Lung-protective Ventilation Strategies and Adjunctive Treatments for the Emergency Medicine Patient with Acute Respiratory Failure

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KEYWORDS

- Acute respiratory failure • Acute respiratory distress syndrome
- Mechanical ventilation

KEY POINTS

- Respiratory failure is a frequent disease process encountered in the emergency department.
- There is significant need for improvement in the care of patients on mechanical ventilation. If not contraindicated, lung-protective ventilation strategies should be used.
- Patient specific disease pathophysiology is important to consider when treating patients that are difficult to oxygenate, ventilate or when Pa_{O_2}, Pa_{CO_2}, and/or pH can only be maintained at unsafe ventilator settings.

INTRODUCTION

Invasive mechanical ventilation (MV) is an essential component of critical care and emergency medicine (EM). Successful resuscitation requires an expedient and parallel assessment of airway maintenance, efficiency and effectiveness of breathing mechanics, and adequacy of circulation and perfusion. Management should be directed at ensuring sufficient oxygenation, ventilation, and prompt reversal of the inciting disease process if possible. This article reviews the evidence for safe MV strategies in the critically ill patient in the emergency department (ED) and provides treatment options for patients who are difficult to oxygenate and ventilate or cannot safely be managed with standard MV strategies.

Disclosure: None.
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Emerg Med Clin N Am ■ (2014) ■–■
http://dx.doi.org/10.1016/j.emc.2014.07.012 **emed.theclinics.com**
0733-8627/14/$ – see front matter

EPIDEMIOLOGY/STATEMENT OF THE PROBLEM

Acute respiratory failure (ARF) requiring MV is a common clinical scenario. Wunsch and colleagues[1] suggested that approximately 3% of all hospital admissions in the United States require invasive MV. MV costs approximately $27 billion dollars nationally.[1] Nearly one-third of patients who are placed on MV die in the hospital and among survivors only 30% are discharged home after their admission.[1] Recent data suggest opportunities for improvement because many patients in the ED and intensive care unit (ICU) do not get optimal MV therapy for ARF.[2,3]

PATHOPHYSIOLOGY

Breathing is essential for homeostasis. In critically ill patients the demands for oxygen supply and carbon dioxide removal are often increased. This increased demand can be superimposed on prior impaired cardiopulmonary reserve. In ARF the cardiopulmonary system fails to oxygenate or ventilate adequately or inefficient breathing mechanics put excessive loads on the cardiopulmonary system. MV is used to offload respiratory muscle work and assist in oxygen delivery and ventilation.

OXYGENATION AND HYPEROXIA

Most oxygen is carried by hemoglobin molecules in red blood cells. MV is often used to correct hypoxemia (low oxygen saturation) to improve total blood oxygen content. In emergent situations it is beneficial to increase the fraction of inspired oxygen (Fio_2) to increase blood oxygen content. Increased Fio_2 should only be considered as a temporary fix because there are downsides to high concentrations of Fio_2.

First, in patients with normal lungs, supernormal Fio_2 concentrations lead to hyperoxia or a Pao_2 greater than or equal to 200.[4] Multiple studies suggest that hyperoxia leads to the formation of reactive oxygen species that can cause tissue damage.[4–8] More recent data in brain-injured patients[4,8] and patients after cardiac arrest[9] suggest worse outcomes with hyperoxia versus normal oxygen concentrations. Hyperoxia is an iatrogenic entity that can be avoided by turning the Fio_2 down.

Second, in patients with abnormal lungs, an Fio_2 of 1.0 (100%) can mask the degree of pulmonary dysfunction.[3] A normal oxygen saturation on pulse oximetry can be falsely reassuring.[3] On a Fio_2 of 1.0, a saturation of 100% may correspond with a Pao_2 of between 100 and 500, the latter being normal and the former evidence of significant respiratory dysfunction. Having a through understanding of the magnitude of pulmonary dysfunction may allow better patient care[3] because these patients may be candidates for other adjunctive therapies and lung-protective ventilation strategies (LPVS). Once stabilized and resuscitated through the peri-intubation period, dial down the Fio_2 using pulse oximetry. An oxygen saturation around 95% is sufficient and in certain conditions (chronic obstructive pulmonary disease [COPD], obesity hypoventilation syndrome, and obstructive sleep apnea) a saturation of between 88% and 92% may be more appropriate.[10] Titrating the Fio_2 helps to determine the degree of respiratory dysfunction and helps limit oxygen toxicity.

OXYGEN DELIVERY AND HEART-LUNG INTERACTIONS

Placing a critically ill patient on MV can have serious untoward effects on cardiac output (CO) and oxygen delivery and can lead to adverse events if not appropriately anticipated and managed proactively.[11] In conditions associated with high afterload, MV can be beneficial by decreasing the force opposing left ventricular contraction and left ventricular transmural wall pressure.[11] In preload-dependent states (hypovolemic

and distributive shock) and diseases with right ventricular (RV) dysfunction (pulmonary embolism, pericardial tamponade, tension pneumothorax) the increase in intrathoracic pressure and RV afterload during MV can impede venous return to the right side of the heart and CO.[11] This decrease in venous return can manifest as a precipitous decrease in blood pressure and even cardiac arrest after initiation of MV. The reader is referred to recent work by Funk and colleagues[12,13] for a more detailed description of RV function and venous return. Focused bedside echocardiography assessing inferior vena cava collapsibility and RV size and function before intubation (if feasible) may clue the clinician into potential postintubation complications and direct the need for aggressive fluid resuscitation and early vasopressor support during the induction and early MV period.

HYPOXEMIA

Hypoxemia is low arterial oxygen saturation. There are multiple physiologic mechanisms for hypoxemia: hypoventilation (airway obstruction or sedative overdose), low Fio_2 or low partial pressure of O_2 (high altitude), diffusion-limited processes (interstitial lung disease), ventilation/blood flow (V/Q) mismatch (COPD), shunt (pulmonary edema), and low venous oxygen content (shock).[14] During MV, persistent hypoxemia can usually be attributed to a combination of shunt physiology and low venous admixture of blood.[15]

The cardiac and pulmonary systems match ventilation and blood flow. Shunt physiology is a V/Q mismatch in which blood passes from the right to the left side of the heart without participating in gas exchange. Desaturated venous blood mixes with oxygenated arterial blood, decreasing the overall arterial oxygen saturation. Supplemental oxygen only partially corrects hypoxemia or has no effect on systemic oxygen saturation because the shunted blood bypasses the delivered supplemental oxygen.[16]

VENTILATION AND HYPERCAPNEA

Effective MV must provide for adequate CO_2 excretion and O_2 saturation while not exposing the patient to excessive airway pressures (barotrauma) or tidal volumes (T_v) (volutrauma). The clearance of CO_2 depends on the relationship between CO_2 production and alveolar ventilation (V_a)[17]:

$$Paco_2 \approx (CO_2 \text{ production})/(V_a).$$

$$V_a = \text{minute ventilation } (V_m) - \text{Dead space ventilation } (V_{ds}).$$

The typical MV adjustment to hypercarbia is to increase the V_m by increasing the respiratory rate (RR) or T_v. In most patients this increase in V_m leads to an increase in V_a and lowering of the $Paco_2$. However, in low cardiac output states, acute respiratory distress syndrome (ARDS), advanced COPD, massive pulmonary embolism, and abdominal compartment syndromes,[17] V_{ds} can increase. In these instances, merely adjusting the set V_m may not improve CO_2 clearance if V_a does not improve. Instead, the clinician should attempt to reverse the underlying process if possible and/or attempt to decrease CO_2 production. Rechecking arterial blood gases (ABGs) after MV adjustments is important. Continuous end-tidal CO_2 monitoring ($ETco_2$) is another helpful tool for the patient needing MV but does not obviate ABGs. $ETco_2$ approximates the $Paco_2$. The difference between the $Paco_2$ and $ETco_2$ depend on V_{ds}. Therefore, it is important to obtain an ABG to correct for patient-specific relationships between the $ETco_2$ and $Paco_2$ and not rely solely on the $ETco_2$. The clinician should be cognizant

of the value of the $ETco_2$ and actual V_m (not merely the set or prescribed V_m if the patient is breathing spontaneously at more than the set ventilator rate) when the ABG is drawn. A high $ETco_2$ is an assurance of a high $Paco_2$ but a low or normal $ETco_2$ can be seen with a normal $Paco_2$ or an increased $Paco_2$ in the setting of high V_{ds}. Large differences between $Paco_2$ and $ETco_2$ can be seen with excessive V_{ds} or low CO.[18] Changes in clinical condition, severity of illness, or lung mechanics should prompt the clinician to consider whether a repeat ABG is necessary to recalibrate the $ETco_2$ with the $Paco_2$.

ARDS AND LUNG-PROTECTIVE VENTILATION

ARDS was first described by Ashbaugh and colleagues[19] in 1967. They described 12 patients with a diffuse alveolar infiltrative chest radiograph pattern that manifested acute onset of tachypnea, hypoxemia, and cyanosis that was refractory to oxygen therapy. ARDS was defined in 1994,[20] and this definition was revised in 2012 (the Berlin definition[21]) to address some limitations of the earlier definition. The major changes and new ARDS criteria are as follows:

1. The term acute lung injury was eliminated and the 2-tiered model was replaced by a 3-tiered scale based on the degree of hypoxemia as measured by the Pao_2/Fio_2 (P/F) ratio: mild ($\leq$300–200 mm Hg), moderate ($\leq$200–100 mm Hg), and severe ($\leq$100 mm Hg). A minimum continuous positive airway pressure (CPAP) or positive end-expiratory pressure (PEEP) must be present.
2. Onset within 1 week of inciting event.
3. Bilateral opacities consistent with pulmonary edema that are nonhydrostatic or noncardiogenic in origin. A wedge pressure is no longer required, but the respiratory failure must not be fully explained by cardiac failure or fluid overload.[21]

The new severity scale that uses the degree of hypoxemia is the most important change to the new definition. Worsening P/F ratio predicts mortality and duration of MV in survivors and can help triage patients who may benefit from more aggressive therapies.[21]

With a few exceptions, MV is usually required in ARDS. Over the last 5 decades, it has been recognized that MV can be injurious. In the 1970s, ventilator settings were titrated to normalize blood gas values. Clinicians used T_v of 12 to 15 mL/kg of body weight.[22] Gross barotrauma in the form of pneumothorax, pneumomediastinum, and pneumoperitoneum was common, and mortality in severe ARDS was as high as 90%.[23] Work by Amato and colleagues[24] and then the landmark ARDSNet (Acute Respiratory Distress Syndrome Network)[25] trial in 2000 showed improved outcomes with low T_v ventilation strategies (4–6 mL/kg of ideal body weight [IBW]) versus higher traditional T_v (10–12 mL/kg IBW). IBW is determined by the patient's height and sex and predicts lung volume better than actual weight.

A better understanding of ventilator induced lung injury (VILI) in recent years has created a renewed impetus on providing LPVS.[26] LPVS was first shown to be beneficial in patients with ARDS but more recent data suggest that lowering the tidal volume in patients without ARDS may be beneficial.[27–30] There are 4 major theories for ventilator-induced lung injury: barotrauma, volutrauma, atelectrauma, and biotrauma.[27] Barotrauma is lung damage secondary to high airway pressure (ie, pneumothorax or pneumomediastinum). Volutrauma is injury induced by high T_v causing overdistention of alveoli. Atelectrauma is damage from the shear and strain of collapsible lung units opening and closing, and biotrauma is damage from the release of proinflammatory cytokines and immune-mediated injury that occurs when lung tissue is exposed to unphysiologic stress or strain.[26]

SELECTION OF OPTIMAL TIDAL VOLUME

The mainstays of LPVS are to (1) limit tidal volume; (2) limit end-inspiratory plateau pressure (P_{plat}); (3) provide adequate PEEP to keep the lung open and prevent alveolar collapse, and (4) limit Fio_2.[30]

The optimal T_v for patients without ARDS who require MV is not known.[30–32] Animal data suggest that normal T_v for mammals is 6.3 mL/kg.[33] Data from ARDSNet[25] as well as multiple additional trials[27–29] suggest that T_v greater than 10 mL/kg IBW is harmful. Lellouche and colleagues[27] showed a lower incidence of organ failure and shorter ICU length of stay (LOS) when using T_v less than 10 mL/kg IBW in patients having cardiac surgery. The IMPROVE[28] study group similarly showed less postoperative respiratory support, less pneumonia, and shorter hospital LOS among patients receiving low intraoperative T_v (6–8 mL/kg IBW) after abdominal surgery. In addition, Serpa Neto and colleagues[29] performed a meta-analysis of the use of LPVS with low T_v and clinical outcomes among patients without ARDS and showed less subsequent lung injury (RR, 0.33; [0.23–0.47], number needed to treat [NNT], 11), less mortality (RR, 0.64; [0.46–0.89]; NNT, 23), and shorter hospital LOS.

If using LPVS and low T_v, it is imperative that the RR is turned up to maintain an adequate V_m. Adequate V_m is especially important in the ED environment when paralytics like succinylcholine and longer acting agents like rocuronium are used for rapid sequence induction and patients are heavily sedated to facilitate management. In these instances respiratory drive is blunted and patients cannot increase their RR to compensate for low T_v. This can lead to alveolar hypoventilation, hypercarbia, and worsening acidosis. Normal V_m is approximately 100 mL/kg. This requirement is greater in critically ill patients. It is helpful to use the patients pre-intubation respiratory rate and depth of ventilation to gauge the post-intubation V_m requirements. A patient with Kussmaul breathing will need a high RR and appropriate T_v to maintain respiratory compensation for their metabolic acidosis post-intubation. Alternatively, if a patient is on Non-Invasive Ventilation (NIV) prior to intubation, post-intubation V_m can be estimated by using the V_m from the NIV respirator.

Maintaining adequate pH should be weighed against the need to provide safe MV settings and safe airway pressures. In many clinical scenarios the goal should not be to normalize blood gas values but to provide LPVS while accepting permissive hypercapnia and a mild acidosis. Some data even suggest that mild hypercapnea is protective against lung injury[30] and improves red blood cell oxygen delivery.[14] ARDSnet[25] tolerated pH levels down to 7.15. However, in certain clinical scenarios (eg, brain injury with increased intracranial pressure, toxicologic emergencies, refractory shock) an increased $Paco_2$ may not be safe. In addition, in ARDSNet, some patients required bicarbonate drips to maintain pH and the low T_v group had a mean respiratory rate of approximately 30 breaths per minute.[25] Higher respiratory rates shorten the expiratory time. In certain patient populations with increased airway resistance and obstructive lung disease this can potentially lead to air-trapping and auto-PEEP. Auto-PEEP in preload-dependent states can decrease venous return and lead to hemodynamic instability, increased vasopressor and fluid needs, and even cardiovascular collapse in severe cases.

In summary, with regard to T_v selection, in patients who meet criteria for ARDS, a low-T_v strategy that replicates the original ARDSNet trial (4–6 mL/kg IBW) should be used (Appendix 1).[3,25] In patients without ARDS, expert opinion and clinical data suggest that LPVS with a T_v of 6 to 8 mL/kg of IBW is prudent.[31] Using T_v greater than 10 mL/kg of IBW is associated with worse clinical outcomes. Whether the optimal tidal volume is 6 or 8 mL/kg is still open to debate.[32,33] When using LPVS, it is important to

ensure an adequate V_m by providing an appropriate RR. ABG, in addition to pulse oximetry and $ETCO_2$, should be used to ensure adequate oxygenation and ventilation.

LIMITING INSPIRATORY P_{plat}

An additional goal of LPVS is to limit airway pressure to avoid barotrauma. The inspiratory hold or P_{plat} estimates the pressure distending the alveolus. This maneuver is done by pausing the flow of air at the end of inspiration. There is no definitive safe P_{plat}.[34] In ARDS, the goal should be a P_{plat} less than 30 cm H_2O.[25] Hager and colleagues,[34] in their analysis of the ARDSNet data, saw improved outcomes with lower P_{plat} values. Whether this was causal or coincidental and whether a lower P_{plat} should be actively sought by lowering T_v is currently unclear. In obese patients or patients with stiff chest walls, P_{plat} may not accurately reflect transpulmonary pressure or the pressure distending the alveoli. In these instances it may be acceptable to tolerate higher P_{plat}.[31] In patients without ARDS, targeting a P_{plat} less than 20 cm H_2O is suggested by some experts.[31] Lowering P_{plat} is accomplished primarily by decreasing T_v but, again, acceptable (albeit not necessarily normal) $PaCO_2$ and pH should be ensured. In addition to lowering T_v, providing adequate sedation to facilitate patient synchrony, adjusting PEEP to optimal levels, ensuring that auto-PEEP is not present, and ruling out pneumothorax or mucous plugging are other measures that can help lower P_{plat}.

SELECTION OF OPTIMAL PEEP AND OPEN LUNG RECRUITMENT

As stated earlier, most oxygenation problems that occur on MV are secondary to shunt physiology. Shunts are caused by pulmonary (pneumonia, pulmonary contusion, pulmonary edema, and so forth) or cardiac (patent foramen oval, atrial or ventricular septal defects) causes.

The typical treatment of hypoxemia from pulmonary shunts is to attempt to recruit collapsed lung units by increasing PEEP. The optimal PEEP settings, or even the best method to go about choosing PEEP, are controversial.[35,36] To simplify management in the ED, I recommend using the PEEP table provided by ARDSNet[37] because it has been validated and is easy to use[35] (see Appendix 1). There is no evidence favoring a high-PEEP versus a low-PEEP strategy in terms of survival, but a high-PEEP strategy has been associated with improved oxygenation.[38] PEEP goals should be reassessed if vasopressor or fluid requirements increase after increasing PEEP, P_{plat} is greater than 30 to 35 cm H_2O (depending on body habitus and clinical condition), or there is evidence of worsening tissue oxygen delivery or worsening oxygen saturation.

If increasing PEEP fails to correct oxygenation, or oxygenation worsens, it is important for the clinician to troubleshoot and not continue with treatment strategies that do not help and potentially complicate the clinical scenario. Cardiac shunts can worsen with increased PEEP because the increase in RV afterload increases right-to-left shunt.[39] Dessap and colleagues[40] in their cohort of 203 patients with ARDS found a prevalence of a moderate to large patent foramen ovale (PFO) shunt in 19.2% of their patients. These patients had a poorer P/F ratio response to PEEP and had longer ICU and ventilator days compared with their counterparts without PFO shunting. Inhaled pulmonary vasodilators and prone positioning (discussed later) may be a more appropriate treatment option in patients with PFO shunts. A transthoracic echocardiogram (or ideally transesophageal echocardiography) bubble study can help to detect cardiac shunts.

In addition, unilateral lung diseases (pneumonia, mucous plugging, pulmonary contusions, and so forth) may have a paradoxic response to increasing levels of PEEP.[41] In these situations the increased airway pressure from applied PEEP may overdistend healthy lung tissue. This will divert perfusion away from aerated lung and through the

shunt worsening oxygenation. These conditions can be difficult to predict, but when a patient has worsening hypoxemia with initiation of MV (ie, after intubation) or with increasing levels of positive airway pressure, it is important for the clinician to consider these disease processes. The treatment of patients with unilateral lung shunts and cardiac shunts is different than the standard open lung recruitment strategies used in most patients with hypoxemic respiratory failure. In these infrequent instances, blindly following a PEEP/Fio_2 table is likely to worsen the clinical scenario. In these patients, limiting PEEP, prone positioning, and pulmonary vasodilators might be more effective techniques.

Fig. 1 summarizes a stepwise strategy for selection of appropriate T_v, RR, Fio_2 and PEEP. In addition to ensuring adequate Pao_2, $Paco_2$, and/or pH, every effort should be made to provide safe LPVS. **Fig. 2** summarizes a stepwise strategy for a patient with a ventilator crisis or with a failure to oxygenate or ventilate.

ADJUNCTIVE MANEUVERS

Multiple new and promising developments that focus on non-MV adjunctive treatment measures for patients with refractory ARDS and respiratory failure have recently been

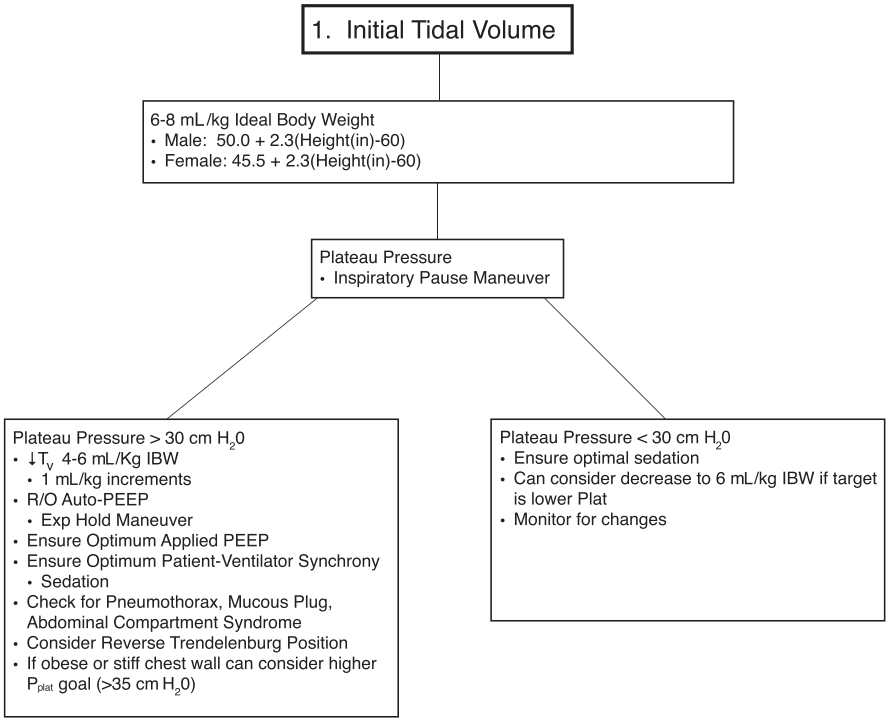


Fig. 1. Algorithm for initiating initial MV settings in the ED. (*Ventilator Waveform from* Santanilla JI, Daniel B, Yeow ME. Mechanical ventilation. Emerg Med Clin N Am 2008; 26:849–62. *PEEP table modified from* Haas CF. Lung protective mechanical ventilation in acute respiratory distress syndrome. Respir Care Clin N Am 2003;9(3):363–96. *Adapted from* The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000;342:1301–8 and Slutsky AS, Ranieri VM. Ventilator-induced lung injury. N Engl J Med 2013;369:2126–36.)

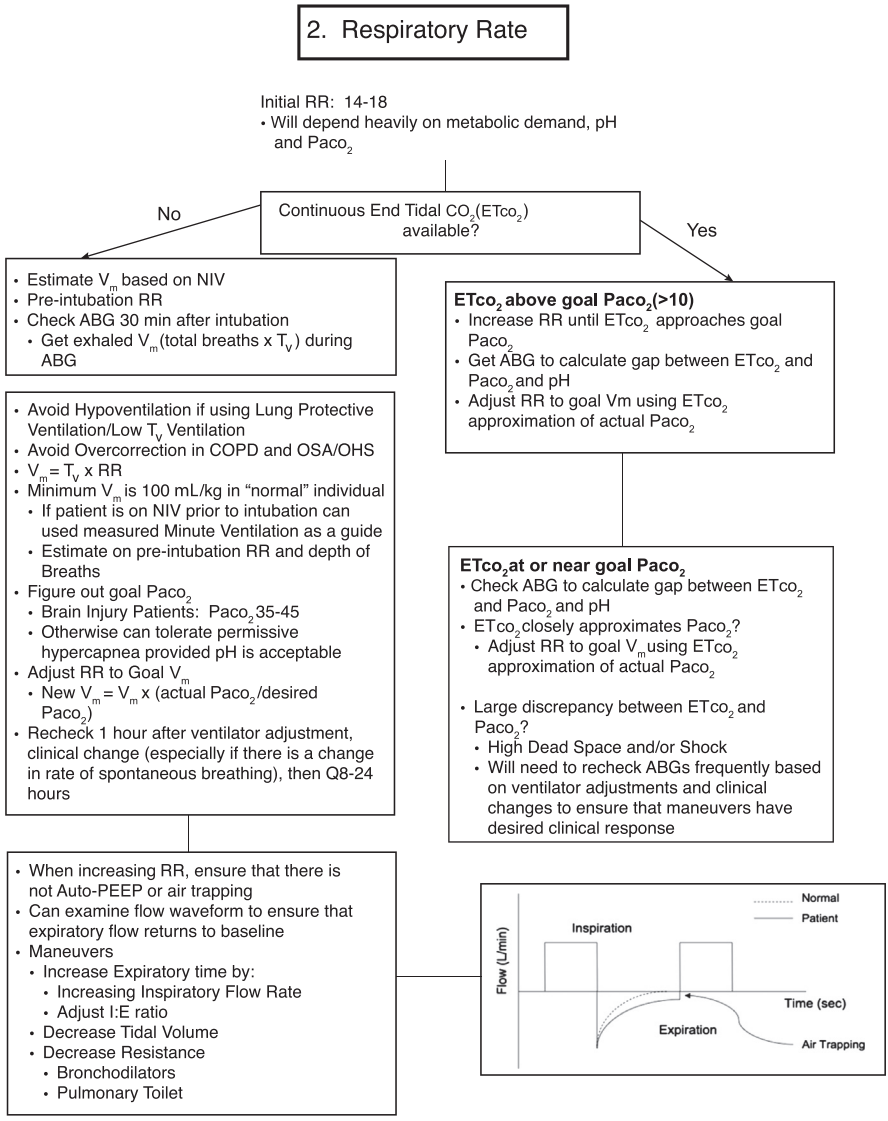


Fig. 1. (*continued*)

developed. These treatments may find a role in the EM management of ARDS and severe respiratory failure. Further information on each can be found in references.[38,42,43]

NEUROMUSCULAR BLOCKING AGENTS

Neuromuscular blocking agents (NMBAs) are used in patients with severe respiratory failure to facilitate ventilator synchrony.[44] A patient who is bucking the ventilator can be exposed to barotrauma, volutrauma from breath stacking, and other serious complications (eg, tube dislodgment). NMBAs have been used to facilitate ventilator synchrony and are associated with improvements in P/F ratio.[31] The rational for this benefit is not fully clear because NMBAs seem to help even in patients who do not

3. Fraction of Inspired Oxygen (Fio_2)

- If acceptable pulse oximetry waveform is present titrate down to lowest possible Fio_2 required for goal Oxygen Saturation (> 95%)
  - COPD, OSA/OHS: 88-92%
- If no lung pathology (ie intubated for airway protection) can do rapidly
- Otherwise ≈ ↓10% Q 10 minutes
- Get ABG to confirm once at goal
- If you can't get Fio_2 less than 50%, see PEEP table below
  - Consider ARDS and other causes of Shunt Physiology and Severe Respiratory Failure

4. Positive End Expiratory Pressure

- Ensure patient is volume resuscitated and monitored
- Adjust PEEP per table to lowest Fio_2 and PEEP value to maintain adequate Spo_2
- Monitor for appropriate response
  - If paradoxical response, ie Oxygen Saturation drops with higher PEEP or initiation of MV consider cardiac shunts and unilateral lung disease and shunt
    - Chest xray and/or Lung US
    - ECHO bubble study
    - Decrease PEEP and consider other treatments for hypoxemia
- If PEEP > 8 is needed consider ARDS and other causes of Shunt Physiology and Severe Respiratory Failure

Fio_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18-24

Fig. 1. (*continued*)

have ventilator dysynchrony.[31] However, concern for ICU-acquired weakness has limited the use of NMBAs, especially in patients receiving steroids.[44] The ACURASYS study,[45] a multicenter trial, recently assessed the use of cisatracurium in the early management (6–29 hours from diagnosis) of patients with severe ARDS (P/F ratio <150) and showed an improvement in 90-day mortality (hazard ratio, 0.68; confidence interval, 0.48–0.98). The incidence of ICU-acquired weakness did not differ between the two groups.[45] EM physician familiarity with NMBA and the early timing of intervention make this a promising study for the ED; however, it is important to ensure that the patient is adequately sedated before initiating NMBA because it is challenging to assess the level of sedation in a paralyzed patient.

INHALED PULMONARY VASODILATORS

Inhaled nitric oxide (INO) and inhaled prostacyclin (IP) are the inhaled pulmonary vasodilators (IPVs) currently used for salvage therapy in refractory hypoxemia. The

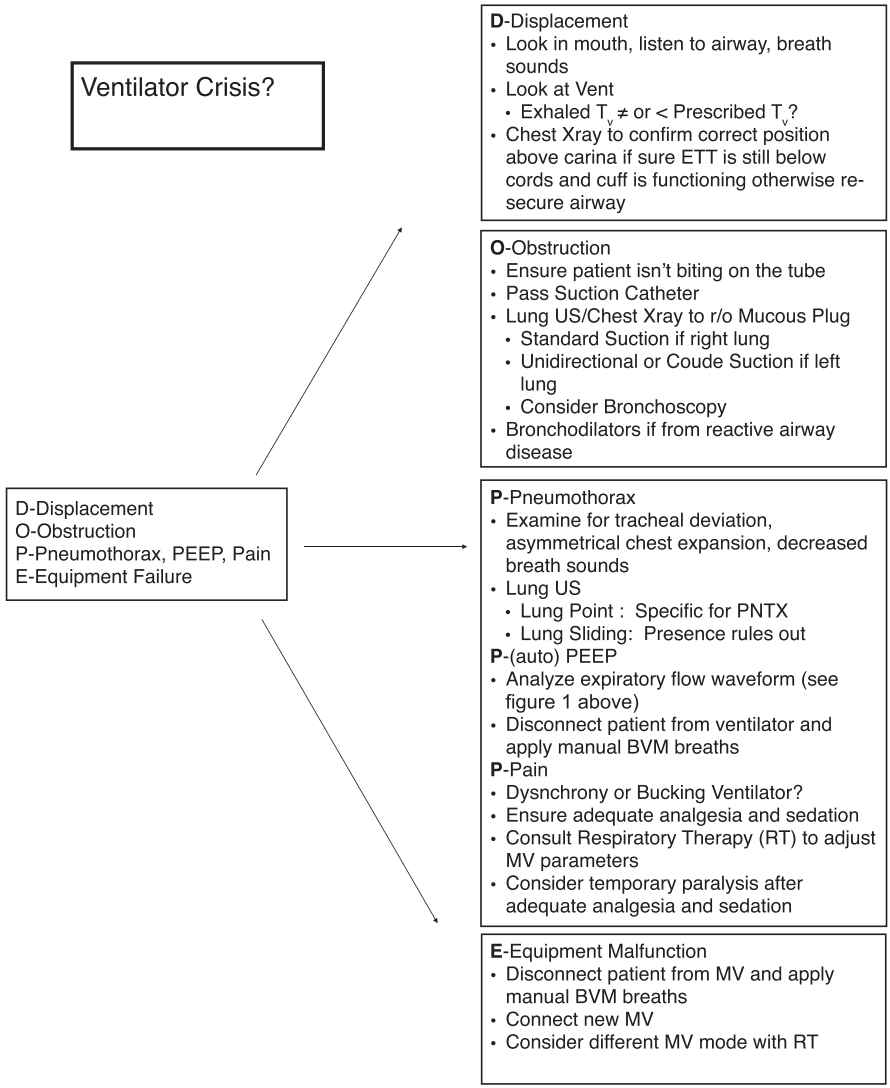
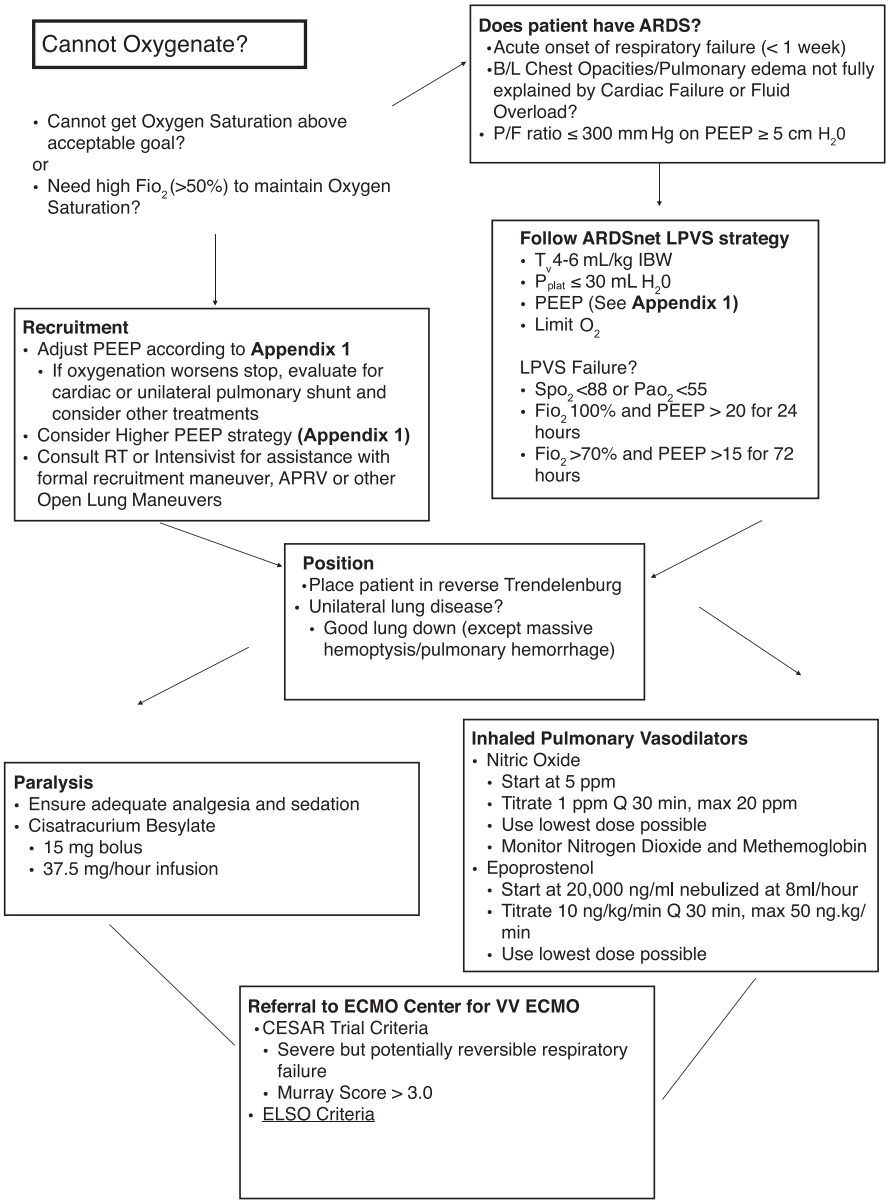


Fig. 2. An algorithm for an approach to the crashing patient on MV. (*Adapted from* Diaz JV, Brower R, Calfee CS, et al. Therapeutic strategies for severe acute lung injury. Crit Care Med 2010;38(8):1646–48.)

reader is encouraged to read a more in-depth review from the clinics series.[46] IPVs work by improving blood flow to ventilated lung units and decreasing shunt magnitude. In many cases this leads to an improvement, albeit transient (24–96 hours), in oxygenation.[42,43,46]

In addition to better V/Q matching, IPV may be beneficial in patients with acute right heart failure (ie, pulmonary embolism) and right-to-left cardiac shunts. **Fig. 2** shows how to titrate INO and IP. The major benefit of IP compared with INO is cost: $275/d versus $3000/d.[46] Tachyphylaxis can occur with both so the lowest effective dose should be used. The beneficial effects should be seen immediately. INO has been



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more extensively studied for refractory hypoxemia than IP.[42,46] Daily blood methemoglobin and inhaled nitrogen dioxide levels should be checked with INO because these byproducts are toxic.[42,43] IP has a longer half-life than INO so there is a theoretic risk of systemic hypotension from nonselective vasodilation, although this has not been shown in small studies of patients with ARDS.[47,48] Neither medication is US Food and Drug Administration approved for treatment of hypoxemia,[46] and neither medication is associated with improved mortality. However, if faced with refractory

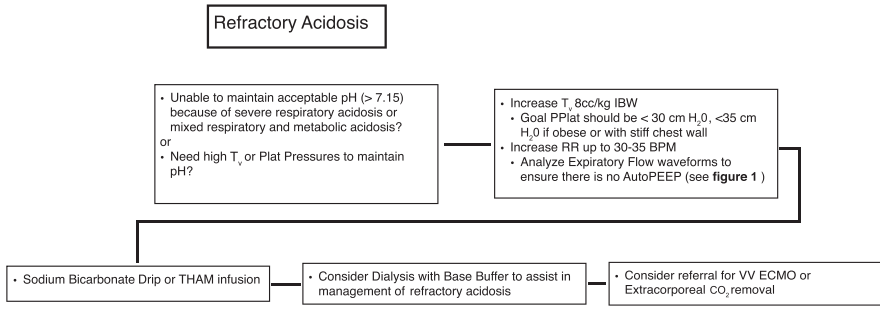

Fig. 2. (*continued*)

hypoxemia, INO and IP can be considered as salvage therapy while planning other interventions (see **Fig. 2**).

PRONE POSITIONING

Prone positioning (PP) involves rotating the patient from the standard supine position to a face-down or prone position. When supine, the inferior and posterior portions of the lung can become atelectatic from compression by the heart, thorax, and diaphragm. Atelectasis can worsen gas exchange, decrease compliance, and increase the risk for volutrauma because the T_v prescribed is now directed to a smaller lung volume. PP in some individuals allows reexpansion of these posterior lung units. Previous data have suggested that PP improved oxygenation and P/F ratio, but did not necessarily improve outcomes across all patients with ARDS.[49–51] However, a trend toward improved survival was seen in the sickest patient with ARDS.[52]

Recent data by the PROSEVA group[53] examined PP in severe ARDS (P/F ratio <150 mm Hg) and found a reduction in 28-day mortality (16.0% vs 32.8%) and no increase in complications in the prone group. The investigators who participated in this trial had significant experience with PP that potentially minimized complications (airway and central line dislodgment, pressure ulcers). They also required a stabilization period of 12 to 24 hours before PP was attempted.

If considering PP, appropriate staff (especially nursing) should be available. If the ICU has experience with this technique they should be consulted for assistance. The reader is encouraged to refer to these practical resources on the logistics of PP and for additional information on indications and contraindications.[53–55] In ED patients with difficult oxygenation, a trial of reverse Trendelenburg or placing the good lung down (provided there is not massive pulmonary hemorrhage) can be attempted.

EXTRACORPOREAL MEMBRANE OXYGENATION

The use of venovenous extracorporeal membrane oxygenation (ECMO) in severe ARDS and refractory hypercarbic respiratory failure has gained renewed interest after recent encouraging data from the United Kingdom[56] and from experience with ARDS during the 2009 H1N1 pandemic.[57] Work from the late twentieth century showed dismal survival[23] and no benefit in patients with ARDS treated with ECMO[58] but improvements in technology have made this a potential modality for severe ARDS.

ECMO has risks and costs so only the sickest patients with potentially reversible lung injury should be considered for this treatment. The Extracorporeal Life Support Organization (ELSO) has guidelines for consideration of ECMO in respiratory failure that can be viewed online (http://elso.org/resources/guidelines).[59] ECMO has risks

and costs so only the sickest patients with potentially reversible lung injury should be considered for this treatment. Indications for VV ECMO include: failure to oxygenate, severe CO_2 retention or the ability maintain acceptable CO_2 levels at unsafe airway pressures (PPlat <30 cm H_2O) or severe air leak syndromes.[59]

The CESAR trial[56] is the major trial to date showing the potential benefit of ECMO in ARDS. A controversy surrounding the study is that some of the benefits found in the CESAR trial might be secondary to treatment of ARDS in a high-volume center with experience in providing best-evidence medicine (ie LPVS) to patients with ARDS and not necessarily related solely to treatment with ECMO.[60]

Current expert opinion suggests that clinicians consider referral of adult patients with severe ARDS or severe respiratory failure with high risk of mortality, as defined by CESAR[56] entry criteria or ELSO guidelines,[59] to an ARDS center with ECMO capabilities if available. Prolonged treatment with unacceptable MV strategies (high Fio_2 or P_{plat}) is a contraindication so these patients should be referred early in the disease process.

The main adverse events associated with ECMO are bleeding, hemolysis, disseminated intravascular coagulation, and infection. In addition, there is significant financial cost associated with ECMO.[56,60]

SUMMARY

Respiratory failure is a frequent disease process encountered in the ED. Better care can lead to better outcomes for patients on MV.[61] If not contraindicated, LPVS should be used. It is important to consider disease pathophysiology when formulating treatment strategies in patients that are difficult to oxygenate or ventilate, or when Pao_2, $PaCo_2$, and pH can only be maintained with unsafe ventilator settings. If MV adjustments do not produce the expected clinical outcome then different treatment strategies should be considered. There are multiple adjunctive therapies for ARDS and severe respiratory failure. Some strategies are straightforward and can potentially be applied in the ED (IPV for refractory hypoxemia or NMBA for severe ARDS), whereas other treatments require a collaborative multidisciplinary approach and the assistance of other health care providers (PP and referral to ECMO-capable ARDS centers). Preemptively developing multidisciplinary treatment protocols assists in treating this complicated patient population.

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APPENDIX 1

NIH NHLBI ARDS Clinical Network
Mechanical Ventilation Protocol Summary

INCLUSION CRITERIA: Acute onset of

1. $Pao_2/Fio_2 \leq 300$ (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

PART I: VENTILATOR SETUP AND ADJUSTMENT

1. Calculate predicted body weight (PBW)
   Males = 50 + 2.3 [height (inches) - 60]
   Females = 45.5 + 2.3 [height (inches) -60]
2. Select any ventilator mode
3. Set ventilator settings to achieve initial V_T = 8 mL/kg PBW
4. Reduce V_T by 1 mL/kg at intervals ≤ 2 hours until V_T = 6mL/kg PBW.
5. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
6. Adjust V_T and RR to achieve pH and plateau pressure goals below.

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pH GOAL: 7.30-7.45
Acidosis Management: (pH < 7.30)
If pH 7.15-7.30: Increase RR until pH > 7.30 or $PaCo_2$ < 25 (Maximum set RR = 35).

If pH < 7.15: Increase RR to 35.
If pH remains < 7.15, V_T may be increased in 1 mL/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded).
May give $NaHCO_3$
Alkalosis Management: (pH > 7.45) Decrease vent rate if possible.

I: E RATIO GOAL: Recommend that duration of inspiration be ≤ duration of expiration.

PART II: WEANING

A. Conduct a SPONTANEOUS BREATHING TRIAL daily when:

1. $Fio_2 \leq 0.40$ and PEEP ≤ 8.
2. PEEP and $Fio_2 \leq$ values of previous day.
3. Patient has acceptable spontaneous breathing efforts. (May decrease vent rate by 50% for 5 minutes to detect effort.)
4. Systolic BP ≥ 90 mm Hg without vasopressor support.
5. No neuromuscular blocking agents or blockade.

OXYGENATION GOAL: Pao_2 55-80 mm Hg or SpO_2 88-95%
Use a minimum PEEP of 5 cm H_2O. Consider use of incremental Fio_2/PEEP combinations such as shown below (not required) to achieve goal.

Lower PEEP/higher Fio_2

Fio_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

Fio_2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/lower Fio_2

Fio_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

Fio_2	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

PLATEAU PRESSURE GOAL: ≤ 30 cm H_2O
Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or V_T.
If Pplat > 30 cm H_2O: decrease V_T by 1mL/kg steps (minimum = 4 mL/kg).
If Pplat < 25 cm H_2O and V_T< 6 mL/kg, increase V_T by 1 mL/kg until Pplat > 25 cm H_2O or V_T = 6 mL/kg.
If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase V_T in 1mL/kg increments to 7 or 8 mL/kg if Pplat remains ≤ 30 cm H_2O.

B. SPONTANEOUS BREATHING TRIAL (SBT):
If all above criteria are met and subject has been in the study for at least 12 hours, initiate a trial of UP TO 120 minutes of spontaneous breathing with $Fio_2 \leq 0.5$ and PEEP ≤ 5:

1. Place on T-piece, trach collar, or CPAP ≤ 5 cm H_2O with PS ≤ 5
2. Assess for tolerance as below for up to two hours.
   a. $SpO_2 \geq 90$: and/or $Pao_2 \geq 60$ mm Hg
   b. Spontaneous $V_T \geq 4$ mL/kg PBW
   c. RR ≤ 35/min
   d. pH ≥ 7.3
   e. No respiratory distress (distress= 2 or more)
      - HR > 120% of baseline
      - Marked accessory muscle use
      - Abdominal paradox
      - Diaphoresis
      - Marked dyspnea
3. If tolerated for at least 30 minutes, consider extubation.
4. If not tolerated resume pre-weaning settings.

Definition of UNASSISTED BREATHING
(Different from the spontaneous breathing criteria as PS is not allowed)

1. Extubated with face mask, nasal prong oxygen, or room air, OR
2. T-tube breathing, OR
3. Tracheostomy mask breathing, OR
4. CPAP less than or equal to 5 cm H_20 **without pressure support or IMV assistance.**