**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).

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

1. **Suspected ARDS** (PF ratio < 300 mmHg)
   - **Tv set at ≤ 6 ml/kg**
   - **PaO2 > 55mmHg or Decreased perfusion**
     - **YES**
     - Recommended Interventions:
       - IVF
       - Pressors
   - **NO**
     - **Pplat < 30?**
       - **NO**
       - **Recommended Interventions:**
         - Airway clearance
         - Reduce Tv by 1ml/kg
         - Evaluate need for sedation
       - **Pplat < 30?**
         - **NO**
           - Refractory hypoxemia therapies should be considered
         - **YES**
           - **PF ratio > 150 mmHg?**
             - **NO**
               - Refractory hypoxemia therapies should be considered
             - **YES**
               - **FiO2 > 0.8 & PEEP ≥ 14 (for at least 12 hours)?**
                 - **NO**
                   - **Allow time for alveolar recruitment**
                   - **Wean per Appendix A**
                 - **YES**
                   - Refractory hypoxemia therapies should be considered

**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.

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Algorithm 2. Recommended Escalation of Treatment for Refractory Hypoxemia

1. **Refractory Hypoxemia**
   - Increase PEEP per Appendix A
   - Consider bolus of paralytic
     - Inhaled epoprostenol can be readily administered and therefore could be considered concurrently with prone or other interventions. No RCT supports primary use of pulmonary vasodilators in favor of lung protective ventilation; however, it can be effective in allowing the time to implement prone or other approaches without added risk.
   - Eligible for prone ventilation (Appendix B)
     - Consider APRV (Airway Pressure Release Ventilation) (Appendix D)
       - Consider goals of care and palliative consult
   - Continuation of current therapy
     - Inhaled epoprostenol
       - OSUWMC epoprostenol guideline
         - Success
           - Yes: Continue current therapy
           - No: Consider stopping therapy
   - Success
     - Yes: Consider continuous paralysis
     - No: Success
       - Yes: Attempt prone ventilation (Appendix C)
         - No: Success
           - Yes: Continue current therapy
           - No: Consider goals of care and palliative consult
   - ECMO
     - OSUWMC ECMO guideline
       - Success
         - Yes: Consult Cardiothoracic Surgery STAT
         - No: Consider goals of care and palliative consult
   - 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.

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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


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

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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.

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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></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Cardiovascular instability including shock</td>
<td>• Open neck, chest or abdominal wounds</td>
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<tr>
<td></td>
<td>• Femoral venous or arterial catheter in use</td>
<td></td>
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<tr>
<td></td>
<td>• Intracranial pressure &gt; 30 mmHg or cerebral perfusion pressure &lt; 60 mmHg</td>
<td></td>
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<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>
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<tr>
<td></td>
<td>• Cardiac pacemaker inserted in the last 2 days</td>
<td></td>
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<tr>
<td></td>
<td>• Unstable spine, femur, pelvic or skull fractures</td>
<td></td>
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<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>
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<tr>
<td></td>
<td>• Sternotomy within the last 30 days</td>
<td></td>
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<tr>
<td></td>
<td>• Burns on more than 20% of the body surface</td>
<td></td>
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<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>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Inhaled Vasodilators</th>
<th>Cardiovascular instability including shock</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ECMO (see OSUWMC Extracorporeal Life Support guideline in reference section for further details)</td>
<td></td>
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<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>
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<tr>
<td></td>
<td>• BMI &gt;40</td>
<td></td>
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<tr>
<td></td>
<td>• Life expectancy &lt; 1 year before onset of acute respiratory failure</td>
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<tr>
<td></td>
<td>• Primary or idiopathic pulmonary hypertension, end-stage cardiopulmonary disease, and home oxygen requirement and not a transplant candidate.</td>
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<tr>
<td></td>
<td>• Neuromuscular blockade infusion &gt; 48 hours</td>
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<tr>
<td></td>
<td>• History of coagulopathy or thrombophilia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Ungrafted severe burns</td>
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<tr>
<td></td>
<td>• Profound metabolic acidosis with pH &lt; 7.1</td>
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<tr>
<td></td>
<td>• Requirement of prolonged high-dose vasoactive drugs</td>
<td></td>
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<tr>
<td></td>
<td>• Severe immunocompromised state</td>
<td></td>
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<tr>
<td></td>
<td>• ANC &lt;400/mm³</td>
<td></td>
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<tr>
<td></td>
<td>• Advanced age (&gt;75 years)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Prolonged ventilation for &gt; 7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Established multi-organ system failure – SOFA Score &gt; 15</td>
<td></td>
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<tr>
<td></td>
<td>• Contraindication to systemic anticoagulation</td>
<td></td>
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<tr>
<td></td>
<td>• Refusal to receive blood products</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Quadriplegia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Bone marrow transplant recipients</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• DNR/DNI status</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Only relevant in patients who are full code prior to evaluation</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: Do not prone patient on a low air mattress.

  - Manually prone patient

  - **Hemodynamic/respiratory instability experienced**
    - YES: Patient failed prone trial - return patient to supine position
    - NO: Maintain prone position

    - **FiO₂ < 1.0 and SpO₂ > 92% or PaO₂ > 70%**
      - YES: Perform SPT for up to 6 hours to allow for pt. care/evaluation
      - NO: Return to prone positioning

    - **Is patient 91-159 kg & 4'6"-6'6"**
      - YES: Evaluate for discontinuation (page 7, figure C)
      - NO: In special situations, consider Rotoprone® bed with a critical care CNS consult

- **Manually prone the patient**
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 $\text{FiO}_2 < 1.0$? 
  - NO: Continue prone ventilation and usual care
  - YES: Is $\text{SpO}_2 > 92\%$ or $\text{PaO}_2 > 70$?
    - NO: Continue prone ventilation and usual care
    - YES: Place patient in supine position

  - $\text{SpO}_2 > 90\%$ 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