Ventilatory Ratio in Hypercapnic Mechanically Ventilated Patients with COVID-19 Associated ARDS

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Introduction

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

Ventilatory ratio (VR), defined as [minute ventilation (mL/min) × $PaCO_2$ (mmHg)] / [predicted body weight × 100 (mL/min) × 37.5 (mmHg)] (4), is a simple bedside index of impaired efficiency of ventilation and correlates well with physiological dead space fraction (dead space to tidal volume ratio, VD/VT) in patients with ARDS (4-6). However, the VR and appropriate lung ventilation strategy for Corona Virus Disease 2019 (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 intensive care unit (ICU) and their individualized ventilation strategy.

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 COVID-19 patients in Guangdong, China. We included eight consecutive patients (7 male;

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mean age 63.2 ± 11.0 years) who were intubated in another hospital before being transferred to our ICU. All patients had a history of exposure in Wuhan City or direct contact with patients with confirmed COVID-19. All patients reported fever, cough, shortness of breath, generalized weakness before hospitalization, and tested positive for SARS-CoV-2 based on real-time polymerase chain reaction of throat swab specimens. All patients were diagnosed with ARDS according to the Berlin definition (7): arterial oxygen pressure/fractional inspired oxygen concentration (PaO_2/FiO_2) ratio 102.0 ± 29.7 mmHg (mean ± SD), with Acute Physiology and Chronic Health Evaluation (APACHE) II score 21.6 ± 5.3 and Sequential Organ Failure Assessment (SOFA) score 9.1 ± 2.7 (Table 1).

A ventilation strategy using a low tidal volume of 6.0 mL/kg predicted body weight (PBW) was used in the first 4 consecutive patients. However, they had respiratory distress with low SPO_2, so we immediately increased VT to 7.0 ± 0.6 mL/kg PBW (Table 2). This resulted in an acceptable plateau pressure (23.3 ± 2.2 cmH_2O) and driving pressure (12.3 ± 1.7 cmH_2O). However, all four patients developed hypercapnia [arterial carbon dioxide pressure ($PaCO_2$), 57.7 ± 5.2 mmHg]. Respiratory system compliance was only moderately reduced (static respiratory system compliance, 35.7 ± 5.8 mL/cmH_2O). To examine this issue, we measured VR; the mean value was 2.1 ± 0.3 in the initial four patients, suggesting high VD/VT (4-6).

WE then performed titration of tidal volume. An increased tidal volume (7.7 ± 0.8 mL/kg PBW) was applied to the initial four patients (Table 2). $PaCO_2$ decreased significantly compared to VT 7.0 mL/kg PBW (57.7 ± 5.2 vs. 44.1 ± 3.6 mmHg, p = 0.003) with permitted plateau pressure (23.3 ± 3.1 cm H_2O) and driving pressure (13.5 ± 2.7 cm H_20). Importantly,

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VR in the four patients was significantly decreased (1.7 ± 0.2 vs. 2.1 ± 0.3, p = 0.018) and PaO_2/FiO_2 was slightly improved (241 ± 38 mmHg vs. 207 ± 61, p = 0.402) compared to VT 7.0 mL/kg PBW. Therefore, an intermediate tidal volume of 7.5 ± 0.6 mL/kg PBW was applied to the subsequent four COVID-19 ARDS patients. The $PaCO_2$ was 41.8 ± 3.7 mmHg and VR was 1.6 ± 0.2.

Discussion

We found that hypercapnia was common in COVID-19-related ARDS patients with low tidal volume ventilation. High VR was found in these patients, indicating inadequacy of ventilation in ARDS patients with COVID-19. An intermediate tidal volume (7-8 ml/kg PBW) ventilation strategy was applied to the first four patients to increase pulmonary efficiency to eliminate CO_2, and this used in the next four patients.

Gas exchange consists of oxygenation and ventilation. Oxygenation is quantified by the PaO_2/FiO_2 ratio and this method has gained wide acceptance, particularly since publication of the Berlin definition of ARDS (7). However, the Berlin definition does not include additional pathophysiological information about ARDS, such as alveolar ventilation, as measured by pulmonary dead space, which is an important predictor of outcome (8). Increased pulmonary dead space reflects the inefficiency of the lungs to eliminate CO_2, which may lead to hypercapnia.

In our ARDS patients with COVID-19, hypercapnia was common at ICU admission with low tidal volume ventilation. Assuming the anatomic portion of dead space is constant, increasing tidal volumes with constant respiratory rate would effectively increase alveolar

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ventilation. Any such increase in VT would decrease $PaCO_2$, which would be captured by VR (6). VR, a novel method to monitor ventilatory adequacy at the bedside (4-6), was very high in our patients, reflecting increased pulmonary dead space and inadequacy of ventilation.

With an acceptable plateau pressure and driving pressure, titration of tidal volume was performed. $PaCO_2$ and VR were significantly decreased when an intermediate tidal volume (7-8 mL/kg PBW) was applied. We suggest that intermediate tidal volumes (7-8 mL/kg PBW) are recommended for such patients. Therefore, low tidal volume may not be the best approach for all ARDS patients, particularly those with a less severe decrease in respiratory system compliance and inadequacy of ventilation.

In summary, we found that hypercapnia was common in patients with COVID-19-associated ARDS while using low tidal volume ventilation. VR was increased in these patients, which reflected increased pulmonary dead space and inadequacy of ventilation. An intermediate tidal volume was utilized to correct hypercapnia efficiently, while not excessively increasing driving pressure. Clinicians must have a high index of suspicion for increased pulmonary dead space when COVID-19-related ARDS patients present with hypercapnia.

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Table 1 Baseline characteristics of eight ARDS patients infected with SARS-CoV-2

Characteristics	Patients (n=8)
Exposure history (n)	8/8
Age(years)	63.2 ± 11.0
Sex (Male)	7/8
Body mass index(kg/m2)	22.7 ± 2.3
Predicted body weight, kg	64.7 ± 6.0
Chronic medical illness (n)	
-Hypertension	4/8
-Diabetes	3/8
-Coronary heart disease	1/8
-Chronic obstructive pulmonary disease	1/8
-Obstructive sleep apnea syndrome	1/8
-Hepatitis B	1/8
-Smoker	3/8
Presenting symptoms onset (n)	
-Fever	8/8
-Cough	7/8
-Generalized weakness	4/8
-Shortness of breath	3/8
Real-time RT-PCR of throat swab (n)	8/8

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Radiologic characteristics (n)	
-Bilateral pneumonia	8/8
-Multiple mottling and ground-glass opacity	8/8
Noninvasive ventilation before intubation (n)	1/8
-Duration of noninvasive ventilation (day)	1
HFNC before intubation (n)	7/8
-Duration of HFNC (day)	2.6 ± 2.2
PaO_2/FiO_2 ratio (mmHg)	102.0 ± 29.7
APACHE II score	21.6 ± 5.3
SOFA score	9.1 ± 2.7
Weaning before day 28 at ICU	5/8
Discharge before day 28 at ICU	5/8
28- day mortality at ICU	0/8

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Table 2 Ventilator settings

Variables	Low VT (initial 4 patients)	Intermediate VT (initial 4 patients)	P value	Intermediate VT (8 patients)
VT (mL/kg PBW)	7.0 ± 0.6	7.7 ± 0.8	0.022	7.5 ± 0.6
$PaCO_2$ (mmHg)	57.7 ± 5.2	44.1 ± 3.6	0.003	41.8 ± 3.7
PaO_2/FiO_2 ratio	207 ± 61	241 ± 38	0.402	230 ± 49
RR (beat/minute)	21.5 ± 2.0	21.0 ± 1.4	0.182	20.1 ± 1.5
VE (L/minute)	9.1 ± 1.0	9.8 ± 1.0	0.020	9.3 ± 1.0
Ventilation Ratio	2.1 ± 0.3	1.7 ± 0.2	0.018	1.6 ± 0.2
Pplat (cmH_20)	23.3 ± 2.2	23.3 ± 3.1	>0.999	23.6 ± 2.7
PEEP (cmH_20)	11.0 ± 1.2	10.0 ± 1.4	0.250	9.6 ± 1.2
ΔP (cmH_20)	12.3 ± 1.7	13.5 ± 2.7	0.080	14.1 ± 2.5
Cst (mL/cmH_2O)	35.7 ± 5.8	36.1 ± 7.9	0.595	33.9 ± 7.6
EELV (mL)	--	2559 ± 61	--	2285 ± 355

Footnote: P value indicates difference between low VT and. intermediate VT of the initial four patients using a paired t test.

Abbreviations: VT: tidal volume; $PaCO_2$: arterial carbon dioxide pressure; PaO_2: arterial oxygen pressure; FiO_2: fractional inspired oxygen concentration; RR: respiratory rate; VE:

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measured minute ventilation; Pplat: plateau pressure; PEEP: positive end-expiratory pressure; ΔP: driving pressure; Cst: static respiratory system compliance; EELV: end-expiratory lung volume.

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