Lung Recruitability in COVID-19–associated Acute Respiratory Distress Syndrome: A Single-Center Observational Study

To the Editor:

The coronavirus disease (COVID-19) outbreak was declared a public health emergency by the World Health Organization on January 30, 2020. A majority (67–85%) of critically ill patients who were admitted to an ICU with a confirmed infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) developed acute respiratory distress syndrome (ARDS) (1, 2). An observational study of 52 cases at a single center, the Jinyintan Hospital (a temporary designated center for critically ill patients with COVID-19) in Wuhan, China, showed that these patients had a high mortality (61.5%) (2). For patients with ARDS, the specific characteristics of this syndrome, such as the respiratory mechanics, remain unknown. In particular, an important clinical question with regard to personalizing the management of these patients is whether the lungs are recruitable with high positive end-expiratory pressure (PEEP) for each individual patient.

Two of the authors of this study (C.P. and H.Q.) were directly in charge of these critically ill patients with SARS-CoV-2–associated ARDS at the Jinyintan Hospital. Clinical decisions about the right PEEP level were challenging, especially when the PEEP was adapted based on the NIH-NHLBI ARDS Network PEEP-$F_{I_{O_2}}$ table. With high PEEP (e.g., 15 cm H_2O), the plateau pressure often became extremely high (>45 cm H_2O) and patients seemed poorly responsive, often displaying only modest improvement in oxygenation, with increased driving pressure and/or development of hypotension. Because of the high clinical workload and the very constrained environment, these bedside observations were not done in a systematic manner or recorded.

Until recently, quantitative assessments of a patient's potential for lung recruitment at the bedside were very imprecise (3). Recently, members of our group (including L.C., M.C.S., and L.B.) described a new mechanics-based index to directly quantify the potential for lung recruitment, called the recruitment-to-inflation ratio (R/I ratio) (4). It estimates how much of an increase in end-expiratory lung volume induced by PEEP is distributed between the recruited lung (recruitment) and the inflation and/or hyperinflation of the "baby lung" when a higher PEEP is applied. It ranges from 0 to 2.0, and the higher the R/I ratio, the higher the potential for lung recruitment. An R/I ratio of 1.0 suggests a high likelihood of recruitment, as the volume will be distributed similarly to the recruited lung and the baby lung. This method can be performed at the bedside and requires only a single-breath maneuver on any ventilator. This maneuver is particularly useful in conditions of high risk of virus transmission by disconnection, transport, or complex procedures. The clinicians in Wuhan decided to use this measure of recruitment in a systematic way in a series of patients with SARS-CoV-2–associated ARDS, and also to assess the effect of body positioning.

Methods

This was a retrospective, observational study conducted in a 35-bed ICU at Wuhan Jinyintan Hospital. The institutional ethics review board approved this study (KY-2020-10.02). Written informed consent was waived owing to the observational design of the study and the urgent need to collect data for this infectious disease. The clinical charts of adult patients with laboratory-confirmed COVID-19 admitted to the ICU were reviewed. The patients received invasive mechanical ventilation and met the criteria for ARDS (Berlin definition) (5), were under continuous infusion of sedatives, and were assessed for respiratory mechanics, including lung recruitability, during the week of February 18, 2020. This week (a 6-d observational window) was selected in order for the clinical team to record these additional measurements in the chart.

Patients were ventilated in volume-controlled mode with VT at 6 ml/kg of predicted body weight. Prone positioning was performed over periods of 24 hours when $Pa_{O_2}/F_{I_{O_2}}$ was persistently lower than 150 mm Hg. Flow, volume, and airway pressure were measured by ventilators (SV300; Mindray). Circuit leakage was excluded through a 6-second end-inspiratory occlusion. Measurements were performed at clinically set PEEP levels and were repeated every morning during the observation days, when possible. Total PEEP and plateau pressure were measured by a short end-expiratory and an end-inspiratory occlusion, respectively. Complete airway closure was assessed by performing a low-flow (6 L/min) inflation and by comparing patients' compliance with circuit compliance as previously described (6). The potential for lung recruitment was assessed by means of the R/I ratio (4), which can be calculated automatically from a webpage (https://crec.coemv.ca). Because of the limited access to computers or the internet while under airborne precautions, one of the authors (L.C.) provided a compact form for calculating the R/I ratio manually. In patients without airway closure,

$$\text{R/I ratio} = \frac{\text{VTe}_{\text{H}\rightarrow\text{L}} - \text{VTe}_{\text{H}}}{\text{VTi}} \times \frac{\text{Pplat}_{\text{L}} - \text{PEEP}_{\text{L}}}{\text{PEEP}_{\text{H}} - \text{PEEP}_{\text{L}}} - 1$$

where $\text{VTe}_{\text{H}\rightarrow\text{L}}$ indicates the VT exhaled from high to low PEEP during the single-breath maneuver, VTe_{H} is the exhaled VT at high PEEP, VTi is the preset inspiratory VT, Pplat_{L} is the plateau pressure at low PEEP, and PEEP_{H} and PEEP_{L} denote high and low PEEP, respectively. In patients with airway closure, the low PEEP was replaced with the measured airway opening

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pressure when the airways were reopened above the airway closure (6).

A threshold of 0.5 was used to define high recruitability (R/I ratio $\geq$ 0.5) and low recruitability (R/I ratio $<$ 0.5). Note that recruitability can differ at different ranges of pressure. In the present study, the R/I ratio was measured from 15 to 5 cm H_2O in all patients.

Results

Twelve patients (seven males and five females, age 59 ± 9 yr) were enrolled. All of the patients had been transferred from other hospitals. On the day of intubation, $Pa_{O_2}/F_{I_{O_2}}$ was 130 ± 55 mm Hg with Pa_{CO_2} 57 ± 27 mm Hg. Of note, the patients received various days of noninvasive or invasive ventilatory support before the first day of observation (Table 1). During the 6-day period of observation, seven patients received at least one session of prone positioning. Three patients received both prone positioning and extracorporeal membrane oxygenation. Three patients (25%) died.

The worst values for gas exchange and respiratory mechanics are reported in Table 1 ("worst" meaning lowest $Pa_{O_2}/F_{I_{O_2}}$, highest driving pressure, or lowest respiratory system compliance). Neither complete airway closure nor auto-PEEP was found in any patient.

Among the 12 patients, 10 (83%) were poorly recruitable (R/I ratio, 0.21 ± 0.14) on the first day of observation. As shown in Figure 1, patients who did not receive prone positioning had persistent poor recruitability (only 1 out of 17 daily measurements showed high recruitability). In contrast, alternating the body position between supine and prone positioning was associated with increased lung recruitability (13 out of 36 daily measurements showed high recruitability; $P = 0.020$ by chi-square test between two groups). Prone positioning is indicated as an upside-down triangle in Figure 1. In patients who received prone positioning, $Pa_{O_2}/F_{I_{O_2}}$ went from 120 ± 61 mm Hg at supine to 182 ± 140 mm Hg at prone ($P = 0.065$ by paired t test).

Discussion

This is the first study to describe respiratory mechanics and lung recruitability in a small cohort of mechanically ventilated patients with SARS-CoV-2–associated ARDS. The main findings may be important for clinical management and can be summarized as follows: *1*) none of the enrolled patients had complete airway closure or auto-PEEP, *2*) driving pressure was high and respiratory system compliance was low, and *3*) a majority of the patients were poorly recruitable, with high PEEP, but the recruitability seemed to change when alternating body positions were used.

Our findings are not generalizable to all cases of SARS-CoV-2–associated ARDS. First of all, the sample was small ($n = 12$) and nonrandom. The patients had severe disease and on average had 22 cm H_2O of driving pressure despite using 6 ml/kg V_T. Although we were not able to compare the recruitability measured by the R/I ratio with that assessed by another technique (e.g., computed tomography), the low R/I ratio at Day 1 seemed consistent with the clinical impression of the clinicians. Of note, these patients had received various durations of noninvasive and invasive mechanical ventilation, and it would have been ideal to obtain these measurements as soon as the patients were intubated. The surprising finding that alternating body position is followed by increased lung recruitability is interesting but needs to be confirmed. The improvement in oxygenation with prone positioning was not statistically significant but seemed to be

Table 1. Worst Gas Exchange and Respiratory Mechanics during Observation Days

Patient No.	NIV/NHF Days*	IMV Days†	ARF Days‡	$F_{I_{O_2}}$	$Pa_{O_2}/F_{I_{O_2}}$ (*mm Hg*)	Pa_{CO_2} (*mm Hg*)	Pplat (*cm H_2O*)	ΔP§ (*cm H_2O*)	Crs‖ (*ml/cm H_2O*)	Prone¶	ECMO	Outcome
1	5	3	8	0.55	163.6	62	24	14	30	No	No	Dead
2	0	2	2	0.45	165	54	32	28	12	No	No	Alive
3	0	21	21	0.5	180	74	29	14	32	No	No	Alive
4	10	0	10	0.5	136	97	25	15	24	No	No	Dead
5	4	0	4	0.5	178	54	25	17	21	No	No	Alive
6	8	4	12	0.7	55	64	23	18	18	Yes	No	Alive
7	0	1	1	0.65	106	70	48**	43**	10	Yes	No	Dead
8	5	0	5	0.7	209	>115	27	23	17	Yes	No	Alive
9	5	4	9	0.55	128	70	22	12	30	Yes	No	Alive
10	4	8	12	1.0	90	69	35	25	9	Yes	Yes	Alive
11	2	1	3	1.0	57	49	35	25	18	Yes	Yes	Alive
12	7	9	16	1.0	68	58	38	30	14	Yes	Yes	Alive
Mean	4	4	9	0.7	128	66	30	22	20	—	—	—
SD	3	6	6	0.21	53	13	8	9	8	—	—	—
Total	—	—	—	—	—	—	—	—	—	7Y/5N	3Y/9N	9A/3D

Definition of abbreviations: ARF = acute respiratory failure; Crs = respiratory system compliance; ΔP = driving pressure; ECMO = extracorporeal membrane oxygenation; IMV = invasive mechanical ventilation; NHF = nasal high flow; NIV = noninvasive ventilation; PEEP = positive end-expiratory pressure; Pplat = plateau pressure.

*Days receiving NIV or NHF before intubation.

†Days on IMV before enrollment in the study.

‡ARF days were defined as days from the onset of respiratory failure with any form of ventilatory support until enrollment in the study.

§Driving pressure was the difference between the plateau pressure and total PEEP, measured at 6 ml/kg of V_T.

‖Crs was calculated as V_T divided by the difference between the plateau pressure and total PEEP.

¶Received at least one session of prone positioning.

**Suspected tension pneumothorax.

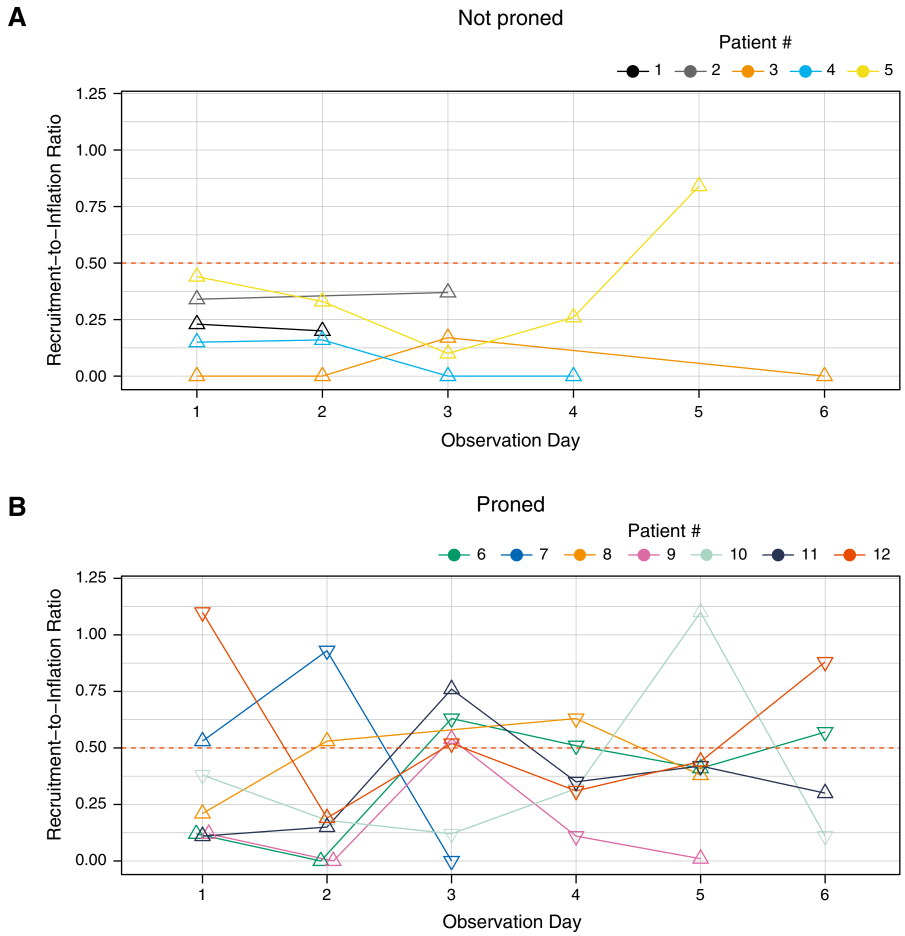

Figure 1. Daily measurements of the recruitment-to-inflation (R/I) ratio for each patient during the observation days. Each patient is indicated by a distinct color. (*A*) Five patients who did not receive prone positioning. Each triangle denotes a measurement in the supine position. (*B*) Seven patients who received at least one session of prone positioning. Each upside-down triangle denotes a measurement in the prone position. Notice that each session of prone positioning was maintained for 24 hours. The dashed line represents the cutoff of the R/I ratio for defining lung recruitability (R/I ratio ⩾ 0.5 suggests highly recruitable).

clinically relevant. Three patients received both prone positioning and extracorporeal membrane oxygenation, which may also affect lung recruitability (7).

During our clinical practice, PEEP was set at the clinicians' own discretion. However, once the R/I ratio was determined, 5–10 cm H_2O of PEEP was usually used if the patient was poorly recruitable. In highly recruitable patients, a higher PEEP was used as long as the plateau pressure was tolerable.

In conclusion, our data show that lung recruitability can be assessed at the bedside even in a very constrained environment and was low in our patients with COVID-19–induced ARDS. Alternating body positioning improved recruitability. Our findings do not imply that all patients with SARS-CoV-2–associated ARDS are poorly recruitable, and both the severity and management of these patients can differ remarkably among regions. Instead, we think these findings might prompt clinicians to assess respiratory mechanics and lung recruitability in this population. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Ventilatory Ratio in Hypercapnic Mechanically Ventilated Patients with COVID-19–associated Acute Respiratory Distress Syndrome

To the Editor:

Lung-protective ventilation with low VT has become a cornerstone of management in patients with acute respiratory distress syndrome (ARDS) (1, 2). However, a consequence of low-VT ventilation is hypercapnia, which has significant physiological effects and may be associated with higher hospital mortality (2, 3).

Ventilatory ratio (VR), defined as [minute ventilation (ml/min) × Pa_{CO_2} (mm Hg)]/[predicted body weight × 100 (ml/min) × 37.5 (mm Hg)] (4), is a simple bedside index of impaired efficiency of ventilation and correlates well with physiological VD fraction (VD-to-VT ratio, VD/VT) in patients with ARDS (4–6). However, the VR and appropriate lung ventilation strategy for coronavirus disease (COVID-19)-associated ARDS remain largely unknown.

Here, we report a case series highlighting ventilatory ratio in hypercapnic mechanically ventilated patients with COVID-19–associated ARDS in our ICU and their individualized ventilation strategies.

Case Series

The study was approved by the ethics committee of the First Affiliated Hospital of Guangzhou Medical University. The requirement for informed consent was waived because the study was observational and the family members were in quarantine.

The First Affiliated Hospital of Guangzhou Medical University is the designated center for patients with COVID-19 in Guangdong, China. We included eight consecutive patients (seven male; mean

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