Lung Recruitability in SARS-CoV-2 Associated Acute Respiratory Distress Syndrome: A Single-center, Observational Study

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Author contributions

P.C., L.C., B.D., L.B., H.Q., conceived the study. P.C., W.Z., and J-A.X. collected the data. L.C. and C.L. conducted data analysis. P.C., L.C., M.C.S., L.B., and H.Q. drafted the manuscript. All authors helped to revise the draft of the manuscript. All authors read and approved the final manuscript.

Funding

This work was partly supported by the research Grant "New Coronavirus Infected Pneumonia Epidemic Emergency Project" (2020YFC0843700) from Ministry of Science and Technology of the People's Republic of China.

Word Count 1440 words

To the Editor:

Coronavirus disease 2019 (Covid-19) outbreak has been declared a public health emergency by the World Health Organization on January 30, 2020. A majority (67-85%) of critically ill patients admitted in intensive care units with confirmed infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) developed the acute respiratory distress syndrome (ARDS) (1, 2). The mortality of these patients was high (61.5%) in an observational study of 52 cases (2) from a single center – the Jinyintan Hospital (a temporary designated center for critically ill patients with Covid-19), Wuhan, China. For patients with ARDS, the specific characteristics of the syndrome, such as respiratory mechanics, remain unknown. In particular, an important clinical question for personalizing the management of these patients is whether the lungs are recruitable with high positive end-expiratory pressure (PEEP) for each individual patient.

During the care of these critically ill patients with SARS-CoV-2 associated ARDS at the Jinyintan Hospital, two of the authors (C.P. and H.Q.) were directly in charge of these patients. Clinical decisions about the right PEEP level were challenging, especially when the PEEP was adapted based on the ARDSnet PEEP-FiO_2 table. With high PEEP (e.g., 15 cmH_2O), the plateau pressure often became extremely high (> 45 cmH_2O) and patients seemed poorly responsive, often displaying only modest improvement in oxygenation, with increased driving pressure and/or developed hypotension. Due to the high clinical workload and the very constrained environment, these bedside observations were not done in a systematic manner nor recorded.

Until recently, quantitatively assessing the potential for lung recruitment was very imprecise at the bedside (3). Recently, our group (LC, MCS, LB) 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: a R/I ratio of 1.0 suggests a high likelihood of recruitment, as the volume will be distributed similarly to the recruited lung and to the baby lung. This method can be done at the bedside and only requires 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 is 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 due to the observational design and the urgent need to collect data for this infectious disease. The clinical charts of adult patients with laboratory-confirmed Covid-19 admitted in the ICU were reviewed. They received invasive mechanical ventilation and met 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-day 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 tidal volume at 6 mL/kg of predicted body weight. Prone positioning was performed over periods of 24 hours when PaO_2/FiO_2 was persistently lower than 150 mmHg. Flow, volume, and airway pressure were measured by ventilators (SV300, Mindray, China). Circuit leakage was excluded through a 6-second end-inspiratory occlusion. Measurements were performed at clinically set PEEP 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 with circuit compliance as previously described (6). Potential for lung recruitment were assessed by the R/I ratio (4), which can be calculated automatically from a webpage (https://crec.coemv.ca). Due to the limited access to computers or internet while under airborne precautions, one author (LC) provided a compact form for calculating the R/I ratio manually. In patients without airway closure:

$$R/I\ ratio = \frac{V_{Te,\,H\rightarrow L} - V_{Te,\,H}}{V_{Ti}} \times \frac{P_{plat,\,L} - PEEP_L}{PEEP_H - PEEP_L} - 1$$

where $V_{Te,\,H\rightarrow L}$ indicates the tidal volume exhaled from high to low PEEP during the single-breath maneuver, $V_{Te,H}$ is the exhaled tidal volume at high PEEP, V_{Ti} is the preset inspiratory tidal volume, $P_{plat,\,L}$ is the plateau pressure at low PEEP, $PEEP_H$ and $PEEP_L$ denotes high and low PEEP, respectively. In patients with airway closure, the low PEEP is replaced with the measured airway opening pressure when airways are reopened above airway closure (6).

A threshold of 0.5 was used as for defining high recruitability (R/I ratio ≥ 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 cmH_2O in all patients.

Results

Twelve patients were enrolled (7 males and 5 females, age 59±9 years). All patients had been transferred from other hospitals. On the day of intubation, PaO_2/FiO_2 was 130±55 mmHg with $PaCO_2$ 57±27 mmHg. Of note, patients received various days of noninvasive or invasive ventilatory support before the 1st day of observation. During the 6-day period of observation, 7 patients received at least one session of prone positioning. Three patients received both prone positioning and ECMO. Three patients died (25%).

The worst values for gas exchange and respiratory mechanics are reported in Table 1 (“worst” meaning lowest PaO_2/FiO_2 or 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) 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 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 position, PaO_2/FiO_2 went from 120±61 mmHg at supine to 182±140 mmHg 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 are outlined below: 1) None of the enrolled patients had complete airway closure nor auto-PEEP; 2) driving pressure was high and respiratory system compliance was low; 4) a majority of them were poorly recruitable with high PEEP but the recruitability seemed to change when alternating body position.

The generalizability of our findings to all cases of SARS-CoV-2 associated ARDS cannot be made. First of all, the sample size (n=12) is small and non-random. The patients were severe and had on average 22 cmH_2O of driving pressure despite using 6 ml/kg tidal volume. Although we were not able to compare the recruitability measured by the R/I ratio with other technique (e.g., computer 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 duration of noninvasive and invasive mechanical ventilation and it would have been ideal to measure these patients as soon as they were intubated. A surprising finding that alternating body position is followed with increased lung recruitability is interesting but needs to be confirmed. The improvement in oxygenation at prone positioning was not statistically significant but seemed to be 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 clinicians' own discretion. However, once the R/I ratio was determined, 5-10 cmH_2O of PEEP was usually used if the patient is 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 is 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 were poorly recruitable, and both the severity and management of these patients can remarkably differ among regions. Instead, we think these findings might incite clinicians to assess respiratory mechanics and lung recruitability in this population.

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Figure Legends

Figure 1. Daily measurements of the Recruitment-to-Inflation (R/I) ratio for each individual patient during the observation days. Each patient is presented in a distinct color. A: Five patients who did not receive prone positioning. Each triangle denotes a measurement in supine position. B: Seven patients who received at least one session of prone positioning. Each upside-down triangle denotes a measurement in prone position. Notice that each session of prone positioning was maintained for 24 hours. The dash line represents the cut-off of R/I ratio for defining lung recruitability (R/I ratio ≥ 0.5 suggests highly recruitable).

Table 1. Worst gas exchange and respiratory mechanics during observation days

Patient No.	NIV/NHF Days*	IMV days#	ARF days**	FiO_2	PaO_2/FiO_2 (mmHg)	$PaCO_2$ (mmHg)	P_{plat} (cmH_2O)	ΔP‡ (cmH_2O)	Crs § (ml/cmH_2O)	Proned¶	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	7Y/5N	3Y/9N	9A/3D
SD	3	6	6	0.21	53	13	8	9	8			

Abbreviations: NIV = non-invasive ventlaiton; NHF = nasal high flow; IMV = invaisve mechanical ventilation; ARF = acute respiratory failure; PaO_2/FiO_2 = the ratio of partial pressure arterial oxygen and fraction of inspired oxygen; PEEP = postive end-expiratory pressure; Pplat = plateau pressure; ΔP = driving pressure; Crs = respiratory system compliance; ECMO = extracorporeal membrane oxygenation

* Days receiving non invasive ventilation or nasal high flow before intubation.

\# Invasivally mechanical ventialtion days before the study enrollment.

** ARF days is defined as the day from the onset of respiratory failure with any form of ventilatory support until the study enrollment.

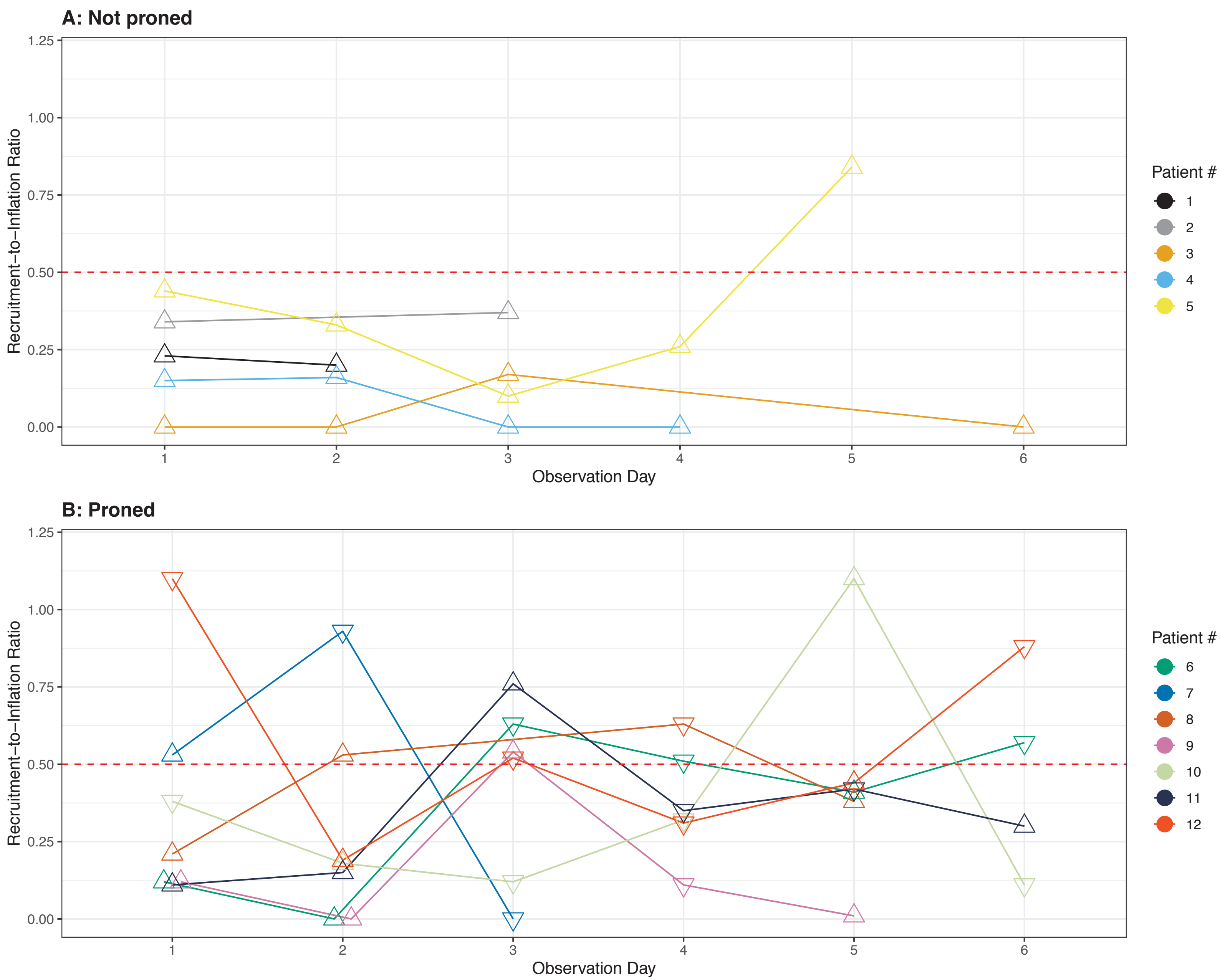
† Suspected tension pneumothorax.

‡ Driving pressure as the difference between plateau pressure and total PEEP, measured at 6 ml/kg of tidal volume.

§ Crs was calcualted as tidal volume divided by the difference between plateau pressure and total PEEP.

¶ Received at least one session of prone positioning.

Figure 1


A: Not proned
Recruitment-to-Inflation Ratio
1.25
1.00
0.75
0.50
0.25
0.00
1
2
3
4
5
6
Observation Day
Patient #
1
2
3
4
5
B: Proned
Recruitment-to-Inflation Ratio
1.25
1.00
0.75
0.50
0.25
0.00
1
2
3
4
5
6
Observation Day
Patient #
6
7
8
9
10
11
12