in patients with Spo_2 less than 85% with Fio_2 100%.

Exclusion criteria were: age less than 18 years old, pregnancy, intubation more than 7 days, confirmed diagnosis of hospital-acquired bacterial pneumonia, contraindications to the prone position or to EIT monitoring (e.g., thoracic wounds), and clinical severity (e.g., need for extracorporeal membrane oxygenation [ECMO] therapy).

The institutional Ethical Committee approved the study (Comitato Etico Milano Area 1; protocol n. 2020/ST/388) and informed consent was obtained according to local regulations.

Data Collection

The following patients' characteristics were recorded at enrollment: age, gender, body mass index, history of hypertension or diabetes mellitus, plasma C-reactive protein (CRP) and D-dimers level, Sequential Organ Failure Assessment (SOFA) score (15), the number of hours spent in prone position before enrollment and days from onset of symptoms, intubation, and pronation. Respiratory system compliance, Pao_2/Fio_2, and ventilatory ratio were measured at enrollment (see **Online Supplement**, http://links.lww.com/CCM/G986).

Study Protocol

Patients were deeply sedated, paralyzed, and mechanically ventilated on pressure-regulated volume-controlled (PRVC) mode. Ventilator settings were standardized for all patients during all study measures: tidal volume (VT) 6–8 mL/kg of predicted body weight, respiratory rate to maintain pH between 7.35 and 7.45, and positive end-expiratory pressure (PEEP)

10 cm H_2O (**Table 1**). Fio_2 was set to obtain a Spo_2 value between 94 and 98% and kept stable during all the study protocol.

After enrollment, patients were initially transported to the CT scan facility in the prone position. Whole thorax scans were performed in the prone and supine position during an end-expiratory occlusion at PEEP 10 cm H_2O (time between scans 15 and 20 min).

After the scan, patients were transported back to the ICU and connected to a ventilator. EIT monitoring was started, and measurements of distribution of ventilation and perfusion were recorded in the supine position and 20–30 minutes after pronation.

Immediately before each EIT measurement, arterial and central venous blood gas analyses were obtained, and respiratory mechanics were measured. Further information on data and statistical computation are provided in the Online Supplement (http://links.lww.com/CCM/G986).

CT Scan Analysis

CT scans were performed by an experienced team, then centralized and analyzed offline, using a standard software (Maluna v3.7, Mannheim, Germany), to provide a quantitative analysis of lung tissue aeration (16). Further information are available in the Online Supplement (http://links.lww.com/CCM/G986).

Ventral and dorsal regions were defined as the upper and lower parts, respectively, of an axis from the sternum to the vertebrae (16). This choice allowed us to obtain more superimposable regions of interest between CT scan and EIT images.

Recruitment (or derecruitment) between supine and prone position at global and regional levels was computed as the respective decrease or increase in nonaerated weight, divided by the global lung weight in the supine position (16).

Electrical Impedance Tomography

EIT data were acquired by standard device (PulmoVista; Draeger, Lubeck, Germany), with a sample rate of 50 Hz. The EIT belt was positioned directly below armpits, between the third and fifth intercostal spaces. The EIT belt was kept in the same position during both supine and prone position.

We measured a so-called impedance curve concavity index based on a similar concept to the stress index (17). Time-impedance curve was fitted to a power equation to assess its concavity. It is assumed that, during ventilation with constant inspiratory pressure, the concavity of the impedance curve may be an acceptable surrogate for the pressure-volume curve, where upper concavity represents ongoing recruitment of collapsed alveoli/small airways (**Fig. E1**, http://links.lww.com/CCM/G986) (18). This index was measured at global and regional scales.

Ventilation-perfusion matching was measured by using the hypertonic saline bolus method (see Online Supplement, http://links.lww.com/CCM/G986) (19, 20).

TABLE 1.
Patients Main Characteristics

Variable	All Patients, $n = 21$
Patients characteristics	
Age, yr	67 (61–72)
Comorbidities, n (%)	
Hypertension	12 (57)
Diabetes mellitus	5 (24)
Male, n (%)	17 (81)
Body mass index, kg/m²	28.6 (26.3–32.0)
Sequential Organ Failure Assessment score	6 (3–7)
C-reactive protein, mg/L	179 (81–211)
d-dimers, µg/L	1,360 (815–5,333)
Severe acute respiratory distress syndrome, n (%)	11 (52)
Days from onset of symptoms, d	12 (8–17)
Days from intubation, d	2 (1–4)
Days from first pronation, d	1 (1–2)
Hours spent in prone position before enrollment, hr	36 (16–72)
Ventilator settings	
Positive end-expiratory pressure, cm H_2O	10 (± 1)
Fio_2, %	83 (± 16)
Tidal volume, mL/kg predicted body weight	7.5 (± 0.8)
Respiratory rate, breaths/min	19 (± 2)
Gas exchange and mechanics in supine at enrollment	
Pao_2/Fio_2, mm Hg	105 (84–121)
Ventilatory ratio	1.74 (1.50–2.25)
Respiratory system compliance, mL/cm H_2O	39 (32–52)

Statistical Analysis

For each variable, Gaussian distribution was assessed by Shapiro-Wilk normality test. After checking for normality, results were expressed as a number (percentage) for qualitative variables and with median (interquartile range) or mean (± SD) for quantitative variables. A paired t test or Wilcoxon signed-rank test, as appropriate, were used to compare between variables measured in the supine and prone position. Based on previous studies on CT scan analysis in C-ARDS patients (21, 22), we hypothesized relatively low lung recruitment induced by the prone position of 5% ± 5%; this, with a type I error of 0.05 and statistical power of 90%, lead to a minimum calculated sample size of 21 patients.

A secondary analysis was also performed to identify subgroups with larger recruitment. Patients were grouped according to: 1) severe versus moderate ARDS and 2) higher or lower respiratory system elastance (< 2 vs > 2 cm H_2O/kg × mL). p value of less than 0.05 was considered significant.

Spearman correlations were used to explore the association between global and regional recruitment and the $\Delta PaO_2/FIO_2$ (defined by PaO_2/FIO_2 prone minus supine, divided by the value in supine position).

All statistical analysis were performed by using Prism (GraphPad Prism v9.0, La Jolla, CA).

RESULTS

Patients'aCharacteristics

Twenty-one patients were enrolled in the study. Twenty-three consecutive patients were screened for enrollment, two patients were excluded due to their clinical severity and indication for ECMO support. Median age was 67 years old (61–72 yr old) and 17 (81%) were men (Table 1). Clinical severity and level of inflammatory markers were elevated, as suggested by median SOFA score of 6 (3–7) and plasmatic CRP of 179 mg/L (81–211 mg/L) (Table 1).

Time between start of symptoms and intubation was 12 days (8–17 d) (Table 1), and all patients were enrolled within 5 days from intubation. Patients underwent 1 day (1–2 d) of pronation before enrollment (Table 1).

As per protocol, mechanical ventilation settings were standardized with a VT of 6–8 mL/kg, PEEP of 10 cm H_2O, and fixed respiratory rate targeted for pH greater than 7.25. Settings remained unchanged during the study (Table 1). In supine position at the time enrollment, PaO_2/FIO_2 was 105 mm Hg (84–121 mm Hg), with a maximal value of 149 mm Hg (Table 1). Respiratory system compliance was 39 mL/cm H_2O (23–52 mL/cm H_2O).

CT Scan Analysis

Quantitative CT scan showed that the nonaerated lung weight decreased significantly in the prone position ($p = 0.001$) (**Table 2**; and **Fig. E2**, http://links.lww.com/CCM/G986). Prone position also induced an increase of the normally aerated lung weight ($p = 0.004$), along with a significant decrease of the hyperinflated tissue ($p = 0.008$) (Table 2; and Fig. E2, http://links.lww.com/CCM/G986). Regional distribution of lung tissue aeration is reported in **Table E1** (http://links.lww.com/CCM/G986).

Considering the whole lung, recruitment induced by prone position was significant ($p < 0.001$) (Table 2) and only two patients (9.6%) experienced derecruitment (**Fig. 1**). Regional response to prone position was dissociated: ventral areas were characterized by derecruitment ($p < 0.001$), while significant recruitment characterized the dorsal regions ($p < 0.001$) (Table 2 and Fig. 1). These changes were associated with an increase in mean Hounsfield Units in the ventral regions and a decrease in the dorsal parts of the lungs (both $p < 0.001$; **Table E2**, http://links.lww.com/CCM/G986).

Figure 2 shows a representative patient with large fraction of recruitment in the dorsal lung when turned prone.

Ventilation and Perfusion by EIT

Data from EIT indicate that recruitment in the dorsal region induced significantly increased regional ventilation, while the ventral derecruited lung was characterized by reduced ventilation ($p < 0.001$ for both) (Table 2).

The concavity index significantly decreased in the prone position only in the dorsal regions of the lung ($p < 0.001$) (Table 2 and Fig. 1).

EIT-based measure of pulmonary perfusion was of acceptable quality in 16 patients (76%). Considering the whole lung, prone position did not affect the fraction of mismatched units (i.e., only ventilated and only perfused) (Table 2), but it induced significant decrease of the dead space/shunt ratio ($p = 0.035$) (Table 2).

At the regional level, the fraction of only ventilated units and the dead space/shunt ratio significantly decreased

TABLE 2.

Regional Quantitative CT Scan and Electrical Impedance Tomography Analysis Between the Supine and Prone Positions

Variable	Supine, $n = 21$	Prone, $n = 21$	p
CT scan global analysis			
Total lung weight, g	1,466 (± 378)	1,394 (± 381)	0.007
Hyperinflated lung weight, g	14 (± 12)	12 (± 9)	0.008
Normally aerated lung weight, g	356 (± 132)	400 (± 164)	0.004
Poorly aerated lung weight, g	525 (± 192)	505 (± 173)	0.335
Nonaerated lung weight, g	571 (± 294)	477 (± 249)	0.001
CT scan recruitment analysis			
Recruitment, %	Baseline	6.0 (± 6.7)	< 0.001
Ventral derecruitment, % of lung weight	Baseline	−6.9 (± 5.2)	< 0.001
Dorsal recruitment, % of lung weight	Baseline	12.5 (± 8.0)	< 0.001
Electrical impedance tomography			
Vt distribution ventral, %	53 (± 8)	40 (± 11)	< 0.001
Vt distribution dorsal, %	47 (± 9)	60 (± 11)	< 0.001
TIC concavity index	1.41 (± 0.16)	1.30 (± 0.16)	0.001
Ventral TIC concavity index	1.40 (± 0.16)	1.35 (± 0.16)	0.186
Dorsal TIC concavity index	1.45 (± 0.20)	1.25 (± 0.19)	< 0.001
Only perfused units, %	5 (1–12)	8 (4–19)	0.105
Only perfused units, ventral, %	2 (0–5)	7 (1–11)	0.023
Only perfused units, dorsal, %	2 (0–8)	2 (0–10)	0.742
Only ventilated units, %	28 (16–36)	22 (15–31)	0.301
Only ventilated units, ventral, %	14 (12–22)	8 (3–12)	< 0.001
Only ventilated units; dorsal, %	11 (4–15)	14 (9–22)	0.133
Dead space/shunt ratio	5.1 (2.3–23.4)	4.3 (0.7–6.8)	0.035
Dead space/shunt ratio, ventral	11.3 (3.7–19.0)	1.5 (0.4–6.0)	< 0.001
Dead space/shunt ratio, dorsal	4.3 (0.8–14.8)	8.6 (0.6–21.5)	0.404

TIC = time-impedance curve, Vt = tidal volume.

in the ventral region ($p < 0.001$ for both), together with a slight increase of the only perfused units ($p = 0.023$) (Table 2; and **Fig. E3**, http://links.lww.com/CCM/G986). The dorsal region did not show any significant change in the ventilation-perfusion matching after pronation.

Figure 2 shows EIT-based pulmonary ventilation and perfusion in supine and prone position in a representative study patient.

Respiratory Mechanics and Gas Exchange

Prone positioning did not induce any change in respiratory mechanics, while oxygenation improved and calculated pulmonary shunt significantly decreased ($p < 0.01$)

(**Table 3**; and **Fig. E4**, **A** and **B**, http://links.lww.com/CCM/G986). There was no difference in Pao_2/Fio_2 nor ventilatory ratio between their values at enrollment and during the study in the supine position after the cycle of pronation ($p = 0.618$, $p = 0.101$, and $p = $ respectively). Respiratory system compliance instead improved after the cycle of prone positioning ($p = 0.020$).

During prone position, hemodynamics remained stable, as indicated by central venous dioxygen saturation (Table 3), and there was no modification of CO_2 clearance by the lungs (Table 3; and **Fig. E4C**, http://links.lww.com/CCM/G986).

Of note, there was no association between global, ventral, or dorsal recruitment, and the $\Delta PaO_2/Fio_2$ between
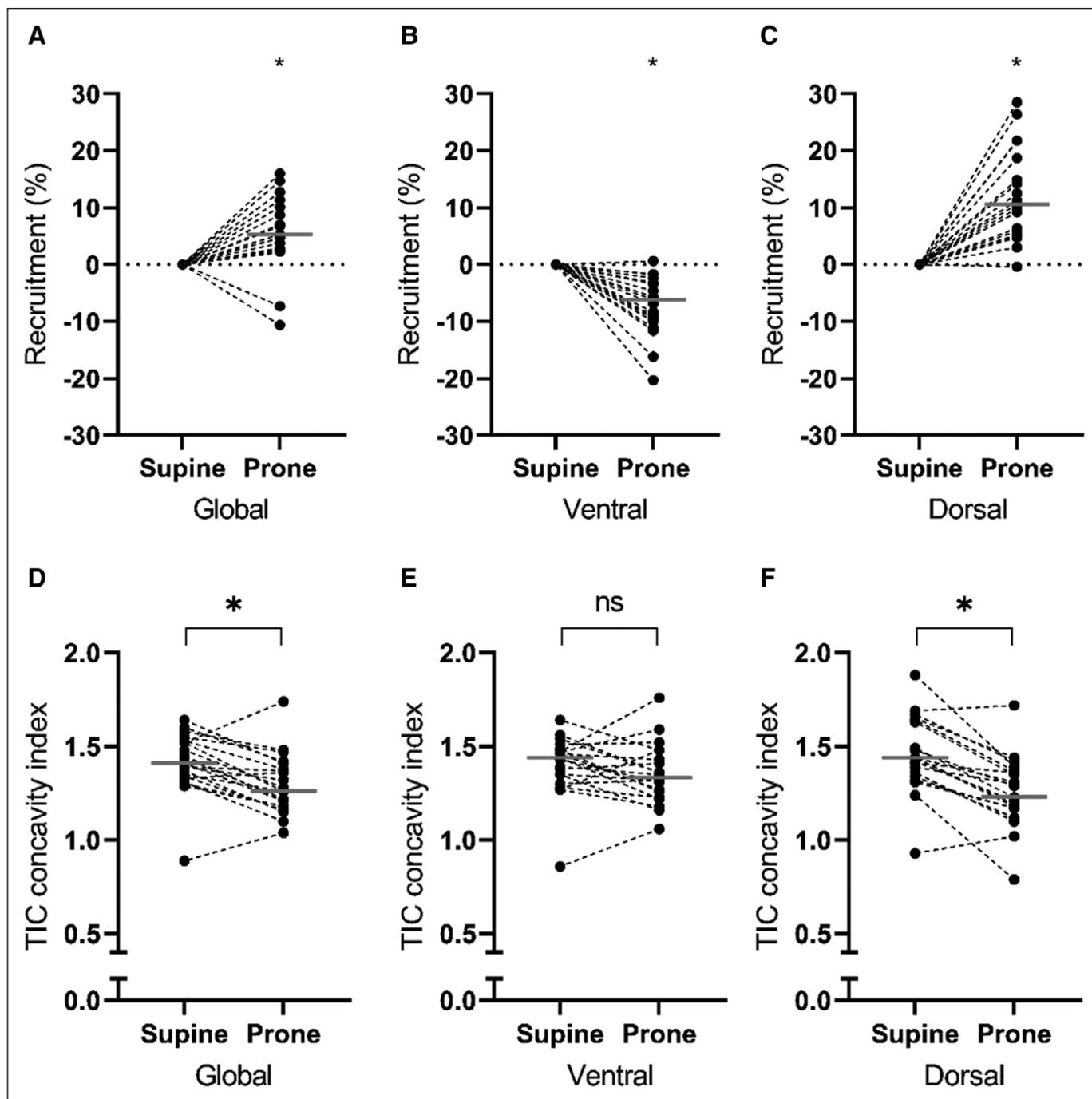
Figure 1. Recruitment measured by CT scan expressed as % of total lung weight and Electrical impedance tomography–based time-impedance curve (TIC) concavity index in the supine and prone position. Recruitment induced by the prone position was significant at the global level (**A**), but ventral lung regions were characterized by derecruitment (**B**) and only dorsal lung was recruited (**C**). The TIC concavity index improved at the global and dorsal regional level (**D** and **F**) without worsening in the ventral derecruited region (**E**). *Red bars* represent mean values. $*p < 0.01$ versus supine. ns = not significant.

the supine and prone positions (rho = 0.091, p = 0.703; rho = 0.317, p = 0.173; and rho = 0.184, p = 0.436, respectively) (**Fig. E5**, http://links.lww.com/CCM/G986).

Subgroups Analysis

To identify patients more likely to respond to prone position in terms of recruitment, we compared the effect of pronation between patients with severe versus moderate ARDS (recruitment: 7% ± 7% vs 5% ± 6%; p = 0.593) (**Fig. E6**, http://links.lww.com/CCM/G986) and with lower versus higher compliance (recruitment: 6% ± 8% vs 6% ± 6%; p = 0.802) (Fig. E6, http://links.lww.com/CCM/G986) but found no difference.
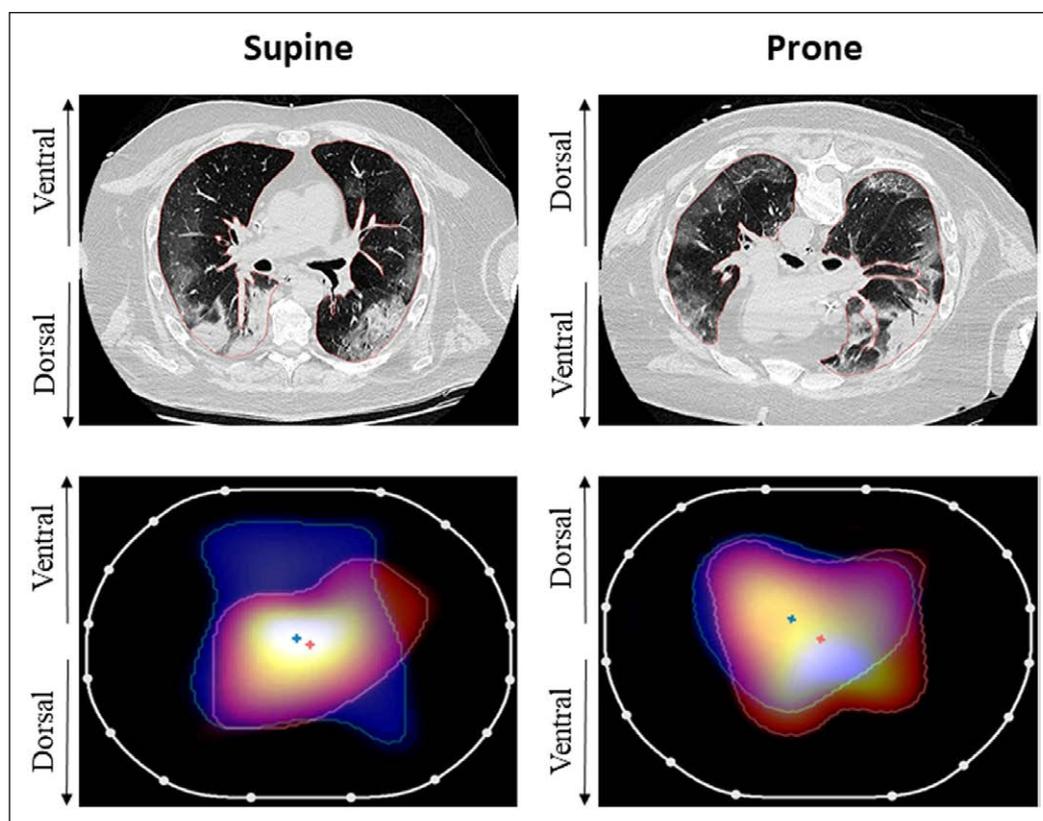
Figure 2. Effects of prone position on recruitment and ventilation-perfusion matching in a representative study patient. *Top*: CT scan images performed in the supine (*left*) and prone position (*right*). Note the recruitment in the dorsal regions and the derecruitment in the ventral part of the right lung. *Bottom*: Electrical impedance tomography assessment of ventilation (*blue*) and perfusion (*red*). Note the large fraction of only-ventilated units (dead space) in the ventral lung regions during supine position (*left*), largely decreased by prone position (*right*); only perfused units (shunt), instead, increased in the same ventral region.

compliance in the supine position, and a low amount of collapsed lung tissue (16). Despite this, prone position induced regional recruitment in the collapsed dorsal regions when they were turned from a gravitationally dependent to nondependent position, similarly to "classical" ARDS (23). Interestingly, the corresponding ventral derecruitment was smaller, likely due to differences in the shape of the chest in the two positions (24). This so-called "sponge-lung" phenomenon (25) may decrease dorsal lung strain and ventral overdistension (26), leading to more protective ventilation (25, 26). The fraction of dorsal recruitment obtained by prone position at constant airway pressure was large with higher values than those obtained by the application of a 45 cm H_2O inspiratory pressure (16) in unselected ARDS patients. A higher PEEP reduces nonaerated lung tissue (22) and improves the recruitment to inflation ratio (27) in patients with C-ARDS, but the prone position may be regarded as more physiologically safe since the maneuver does not increase the inspiratory and driving pressures. Interestingly, in this study, the amount of recruitment was not associated with disease severity nor with oxygenation improvement. These findings highlight the complexity of hypoxemia mechanisms in C-ARDS and may be a reason to expend criteria for pronation, even to patients with moderate hypoxemia (3, 6).

DISCUSSION

This study describes the lung protective effects of prone position in patients with C-ARDS, when performed in the first days after intubation. The main findings can be summarized as follows: 1) despite mild derangement of respiratory mechanics and relatively preserved lung aeration in the supine position, prone position induces extensive alveolar recruitment in the dorsal regions; 2) alveolar derecruitment occurs in the ventral lung regions, albeit by far smaller extent than dorsal recruitment; 3) dorsal recruitment reduces the risk of regional atelectrauma in comparison to the supine position; and 4) ventral lung regions, after pronation, are characterized by decreased fraction of ventilated non-perfused units and reduced dead space/shunt ratio.

Study patients, as previously described for C-ARDS (21, 22), had relatively preserved respiratory system

In the present study, significant recruitment induced by the prone position was not associated with an increase in respiratory system compliance. As this

TABLE 3.
Respiratory Mechanics and Gas Exchange Between the Supine and Prone Positions

Variable	Supine, $n = 21$	Early Prone, $n = 21$	p
Respiratory mechanics			
Plateau pressure, cm H_2O	23 (± 3)	23 (± 4)	0.294
Driving pressure, cm H_2O	12 (± 3)	12 (± 4)	0.456
Respiratory system compliance, mL/cm H_2O	45 (± 15)	45 (± 18)	0.957
Oxygenation			
Pao_2, mm Hg	85 (± 21)	142 (± 90)	< 0.001
Pao_2/Fio_2, mm Hg	108 (± 41)	176 (± 100)	0.002
Arterial dioxygen saturation, %	95 (± 4)	97 (± 3)	0.003
Alveolo-arterial difference in dioxygen partial pressure, mm Hg	441 (± 124)	379 (± 134)	0.003
Measured venous admixture, %	49 (39–55)	35 (27–46)	0.007
Central venous dioxygen saturation, %	81 (± 6)	81 (± 10)	0.973
CO_2 clearance			
$Paco_2$, mm Hg	53 (± 7)	53 (± 8)	0.542
pH	7.38 (± 0.07)	7.37 (± 0.06)	0.134
Corrected minute ventilation, L/min	11.9 (± 2.3)	12.2 (± 2.6)	0.369
Ventilatory ratio	2.03 (± 0.41)	2.06 (± 0.44)	0.477

finding could indicate that the fraction of ventilated units did not change between positions, we hypothesized that these units might be subject to cyclical opening and closing in the supine position, which is then reduced by turning the patients to prone. The EIT technology allowed us to assess the global and regional dynamics of intra-tidal ventilation by analyzing the slope of the time-impedance curve (18, 28). We assumed that, everything being equal and with a constant pressure (as in PRVC), the time-impedance curve was an acceptable surrogate for the pressure-volume curve (18). Following this assumption, concavity of the impedance curve to values closer to 1 in the prone position would likely be due to a reduced fraction of alveolar units (or of small airways) opening along inspiration and to reduced atelectrauma. These data would be coherent with previous results in ARDS from other etiologies (29).

Although chest wall and lung compliance were not measured in this study, decreased atelectrauma potentially could have been determined by an increase in chest wall stiffness coupled with decreased lung elastance (29, 30). Interestingly, in the ventral regions, the impedance curve concavity remained stable, while derecruitment occurred. This result could be explained by complete collapse of alveoli and airways in these regions secondary to increased superimposed lung weight, which might have determined also a decrease of the regional chest wall compliance.

Prone position was also associated with changes in ventilation-perfusion matching. First, ventral fraction of ventilated nonperfused units (i.e., pure dead space) decreased, while perfused nonventilated units (i.e., pure shunt) from the same region slightly increased. These data confirm previous results from animal models (31, 32) and pilot clinical studies in C-ARDS patients (13). Interestingly, decreased dead space could be regarded as protective due to decreased risk of regional hypocapnia (14), while minimal increase in shunt should not affect lung protection. Second, the dead space/shunt ratio decreased with prone position. This ratio is elevated in patients with C-ARDS (19, 33) and a recent prospective study in "classical" ARDS showed a correlation with outcome (33). Thus, its decrease could be regarded as another marker of improved lung protection by prone position. Finally, calculated venous admixture significantly decreased with pronation (Table 2), while pure shunt measured by EIT did not change. These results could indicate decreased areas with low ventilation/perfusion ratio after pronation, as these contribute only to calculated and not to pure shunt, further increasing lung

protection by reduced lung inhomogeneities (33). The recent clinical study reporting a correlation between improved oxygenation during early pronation and survival of patients with C-ARDS may confirm a causal relationship between changes in ventilation-perfusion matching in the prone position and outcome (34).

There are limitations to this study: 1) the sample size was limited, albeit larger than most physiologic studies on this topic (13, 19); 2) patients were enrolled early in the course of C-ARDS and findings may change with clinical evolution; 3) partitioned respiratory mechanics by use of esophageal pressure (especially chest wall and lung compliances) were not measured, leaving the explanation of the effects of chest wall properties in the prone position remained speculative; 4) the EIT characterization of pulmonary regional perfusion by EIT is limited to three-compartment model (ventilated nonperfused, perfused nonventilated, and normal units), while exploration of the larger spectrum of ventilation-perfusion defects might be more accurate for understanding the physiologic effects of prone position; and 5) central hemodynamics, and especially cardiac output were not measured in this cohort, even though they can impact pulmonary perfusion and ventilation-perfusion matching (35). However, central venous saturation remained stable, suggesting unchanged oxygen delivery.

CONCLUSIONS

Prone position in patients with C-ARDS is associated with lung recruitment, decreased risk of atelectrauma, and improved indexes of ventilation-perfusion matching when performed early after intubation. These physiologic mechanisms may represent the causal link between prone position, lung protection, and improved clinical outcomes in C-ARDS.

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