Guideline Goal
Provide clinical guidance regarding the diagnosis of refractory hypoxemia (algorithm 1) and a stepwise approach to the treatment of refractory hypoxemia (algorithm 2).

Key Points
- When employing a higher PEEP strategy for refractory hypoxemia, it is recommended to wait at least 2 hours to determine adequacy of clinical response. This interval can be shortened if clinical situation necessitates.
- While a determination regarding the adequacy of clinical response is based on bedside judgment, a PaO2 >55mmHg is recommended.
- Prone ventilation for 16 hours/day has demonstrated benefits for patients with Refractory Hypoxemia due to ARDS or other etiologies (Appendix B).
- Patients in prone ventilation require a supine position trial daily for routine care and assessment.

Algorithm 1. Usual Care and Escalation to Consideration for Refractory Hypoxemia Therapies

Suspected ARDS (PF ratio < 300 mmHg)

Tv set at ≤ 6 ml/kg

\( \text{PaO}_2 \) >55mmHg or Decreased perfusion

YES

Recommended Interventions:
- IVF
- Pressors

NO

Pplat < 30?

YES

Refractory hypoxemia therapies should be considered

NO

Recommended Interventions:
- Airway clearance
- Reduce Tv by 1ml/kg
- Evaluate need for sedation

\( \text{PF ratio} > 150 \text{ mmHg?} \)

YES

Refractory hypoxemia therapies should be considered

NO

\( \text{FiO}_2 > 0.8 \) & PEEP ≥ 14 (for at least 12 hours)?

NO

YES

Allow time for alveolar recruitment
Wean per Appendix A

Refractory hypoxemia therapies should be considered
Algorithm 2. Recommended Escalation of Treatment for Refractory Hypoxemia

**Refractory Hypoxemia**
- Increase PEEP per Appendix A
  - **Success**
    - **YES** → Continue current therapy
    - **NO** → Consider bolus of paralytic
      - Inhaled epoprostenol (OSUWMC epoprostenol guideline)
        - **Success**
          - **YES** → Consider continuous paralysis
          - **NO** → Eligible for prone ventilation (Appendix B)
            - **YES** → Attempt prone ventilation (Appendix C)
            - **NO** → Consider APRV (Airway Pressure Release Ventilation) (Appendix D)
              - **Success**
                - **YES** → Continue current therapy
                - **NO** → Consider goals of care and palliative consult
      - **NO** → Consider stopping therapy

**ECMO**
- Takes significant time and resources to initiate. Therefore, in patients with refractory hypoxemia who are likely to be non-responsive to other therapies, it is reasonable to initiate CT surgery consultation at any point after refractory hypoxemia is recognized. If ECMO is considered, immediate evaluation is required. Direct physician to physician communication is also required.
Resources

- OSUWMC Extracorporeal Life Support (ECLS) – Adult Veno-Venous Extracorporeal Membrane Oxygenation (VV-ECMO) guideline
- OSUWMC Epoprostenol (Veletri®) Intravenous Solution for Inhalation
- OSUWMC Continuous Pharmacologic Neuromuscular Blockade of the Critically Ill Patient

References


Guideline Authors

- James Bott, RRT, RCP
- Timothy Dunlea, RRT, RCP
- Matthew Exline, MD
- Ravi Tripathi, MD
- Michael Zellers, BS, RRT, RCP
- Cheryl Newton, CNS
- Sheila Chucta, CNS
- Michele Weber, CNS
- Sonal Pannu, MBBS
- Bryan Whitson, MD, PhD
- S. Veena Satyapriya, MD

Guideline Approved


Disclaimer: Clinical practice guidelines and algorithms at The Ohio State University Wexner Medical Center (OSUWMC) are standards that are intended to provide general guidance to clinicians. Patient choice and clinician judgment must remain central to the selection of diagnostic tests and therapy. OSUWMC’s guidelines and algorithms are reviewed periodically for consistency with new evidence; however, new developments may not be represented.

Copyright © 2018. The Ohio State University Wexner Medical Center. All rights reserved. No part of this document may be reproduced, displayed, modified, or distributed in any form without the express written permission of The Ohio State University Wexner Medical Center.

Quality Measures

- Proportion of patients eligible for prone ventilation receiving a trial of prone ventilation by 24 hours
- Proportion of patients on iNO without prior trial of epoprostenol

Guideline reviewed by: Critical Care Quality Committee.
## Appendix A. PEEP/FiO₂ Table

<table>
<thead>
<tr>
<th>FiO₂</th>
<th>0.21-0.40</th>
<th>0.40-0.50</th>
<th>0.50-0.70</th>
<th>0.70-1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP</td>
<td>6</td>
<td>8</td>
<td>10-12</td>
<td>14-20</td>
</tr>
</tbody>
</table>

## Appendix B. Relative and Absolute Contraindications for Selected Refractory Hypoxemia

<table>
<thead>
<tr>
<th>Intervention or Procedure</th>
<th>Relative Contraindications</th>
<th>Absolute Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prone Ventilation*</td>
<td>• Cardiovascular instability including shock</td>
<td>• Open neck, chest or abdominal wounds</td>
</tr>
<tr>
<td></td>
<td>• Femoral venous or arterial catheter in use</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Intracranial pressure &gt; 30 mmHg or cerebral perfusion pressure &lt; 60 mmHg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Massive hemoptysis requiring an immediate surgical or interventional radiology procedure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Tracheal surgery or sternotomy during the previous 15 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Serious facial trauma or facial surgery during the previous 15 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Deep venous thrombosis treated for less than 2 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Cardiac pacemaker inserted in the last 2 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Unstable spine, femur, pelvic or skull fractures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Mean arterial pressure lower than 65 mmHg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Pregnant women</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Single anterior chest tube with air leaks</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Sternotomy within the last 30 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Burns on more than 20% of the body surface</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Chronic respiratory failure requiring oxygen therapy or non-invasive ventilation (NIV)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• End-of-life decision before inclusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Intra-aortic balloon pump</td>
<td></td>
</tr>
<tr>
<td>Inhaled Vasodilators</td>
<td>Cardiovascular instability including shock</td>
<td></td>
</tr>
<tr>
<td>ECMO (see OSUWMC Extracorporeal Life Support guideline in reference section for further details)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Inadequate cardiopulmonary resuscitation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• CPR &gt; 5 minutes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Evidence of neurologic insult or compromised neurologic status prior to acute illness/shock</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Intracranial hemorrhage</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• BMI &gt;40</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Life expectancy &lt; 1 year before onset of acute respiratory failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Primary or idiopathic pulmonary hypertension, end-stage cardiopulmonary disease, and home oxygen requirement and not a transplant candidate.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Neuromuscular blockade infusion &gt; 48 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• History of coagulopathy or thrombophilia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Ungrafted severe burns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Profound metabolic acidosis with pH &lt; 7.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Requirement of prolonged high-dose vasoactive drugs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Severe immunocompromised state</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ANC &lt;400/mm³</td>
<td></td>
</tr>
</tbody>
</table>

Appendix C. Usual Prone Ventilation Procedures

Figure A. Initial Prone Ventilation Trial, Daily Supine Positioning Trials, and Determining Need for Specialty Bed

- **Patient > 200 kg**
  - **YES**: Consider safety of manual prone trial and modify based on need
  - **NO**: Manually prone patient

  - **Manually prone patient**
    - **YES**: Perform SPT for up to 6 hours to allow for pt. care/evaluation
    - **SPT tolerated? (SpO₂ > 92% ≥6h)**
      - **YES**: Evaluate for discontinuation (page 7, figure C)
      - **NO**: Return to prone positioning
    - **NO**: Maintain prone position
      - **YES**: Patient failed prone trial- return patient to supine position
      - **NO**: Hemodynamic/ respiratory instability experienced
        - **YES**: Patient failed prone trial- return patient to supine position
        - **NO**: Maintain prone position
          - **YES**: Perform SPT for up to 6 hours to allow for pt. care/evaluation
          - **SPT tolerated? (SpO₂ > 92% ≥6h)**
            - **YES**: Evaluate for discontinuation (page 7, figure C)
            - **NO**: Return to prone positioning
          - **NO**: Maintain prone position

- **Is patient 91-159 kg & 4'6"-6'6"**
  - **YES**: Manually prone the patient
  - **NO**: Do not prone patient on a low air mattress
Appendix C. Usual Prone Ventilation Procedures

Figure B. Daily assessments for prone ventilation need and general care (Daily supine positioning trial)

Prone ventilation in use for at least 16 hours with plans to continue

- Is FiO₂ < 1.0? NO → Continue prone ventilation and usual care
  YES

- Is SpO₂ > 92% or PaO₂ > 70? NO → Continue prone ventilation and usual care
  YES → Place patient in supine position

- SpO₂ >90% and Clinically stable NO → Place in prone position and initiate prone ventilation for at least 16 hours
  YES → Tolerates supine position. See Appendix C, Figure C.
Appendix C. Usual Prone Ventilation Procedures

Figure C. Terminating Prone Ventilation

Patient placed in **supine** position
(Decision: See Figure B)

- Patient tolerates turn?
  - YES
    - While supine, titrate $\text{FiO}_2 \leq 0.6$
      - $\text{PEEP} \leq 10$ to maintain $\text{SpO}_2 > 92$
  - NO
    - Refer to Appendix C, Figure B

- Pt. tolerates
  - YES
    - Consider discontinuing daily **prone** ventilation
  - NO

Refer to Appendix C, Figure B
Appendix D. APRV Guideline

Initial APRV Settings and Adjustments

*Note: Before initiating APRV, determine the current minute volume, mean airway pressure and plateau pressure when applicable.

<table>
<thead>
<tr>
<th>Settings</th>
<th>Adjustments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure High</td>
<td>20-30 cm H₂O (Use patient’s current plateau pressure or mean airway pressure + 5 cm H₂O)</td>
</tr>
<tr>
<td>Pressure Low</td>
<td>0 cm H₂O</td>
</tr>
<tr>
<td>Time High</td>
<td>4.0 – 6.0 sec</td>
</tr>
<tr>
<td></td>
<td>Release Rate = 60/(Time High + Time Low)</td>
</tr>
<tr>
<td>FIO₂</td>
<td>1.0</td>
</tr>
<tr>
<td>Pressure Support</td>
<td>5-10 cm H₂O or Tubing Compensation = 100%</td>
</tr>
</tbody>
</table>

Weaning APRV

- Weaning to extubation on APRV is more efficient than changing to PSV or other ventilator modes
- “Drop and Stretch”
  - “Drop”: Reduce Pressure High by 2 cm H₂O
  - “Stretch”: Increase Time High by 0.5-1.0 sec
- Maintain Time Low between 0.5 to 0.8 sec
- Once the Pressure-high is at 10-15 cm H₂O, the settings become similar to “CPAP.”
- PS can be added for comfort or ventilation in patients who require prolonged weaning on lower levels of Pressure-high
- Consider SBT when Pressure-high < 15 and FIO₂ < 0.5

Subsequent Adjustments for APRV

To Improve Oxygenation

- Increase FIO₂
- Increase Pressure High
- Increase Time High

To Improve Ventilation

- Increase Release Rate to increase minute ventilation
- Decrease Time High to increase minute ventilation
- Increase Pressure High and/or decrease Pressure Low to increase release volume
- Increase Pressure Support to increase spontaneous volume
- Increase in Time Low to increase release volume

To Decrease Release Volume

- Decrease Time Low