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 \([\text{minute ventilation} \times \text{PaCO}_2] / \text{predicted body weight} \times 100\) (6), 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 age 47 ± 14 years) with community-acquired pneumonia infected with SARS-CoV-2 who were admitted to the ICU between March 10 and March 23, 2020. Two patients had been together at a restaurant prior to hospital admission.

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Table 1. Baseline Characteristics of Eight Patients with Acute Respiratory Distress Syndrome Infected with SARS-CoV-2

| Characteristic                        | Patients (N = 8) |
|---------------------------------------|-----------------|
| Exposure history                      | 8/8             |
| Age, yr                               | 63.2 ± 11.0     |
| Sex, M                                | 7/8             |
| Body mass index, kg/m²                 | 22.7 ± 2.3      |
| Predicted body weight, kg              | 64.7 ± 6.0      |
| Chronic medical illness                |                 |
| 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             |                 |
| Fever                                 | 8/8             |
| Cough                                 | 7/8             |
| Generalized weakness                  | 4/8             |
| Shortness of breath                   | 3/8             |
| Real-time RT-PCR of throat swab       | 8/8             |
| Radiologic characteristics            |                 |
| Bilateral pneumonia                   | 8/8             |
| Multiple motting and ground-glass opacity | 8/8             |
| Noninvasive ventilation before intubation | 1/8             |
| Duration of noninvasive ventilation, d | 1               |
| HFNC before intubation                | 7/8             |
| Duration of HFNC, d                   | 2.6 ± 2.2       |
| PaCO₂/FIO₂ ratio, mm Hg               | 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-d mortality at ICU                 | 0/8             |

Definition of abbreviations: APACHE = Acute Physiology and Chronic Health Evaluation; HFNC = high-flow nasal cannula oxygen therapy; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SOFA = Sequential Organ Failure Assessment.

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                  |
| PaCO₂, mm Hg                     | 57.7 ± 5.2                 | 44.1 ± 3.6                          | 0.003   | 41.8 ± 3.7                 |
| PaO₂/FIO₂ ratio                  | 207 ± 61                   | 241 ± 38                            | 0.402   | 230 ± 49                   |
| RR, beats/min                    | 21.5 ± 2.0                 | 21.0 ± 1.4                          | 0.182   | 20.1 ± 1.5                 |
| Vt, L/min                        | 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, cm H₂O                    | 23.3 ± 2.2                 | 23.3 ± 3.1                          | <0.001  | 23.6 ± 2.7                 |
| PEEP, cm H₂O                     | 11.0 ± 1.2                 | 10.0 ± 1.4                          | 0.250   | 9.6 ± 1.2                  |
| ΔP, cm H₂O                       | 12.3 ± 1.7                 | 13.5 ± 2.7                          | 0.080   | 14.1 ± 2.5                 |
| Cst, ml/cm H₂O                   | 35.7 ± 5.8                 | 36.1 ± 7.9                          | 0.595   | 33.9 ± 7.6                 |
| EELV, ml                         | —                          | 2,559 ± 61                          | —       | 2,285 ± 355                |

Definition of abbreviations: Cst = static respiratory system compliance; ΔP = driving pressure; EELV = end-expiratory lung volume; PBW = predicted body weight; PEEP = positive end-expiratory pressure; Pplat = plateau pressure; RR = respiratory rate.

Discussion

We found that hypercapnia was common in patients with COVID-19-related ARDS with low Vt ventilation. High VR was found in these patients, indicating inadequacy of ventilation in patients with age, 63.2 ± 11.0 yr) 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, and generalized weakness before hospitalization and tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on the basis of real-time PCR of throat swab specimens. All patients were diagnosed with ARDS according to the Berlin definition (7): PaCO₂/FIO₂ ratio, 102.0 ± 29.7 mm Hg (mean ± SD), with Acute Physiology and Chronic Health Evaluation II score 21.6 ± 5.3 and Sequential Organ Failure Assessment score 9.1 ± 2.7 (Table 1).

A ventilation strategy using a low Vt of 6.0 ml/kg predicted body weight (PBW) was used in the first four consecutive patients. However, they had respiratory distress with low oxygen saturation as measured by pulse oximetry, 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 cm H₂O) and driving pressure (12.3 ± 1.7 cm H₂O). However, all four patients developed hypercapnia (PaCO₂, 57.7 ± 5.2 mm Hg). Respiratory system compliance was only moderately reduced (static respiratory system compliance, 35.7 ± 5.8 ml/cm H₂O). 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 Vt. An increased Vt (7.7 ± 0.8 ml/kg PBW) was applied to the initial four patients (Table 2). PaCO₂ decreased significantly compared with Vt 7.0 ml/kg PBW (57.7 ± 5.2 vs. 44.1 ± 3.6 mm Hg; P = 0.003) with permitted plateau pressure (23.3 ± 3.1 cm H₂O) and driving pressure (13.5 ± 2.7 cm H₂O). Importantly, VR in the four patients was significantly decreased (1.7 ± 0.2 vs. 2.1 ± 0.3; P = 0.018) and PaCO₂/FIO₂ was slightly improved (241 ± 38 mm Hg vs. 207 ± 61; P = 0.402) compared with Vt 7.0 ml/kg PBW. Therefore, an intermediate Vt of 7.5 ± 0.6 ml/kg PBW was applied to the subsequent four patients with COVID-19 ARDS. The PaCO₂ was 41.8 ± 3.7 mm Hg, and VR was 1.6 ± 0.2.

Discussion

We found that hypercapnia was common in patients with COVID-19-related ARDS with low Vt ventilation. High VR was found in these patients, indicating inadequacy of ventilation in patients with...
ARDS with COVID-19. An intermediate $V_t$ (7–8 ml/kg PBW) ventilation strategy was applied to the first four patients to increase pulmonary efficiency to eliminate CO$_2$, and this was used in the next four patients.

Gas exchange consists of oxygenation and ventilation. Oxygenation is quantified by the Pa$_{O_2}$/Fi$_{O_2}$ 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 patients with ARDS with COVID-19, hypercapnia was common at ICU admission with low $V_t$ ventilation. Assuming the anatomic portion of dead space is constant, increasing $V_t$ with constant respiratory rate would effectively increase alveolar ventilation. Any such increase in $V_t$ would decrease Pa$_{CO_2}$, 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 $V_t$ was performed. Pa$_{CO_2}$ and VR were significantly decreased when an intermediate $V_t$ (7–8 ml/kg PBW) was applied. We suggest that intermediate $V_t$ (7–8 ml/kg PBW) is recommended for such patients. Therefore, low $V_t$ may not be the best approach for all patients with ARDS, 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 $V_t$ ventilation. VR was increased in these patients, which reflected increased pulmonary dead space and inadequacy of ventilation. An intermediate $V_t$ was used to correct hypercapnia efficiently, while not excessively increasing driving pressure. Clinicians must have a high index of suspicion for increased pulmonary dead space when patients with COVID-19–related ARDS present with hypercapnia. ■

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

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COVID-19 Does Not Lead to a “Typical” Acute Respiratory Distress Syndrome

To the Editor:

In northern Italy, an overwhelming number of patients with coronavirus disease (COVID-19) pneumonia and acute respiratory failure have been admitted to our ICUs. Attention is primarily focused on increasing the number of beds, ventilators, and intensivists brought to bear on the problem, while the clinical approach to these patients is the one typically applied to severe acute respiratory distress syndrome (ARDS), namely, high positive end-expiratory pressure (PEEP) and prone positioning. However, the patients with COVID-19 pneumonia, despite meeting the Berlin definition of ARDS, present an atypical form of the syndrome. Indeed, the primary characteristic we are observing (and has been confirmed by colleagues in other hospitals) is a dissociation between their relatively well-preserved lung mechanics and the severity of hypoxemia. As shown in our first 16 patients (Figure 1), a respiratory system compliance of 50.2 ± 14.3 ml/cm H$_2$O is associated with a shunt fraction of 0.50 ± 0.11. Such a wide discrepancy is virtually never seen in most forms of ARDS. Relatively high compliance indicates a

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