Journal of Acute Disease

Communications

jadweb.org

doi: 10.4103/jad.jad_123_25

Oxygenation adjustment of ventilator combined with venovenous extracorporeal membrane oxygenation

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ABSTRACT

In recent years, venovenous extracorporeal membrane oxygenation (VV-ECMO) has emerged as a critical intervention in the management of adult respiratory failure, with its clinical application expanding at a rapid pace annually. For critically ill patients receiving VV-ECMO support, achieving and maintaining a balance between oxygen supply and oxygen consumption is of paramount importance. Oxygen supply primarily relies on cardiac output and arterial oxygen content; notably, in patients under VV-ECMO support, arterial oxygen content is closely linked to the parameter configurations of both VV-ECMO and mechanical ventilators. Therefore, based on national and industrial needs, this document has been formulated by integrating the latest advancements and practical experience in this field from both domestic and international sources. Its core objectives are to standardize the adjustment of oxygen supply during the combined use of mechanical ventilators and VV-ECMO, provide unambiguous guidance for healthcare professionals, and ultimately enhance the success rate in the treatment of severe respiratory conditions.

KEYWORDS: Respiratory failure; VV-ECMO; Mechanical ventilation; Adjustment; Oxygen supply

As the use of venovenous extracorporeal membrane oxygenation (VV-ECMO) for adult respiratory failure increases, managing oxygen delivery is critical. 49 Experts in the field of emergency medicine draft this guideline for regulating oxygen supply during combined VV-ECMO and mechanical ventilator support. Based on the latest evidence, it aims to provide clinicians with clear guidance to improve patient outcomes.

1. Scope

This document outlines the basic conditions, indications, contraindications, and oxygenation management protocol for

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How to cite this article: Lv CZ, Guo W, Chen XF, Mei Y, Sun J, Wang L, et al. Oxygenation management in the combined use of ventilator and venovenous extracorporeal membrane oxygenation. J Acute Dis 2025; 14; 21.

Article history: Received 31 August 2025; Revision 13 October 2025; Accepted 23 October 2025; Available online 29 November 2025

the combined use of mechanical ventilation and VV-ECMO.

This document applies to oxygenation management by medical staff using ventilators in conjunction with VV-ECMO.

This document is not applicable to pediatric and infant patients.

2. Normative references

The document has no normative references.

3. Terms and definitions

The following terms and definitions apply to this document.

3.1. VV–ECMO[1]

This technique involves draining venous blood from the body *via* percutaneous cannulation or surgical cutdown; the blood is then oxygenated and cleared of carbon dioxide by a membrane oxygenator before being infused back into the patient's venous system *via* a centrifugal pump, thereby assuming the gas exchange function and providing respiratory support.

Note: Refer to the "*Technical operation standard for adult extracorporeal membrane oxygenation*" (2024 Edition)[2].

3.2. Positive end–expiratory pressure (PEEP)

PEEP is a technique used in mechanical ventilation. It maintains positive pressure in the airways at the end of exhalation to prevent collapse of the small airways and alveoli and to improve functional residual capacity.

Source: WS 392-2012, 3.14, with revisions[3].

3.3. Predicted body weight (PBW)

PBW is a theoretical standard of healthy body weight used to assess nutritional status, guide drug dosage calculations, and set mechanical ventilation parameters.

Note 1: Formula: Adult male: PBW=50+0.91×[height (cm)-152.4]; Adult female: PBW=45.5+0.91×[height (cm)-152.4].

Note 2: Refer to the "*Perioperative mechanical ventilation for adult non-cardiothoracic surgical patients: A Delphi consensus*" (2024 Edition)[4].

4. Abbreviations

The following abbreviations are used in this document.

FiO_2: Fraction of inspired oxygen

Hb: Hemoglobin

$PaCO_2$: Arterial carbon dioxide pressure

PaO_2: Arterial oxygen pressure

pH: Potential of hydrogen

SaO_2: Arterial oxygen saturation

SpO_2: Pulse oxygen saturation

SvO_2: Venous oxygen saturation

5. Basic conditions[5]

5.1. Environment, facilities and equipment

A unit must have at least the following equipment: blood gas analyzer, hemodynamic monitoring devices, invasive ventilators, and continuous renal replacement therapy equipment and be set up in an intensive care unit (ICU) or equivalent resuscitation facilities.

All VV-ECMO devices, consumables, and related supporting facilities must be certified as compliant with technical and safety standards.

5.2. Personnel and team

Physicians performing VV-ECMO procedures must possess the following qualifications: a) At least 5 years of clinical experience; b) Professional qualifications in one of the following specialties: emergency medicine, critical care medicine, internal medicine, or surgery; c) Completion of specialized VV-ECMO training and the corresponding assessment.

Nurses performing VV-ECMO procedures must undergo systematic training and pass the assessment.

The VV-ECMO team shall consist of at least three members, including two licensed physicians and one nurse. Among the two licensed physicians, one should be the ECMO team leader, who is a physician with experience in VV-ECMO operation and holds a professional title of deputy chief physician or a higher rank. a) Physicians are responsible for: indications assessment, catheterization operations, formulation and operation management of VV-ECMO treatment strategies (formulation of anticoagulation plans, hemodynamic regulation), weaning from the machine and complications management, *etc*. b) Nurses are responsible for: equipment management, parameter monitoring, anticoagulation implementation, complications prevention, meticulous patient care, transfer and emergency response, *etc*.

6. Indications and contraindications[6,7]

6.1. Indications

Patients with respiratory failure who still have poor treatment outcomes under optimal mechanical ventilation conditions ($FiO_2 \geqslant 80\%$, tidal volume 4-6 mL/kg PBW, PEEP $\geqslant 10$ cmH_2O) despite the combined use of protective lung ventilation strategies, lung recruitment maneuvers, and prone position ventilation, *etc.*, with a PaO_2/FiO_2 ratio <80 mmHg.

Patients with respiratory failure who still have hypercapnia, with a pH $\leqslant 7.25$ and $PaCO_2 \geqslant 60$ mmHg, even after optimizing mechanical ventilation (respiratory rate $\geqslant 35$ breaths/min, airway plateau pressure $\leqslant 30$ cmH_2O).

6.2. Contraindications

There are no absolute contraindications. Relative contraindications include:

-Advanced age ($\geqslant 65$ years);

-Immunosuppression;

-Cerebral hemorrhage, severe central nervous system injury, or irreversible and debilitating central nervous system pathological changes;

-Systemic hemorrhage, contraindication to anticoagulant therapy;

-Mechanical ventilation for more than 7 days (airway plateau pressure >30 cmH_2O and FiO_2 >90%).

7. Oxygenation management protocol for combined ventilator and VV–ECMO therapy

7.1. Oxygenation management indicators during combined therapy

7.1.1. General guidelines

During the process of combined mechanical ventilation and VV-ECMO, oxygenation status is dynamically assessed using oxygenation management indicators. These indicators should always remain within a reasonable range of 3 to 5. This range is derived through laboratory measurements of the patient's blood samples, followed by calculation using Formula (1).

7.1.2. Calculation formula

Oxygenation Management Index=$(Hb \times SaO_2 \times 1.34 + PaO_2 \times 0.0031)/[Hb \times (SaO_2 - SvO_2) \times 1.34]$ (1)

Where:

Oxygenation Management Index—The target range for oxygenation management when using ventilator and VV-ECMO should consistently be maintained within a reasonable range of 3-5.

Hb—Measured from a venous blood sample, in g/dL.

SaO_2—Measured from an arterial blood sample, in %.

PaO_2—Measured from an arterial blood sample, in mmHg.

SvO_2—Measured from a blood sample drawn upstream of the ECMO membrane, in %.

7.2. Initial oxygenation management

7.2.1. Initial ventilator settings[8]

a) Initially provide a moderate to high level of PEEP ($\geqslant 10$ cmH_2O).

b) Dynamically adjust tidal volume, respiratory rate, PEEP, and FiO_2, with consideration of such factors as alveolar recruitment potential, risk of barotrauma, lesion homogeneity, hemodynamics, and body weight.

7.2.2. Initial VV–ECMO settings

a) Blood flow: 60-80 mL/kg/min. If blood volume is sufficient but venous drainage is significantly lower than this value, potential causes such as tubing, cannula placement, or intrathoracic/intra-abdominal pressure should be investigated.

b) Gas flow: Blood flow ratio≈1:1. For patients with hypercapnia and marked acidemia, gas flow may be increased appropriately.

c) Air-oxygen blender: Initial oxygen concentration is set to 100%.

7.2.3. Initial oxygenation indicator evaluation

After initial settings, calculate using Formula (1) is used to assess whether oxygenation is within the reasonable range as described in 7.1. If so, proceed to 7.3; if not, follow the steps in 7.4.

7.3. Oxygenation management during operation

7.3.1. Monitoring and management of barotrauma risk

During operation: During the operation period, evaluate for any signs of barotrauma (*e.g.*, pneumothorax, subcutaneous emphysema) or high risk of barotrauma [*e.g.*, progressive increase in peak inspiratory pressure (PIP)/plateau pressure (Pplat), presence of lung bullae on chest imaging]. If present, implement ventilator protective ventilation settings. Simultaneously, consider adjusting and re-assessing VV-ECMO parameters.

7.3.2. Ventilator ultra-protective ventilation parameter settings[9,10]

Parameter settings are as follows:

a) FiO_2: 30%-50%.

b) Tidal volume: Tidal volum ⩽4 mL/kg PBW.

c) PEEP: Maintain PEEP ⩾10 cmH_2O during VV-ECMO support. Individualize settings based on transpulmonary pressure monitoring, lung electrical impedance tomography, lung ultrasound, *etc.*

d) Respiratory rate: 4-15 breaths/min.

e) Plateau pressure: Keep <25 cmH_2O.

f) Driving pressure: ⩽15 cmH_2O. May be increased slightly in pulmonary fibrosis or reduced chest wall compliance.

7.3.3. VV-ECMO parameter adjustment[11,12]

VV-ECMO parameter adjustments are as follows:

a) Hypoxemia and hypercapnia should be prevented during combined use. The gas exchange targets are PaO_2: 65-90 mmHg, $PaCO_2$: 35-45 mmHg.

b) Avoid rapid correction of hypercapnia after starting VV-ECMO to prevent respiratory alkalosis. $PaCO_2$ should not be reduced by more than 10 mmHg per hour. After 24 hours, $PaCO_2$ should not decrease more than 50% of its pre-VV-ECMO level to prevent neurological complications.

7.3.4. Oxygenation metric assessment during operation

During operation, Formula (1) is used to assess whether oxygenation is within the reasonable range described in 7.1. If so, proceed to 7.2; if not, follow the steps in 7.4.

7.4. Oxygenation management when assessment is outside the target range

VV-ECMO parameter adjustments: Prioritize adjusting VV-ECMO parameters, such as blood flow, oxygen concentration, and gas flow rate.

Ventilator parameter adjustments: If the index calculated per Formula (1) still does not fall within the reasonable range after adjusting VV-ECMO parameters, increase the ventilator FiO_2, appropriately increase tidal volume, adjust PEEP and respiratory rate, then recalculate and assess using Formula (1) until the index reaches the reasonable range.

Concurrently with oxygenation adjustments, actively identify the causes of inadequate oxygen supply and administer targeted treatment for these causes.

7.5. Oxygenation management during the weaning process

Once the patient's primary condition has been controlled and with stable ventilator settings, gradually reduce VV-ECMO support. Using Formula (1), evaluate whether oxygenation reaches the reasonable range. If within range and the weaning criteria are met, proceed with a VV-ECMO weaning trial. Adjust ventilator parameters as necessary during the weaning trial.

VV-ECMO weaning criteria[13]: a) Effective control of the primary condition and improved findings in lung imaging. b) PaO_2 ⩾70 mmHg with FiO_2 ⩽60% and PEEP ⩽10 cmH_2O under ventilator support. c) With ventilator settings of tidal volume 6-8 mL/kg PBW, plateau pressure ⩽28 cmH_2O, and respiratory rate ⩽28 breaths/min, arterial blood gas analysis should show pH 7.35-7.45, and $PaCO_2$ 35-45 mmHg, with no excessive respiratory effort from the patient.

VV-ECMO weaning trial protocol: a) Oxygen reduction: When the patient's lung function begins to improve, the VV-ECMO oxygen concentration should be tapered from 100% to 21%, decreasing by approximately 20% each time. Assess whether SpO_2 remains >92% or PaO_2 remains ⩾70 mmHg after each reduction. If the criteria are met, proceed with step b. If not, pause the weaning trial. b) Gas flow reduction: Gradually reduce the VV-ECMO gas flow from its current setting to zero, at a rate of 0.5-1 L/min each time. After each adjustment, observe for 30 mins and repeat arterial blood gas analysis. Assess PaO_2, pH, and $PaCO_2$ to see if they meet the criteria of PaO_2 ⩾70 mmHg, pH 7.35-7.45, and $PaCO_2$ 35-45 mmHg, and if the patient exhibits no excessive respiratory effort. If these criteria are met, proceed with step c; if not, pause the weaning trial. c) Clamp gas line: Maintain the gas flow cessation for a minimum of 2-3 hours, which may need to be extended to 24 hours or longer for some patients. Subsequently, repeat arterial blood gas analysis and evaluate arterial PaO_2, pH, and $PaCO_2$ to assess if they meet the criteria of PaO_2 ⩾70 mmHg, pH 7.35-7.45, and $PaCO_2$ 35-45 mmHg, and if the patient exhibits no excessive respiratory effort. If these criteria are met, proceed with step d; if not, pause the weaning trial. d) Decannulation: Following the steps described above, ECMO removal can proceed if the evaluation criteria are met after step c; if not, pause the weaning trial.

Ventilator parameter adjustments[14]: During the weaning trial, gradually adjust ventilator parameters to achieve tidal volume 6-8 mL/kg PBW, plateau pressure ⩽28 cmH_2O, and respiratory rate ⩽28 breaths/min. After VV-ECMO withdrawal, continue respiratory support according to standard principles.

7.6. Oxygenation regulation following failed VV-ECMO weaning trial

If the weaning trial fails, the VV-ECMO and ventilator settings are restored to the parameters used during the VV-ECMO operation period (7.3), and dynamic reassessment should be continued. If the weaning criteria are met, the weaning trial is repeated until successful withdrawal.

This document was drafted in accordance with GB/T 1.1—*2020 Directives for standardization—Part 1: Rules for the structure and drafting of standardizing documents*[15].

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Conflict of interest statement

Chuan Zhu Lv is an Editor-in-Chief of *Journal of Acute Disease*, The article was subject to the journal's standard procedures, with peer review handled independently of this Editor-in-Chief. All authors declare no conflict of interest with publications of this guideline.

Publisher's note

The Publisher of the *Journal* remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Edited by Liu JJ

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This document was proposed by the Emergency Medicine Branch of Chinese Geriatrics Society.

This document is under the jurisdiction of Chinese Geriatrics Society.

English version of this article is co-published in *Journal of Acute Disease* (doi: 10.4103/jad.jad_123_25) and *Emergency and Critical Care Medicine* (doi: 10.1097/EC9.0000000000000174). Chinese version of this article is co-published in *Journal of Clinical Emergency* (doi: 110.13201/j.issn.1009-5918.2025.10.001) and *Chinese Journal of Critical Care Medicine* (doi: 10.3969/j. issn.1002-1949.2025.10.002).