Norms and Advice | Expert advice on Procedure of Respiratory Therapy for Severe Novel Coronavirus Pneumonia

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Novel coronavirus pneumonia is mainly manifested as fever, dry cough and fatigue. Most patients may develop dyspnoea 1 week later, and severe patients may rapidly develop acute respiratory distress syndrome (ARDS). The main clinical diagnostic criteria for severe and critical cases in the Schemes of Diagnosis and Treatment of Severe and Critical Cases of Novel Coronavirus Pneumonia (Trial)[1] released by the National Health Commission is presence of ARDS of different severities that requires respiratory supportive treatment. The Schemes have pointed out that the treatment regimens include oxygen therapy, high-flow nasal cannula oxygen therapy (HFNC), non-invasive ventilation (NIV), invasive mechanical ventilation and extracorporeal membrane oxygenation (ECMO). The Schemes have especially pointed out that when receiving HFNC or NIV, patients need to be closely observed for 2 hours, and if the patients are not improved or cannot tolerate, tracheal intubation should be performed timely for invasive mechanical ventilation; invasive mechanical ventilation should be combined with the "lung protective ventilation strategy"; prone position ventilation should be performed for patients with severe ARDS, and ECMO should be performed if mechanical ventilation still fails

to improve oxygenation. On 28 JAN 2020, the World Health Organization (WHO) also published the updated Clinical Guidelines for 2019-nCoV-related Severe Infections[2], which states that when standard oxygen therapy for patients with severe acute respiratory infection (SARI) fails, HFNC or NIV should be used only for patients with specific hypoxemia-induced respiratory failure, and patients treated with HFNC or NIV should be closely monitored for clinical deterioration. In terms of mechanical ventilation, it also proposes the strategies of low tidal volume (Vt) and prone position, as well as ECMO for patients with repeated hypoxemia after lung protective ventilation.

The available guidelines have not provided specific monitoring and implementation indicators. Under the current situation that tens of medical teams in different provinces and many designated hospitals are treating patients, it is urgent to unify the standard procedure of respiratory therapy to improve the homogeneity of treatment, thereby reducing the fatality rate of patients. To this end, under the guidance of the experts in the National Health Commission, in accordance with the Schemes of Diagnosis and Treatment released by the National Health Commission and the WHO Clinical Guidelines, and based on the ARDS treatment procedures in China and foreign countries[4-5], the expert group for the treatment of severe and critical cases of novel coronavirus pneumonia has formulated the procedure of respiratory therapy for severe and critical cases of novel coronavirus pneumonia (Figure 1).

Figure 1 Procedure of respiratory therapy for severe novel coronavirus pneumonia

In this procedure, the severity is stratified and graded by the modified oxygenation index [arterial partial pressure of oxygen (PaO2) / fraction of inspiration O2 (FiO2), P/F] of patients with severe novel coronavirus pneumonia patients, and different strategies of respiratory support are adopted.

I. Patients with mild **ARDS**

HFNC is preferred for patients with P/F of 200-300 mmHg (1 mmHg = 0.133 kPa), and the HFNC parameters are set as flow rate 40-50 L/min and FiO2 100%. During the treatment, vital signs and oxygenation shall be closely observed for 2 h according to the regimen of Roca et al[6], and the ROX index shall be evaluated, where ROX index = pulse oxygen saturation (SpO2) / [FiO2 × respiratory rate (RR)]. After 2 h of HFNC treatment, ROX index ≥ 3.85 or SpO2 ≥93% and RR <25 times/min indicate a high success rate of HFNC treatment, and HFNC treatment shall be continued; ROX index <2.85 or SpO2 <93% and RR >30 times/min indicate a low success rate of HFNC treatment, and it shall be changed to non-invasive ventilation, and if accompanied by any of the following: disturbance of consciousness, malignant arrhythmia, severe shock [noradrenaline dose >0.1 μg/(kg•min)], acute respiratory acidosis (pH <7.25) and airway drainage disorder, it shall be changed to tracheal intubation for invasive mechanical ventilation. If 2.85≤ ROX index <3.85 or SpO2 >93% but RR >25 times/min, the HFNC treatment shall be continued, the conditions and vital signs shall be closely observed for 6 h and the ROX index shall be calculated again, and if the ROX index is still <3.85 or SpO2 <93% and RR >30 times/min, tracheal intubation shall be immediately performed for invasive mechanical ventilation. If ROX index >3.85 or SpO2 >93% but RR >25 times/min, the HFNC treatment shall be continued, the conditions and vital signs shall be closely observed for 12 h and the ROX index shall be calculated again, and if ROX index is still >4.88 or SpO2 ≥93% and RR <25 times/min, the HFNC treatment shall be continued and the vital signs shall be closely observed; if the ROX index <4.88 or SpO2 >93% but RR >25 times/min, tracheal intubation shall be performed for invasive mechanical ventilation. In a previous study[7], after HFNC failed, it was changed to NIV, and if NIV failed again, tracheal intubation for invasive mechanical ventilation would be significantly delayed, which might increase the fatality rate of patients. In the patients who switched to NIV after failure of HFNC in Wuhan Lung Hospital, the support conditions of HFNC were already very high (oxygen flow rate 40.50 L/min, FiO2 100%), so NIV was hardly successful, and all the patients switched to invasive mechanical ventilation finally. Therefore, for those who cannot succeed under the given HFNC support conditions, it is recommended to switch directly to tracheal intubation for invasive ventilation,

but not NIV followed by invasive ventilation if fails.

II. Patients with mild to moderate **ARDS**

For patients with P/F of 150-200 mmHg, NIV shall be initially selected. The NIV parameters are initially set as inspiratory positive airway pressure (IPAP) 8-10 cmH2O (1 cmH2O = 0.098 kPa), expiratory positive airway pressure (EPAP) 5-8 cmH2O, and FiO2 100%. A previous study on NIV in the treatment of ARDS suggests that Vt >9 ml/kg is an independent risk factor of NIV failure and even increased fatality rate[8]. Therefore, it is recommended that patients be observed for 2 hours when undergoing NIV. If Vt is ≤9 ml/kg, NIV shall be continued, and if Vt is >12 ml/kg, NIV shall be immediately changed to tracheal intubation for invasive mechanical ventilation. If Vt is 9-12 ml/kg, NIV shall be continued and patients be observed for 6 hours, if Vt is ≤ 9 ml/kg, NIV shall be continued, and if Vt is > 9 ml/kg, NIV shall be stopped and changed to tracheal intubation for invasive mechanical ventilation.

III. Patients with moderate to severe **ARDS**

(I) Lung protective ventilation strategy with low **Vt** as the core

For patients with P/F below 150 mmHg, initially undergoing HFNC or NIV and reaching the criteria for tracheal intubation for invasive mechanical ventilation, medical staff performing tracheal intubation shall protect themselves with sealed protective helmets and immediately perform mask oxygen inhalation, analgesia and sedation. Visual laryngoscope is recommended for tracheal intubation.

Invasive mechanical ventilation cannot be performed until successful intubation, and in accordance with the invasive mechanical ventilation process for ARDS[5], the “lung protective ventilation strategy” shall be adopted.

Vt shall be initially set as 6 ml/kg (ideal body weight), and ideal body weight shall be calculated by the following formula: Ideal body weight for males (kg) = 50 + 0.91 × [body height (cm) - 152.4], and ideal body weight for females (kg) = 45.5 + 0.91 × [body height (cm) - 152.4].

After Vt is set, it is necessary to monitor the pressure during mechanical ventilation and control the inspiration plateau pressure below 30 cmH2O. If the plateau pressure is >30 cmH2O, Vt must be gradually reduced at a speed of 1 ml/kg until the inspiration plateau pressure is <30 cmH2O or Vt is reduced to 4 ml/kg.

To ensure alveolar minute ventilation and avoid CO2 retention while reducing Vt, we shall increase RR accordingly. When Vt is reduced by 1 ml/kg , RR shall be increased by 5 times. After RR is increased, the expiratory flow rate on the flow rate-time curve of the ventilator shall

reach zero at the end of expiration. If it fails to reach zero, it is necessary to reduce the RR or adjust the expiration/inspiration ratio to increase the expiration time.

To ensure patient safety, it is recommended that the initial FiO2 be set to 100%, and then after the severity of respiratory failure is determined, it can be adjusted according to the status of oxygenation. According to correlation between FiO2 and positive end expiratory pressure (PEEP) recommended by ARDSnet, appropriate FiO2 and PEEP shall be selected to maintain SpO2 at 88%-95%.

(II) Pulmonary re-expandability evaluation, pulmonary re-expansion performing and **PEEP** titration

For patients undergoing invasive mechanical ventilation according to the lung protective ventilation strategy, when FiO2 >50% is required to maintain the target oxygenation, pulmonary re-expandability evaluation is required, including CT, ultrasound, P-V curve, EIT, etc.

To improve the bedside operability for the medical staff, it is recommended to: increase the ventilator PEEP from the basic value to 15 cmH2O, and 15 minutes later, evaluate whether P/F improves, whether the partial pressure of carbon dioxide (PaCO2) decreases and whether lung compliance improves. Lungs can be considered re-expandable if 2 of the above 3 criteria are met. Patients with pulmonary re-expandability shall undergo pulmonary re-expansion. At present, there are mainly three methods of pulmonary re-expansion: (1) Sustained inflation (SI): adopt continuous positive airway pressure, and set the positive pressure at 30-45 cmH2O for 30 s; (2) PEEP stepwise increase: use the pressure control mode, set the upper limit of airway pressure as 35 cmH2O, and increase PEEP by 5 cmH2O and pressure by 5 cmH2O every 30 s. When the airway pressure reaches the upper limit of 35 cmH2O, only increase the PEEP to 35 cmH2O and maintain for 30 s; (3) pressure control: increase the pressure and PEEP. Generally, the pressure is increased to 40-45 cmH2O and PEEP to 15-25 cmH2O and maintained for 1-2 min. It is recommended to use pulmonary re-expansion method most familiar to medical staff. If pulmonary re-expansion is effective, it means that the original PEEP is low and not adequate to avoid end-expiratory alveolar collapse, so PEEP should be titrated after pulmonary re-expansion. Generally, appropriate PEEP is determined by the optimal oxygenation method: PEEP is initially set as 20 cmH2O and decreased by 2 cmH2O every 2 min until oxygenation decreases significantly, PEEP before oxygenation decrease is considered as the best PEEP required by patients, and then PEEP is set as the best measured value after pulmonary re-expansion.

(III) Driving pressure-guided ventilation strategy

For patients with no pulmonary re-expandability and those who have pulmonary re-expandability but still require P/F <150 mmHg at FiO2 >60% after pulmonary re-expansion and PEEP titration, under the condition of volume-controlled ventilation, the driving pressure (DP) shall be calculated by measuring end-inspiratory plateau pressure and end-expiratory positive pressure, and oesophageal pressure shall be measured if possible for DP calculation. Patients with DP >15 cmH2O shall receive neuromuscular blockers, and Vt and PEEP shall be titrated again according to DP. For patients with DP <15 cmH2O but Vt <6 ml/kg complicated with CO2 retention, Vt can be appropriately increased to achieve DP ≤15 cmH2O. After the above treatment and adjustments, if P/F is still <150 mmHg at FiO2 >60%, the patients shall undergo prone position ventilation for ≥12 h and be observed for 24 h. If FiO2 is >60%, P/F <100 mmHg, Pplat >35 cmH2O, PaCO2 >50 mmHg and pH <7.25, intravenous ECMO shall be performed.

(IV) Hypercapnia treatment strategy

After low Vt ventilation strategy is performed, if PaCO2 is ≤50 mmHg, it is just respiratory acidosis, and pH is usually above 7.25, so no special treatment is needed. If PaCO2 is >50 mmHg and pH <7.25, it is recommended to increase RR first to increase CO2 emission by increasing minute ventilation, but if RR is increased to 35 times/minute, PaCO2 is still >50 mmHg, and pH of acidosis due to respiratory factors is <7.25, it is recommended to perform ECMO for rescue.

(V) Invasive mechanical ventilation withdrawal

If patient's condition improves after treatment, and the plateau pressure is <30 cmH2O, FiO2 ≤40% and PEEP ≤5 cmH2O, the ventilator can be switched from the control mode to the pressure support mode. Withdrawal of invasive ventilator can be considered when the following criteria are met: (1) conscious; (2) with stable circulation, i.e., no vasoactive drugs or dopamine <5 μg/(kg•min) or noradrenaline <20 μg/min; (3) receiving pressure support ventilation, FiO2 ≤40%, PEEP ≤5 cmH2O, SpO2 >95% or P/F ≥250 mmHg, 35 mmHg≤ PaCO2 ≤50 mmHg or rapid shallow breath index [Vt (ml) / RR] ≤105.

Spontaneous breathing trial (SBT) is recommended before extubation, and SBT can be performed using the following methods: (1) T-tube method: disconnect the ventilator, and inhale oxygen through tracheal intubation; (2) continuous positive airway pressure (CPAP): set the pressure at 5 cmH2O; (3) pressure support ventilation (PSV): PEEP ≤5 cmH2O, and set the pressure support level at 5-7 cmH2O. Patients shall be observed for about 30 min. Indicators of successful SBT: rapid shallow breath index <105, 8 times/min< RR <35 times/min, Vt >4 ml/kg, HR <140 beats/min or changed by <20% during SBT, no new arrhythmia, and SpO2 >90%.

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