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# Critical Care [ALERT]

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SPECIAL FEATURE

## A Perspective on PEEP at 50 Years

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Mr. Kallet reports he is a major stockholder of and a business advisory board member for the Asthma & Allergy Prevention Company and receives grant/research support from Nihon-Kohden.

Fifty years ago, positive end-expiratory pressure (PEEP) was introduced as an effective technique for improving oxygenation in patients with large intrapulmonary shunt, the hallmark of acute respiratory distress syndrome (ARDS).[1] Although PEEP remains the primary means for stabilizing oxygenation in ARDS, consensus on how to approach setting it remains elusive.[2] This is a narrative review on how our understanding and approach to PEEP has evolved over the past half century.

### RATIONALE

Functional residual capacity (FRC) is essentially the alveolar volume and, as such, the primary determinant of both oxygenation and respiratory system compliance ($C_{RS}$).[3] Historically, the impact of PEEP has been assessed according to its effect on oxygenation or $C_{RS}$ as signifiers of changes in FRC. This is a matter of bedside expedience understood implicitly but rarely stated explicitly. A historically accurate statement might read: The primary impact of PEEP is the stabilization of underinflated alveoli and the recruitment of collapsed small airways and alveoli, thereby increasing FRC and $C_{RS}$ while reducing intrapulmonary shunt so as to allow mechanical ventilation at a relatively safer inspired oxygen fraction ($FiO_2$; i.e., < 0.70).[4-6]

PEEP also produces lung-protective effects. Repetitive opening and closing of small airways and alveoli causes shearing of both the airway epithelium (from breaking and displacing liquid bridges/plugs) and the alveolar epithelium (from asymmetrical stress/strain development between patent alveoli adjacent to collapsed but recruitable alveoli).[7] Restoring FRC toward normal is lung-protective in that it: 1) reduces the formation of liquid bridges and promotes alveolar edema fluid translocation from airspaces to the interstitium, 2) increases alveolar surface area to accommodate tidal ventilation (thus, reducing excessive tidal strain), and 3) allows ventilation at relatively nontoxic $FiO_2$. Particularly noteworthy in this regard is emerging evidence that hyperoxia appears to potentiate stretch-related injury.[8]

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## MISCONCEPTIONS REGARDING RECRUITMENT AND ADVERSE EFFECTS

PEEP does not "recruit" collapsed alveoli but rather stabilizes partially inflated alveoli by counteracting forces that promote collapse, such as increased alveolar surface tension and superimposed hydrostatic forces, and, therefore, prevents tidal "de-recruitment" in mid-level and some dependent regions. On the other hand, recruitment is an inspiratory phenomenon. Its goal is to achieve a threshold opening pressure sufficient to overcome both retractile and compressive forces as well as rupturing liquid bridges and displacing liquid plugs that obstruct the peripheral airspaces.[7,9]

The clinical surrogate for threshold opening pressure is plateau pressure (Pplat), which represents the mean, quasi-static alveolar pressure at end inspiration. The confusion over the role of PEEP in recruitment stems from the fact that PEEP almost invariably increases Pplat. This was particularly true when a traditional tidal volume ($V_T$) of 12-15 mL/kg was used, often producing a Pplat ranging from 35-50 cm $H_2O$. In ARDS, threshold opening pressures follow a bimodal distribution. Whereas most lung units achieve full recruitment with a Pplat of 20-35 cm $H_2O$, in severe ARDS, dorsal-caudal regions exposed to substantial compressive/occlusive forces require opening pressures of 40-60 cm $H_2O$.[9] This explains why moderate levels of PEEP usually are sufficient to stabilize oxygenation in most ARDS cases.

The historical reluctance to use high PEEP levels stems from a misinterpretation of the foundational studies conducted in the 1970s. Without question, high PEEP levels can cause hemodynamic compromise, reduced systemic oxygen delivery, and barotrauma. Yet, these studies were performed using a $V_T$ of 10-15 mL/kg or higher. This often resulted in extraordinarily high alveolar pressures. It also increased the time needed for pressure dissipation during the expiratory phase (i.e., the "amplitude constant" that governs pressure-volume equilibration in the lungs),[10] further impeding venous return and right ventricular output.

The conclusions drawn from these studies were that setting PEEP above 10 cm $H_2O$ increased the risk of hemodynamic instability and barotrauma, and that levels > 15 cm $H_2O$ should be avoided.[3] In this context, it was particularly unfortunate that a crucial PEEP study from 1978 was essentially ignored. Suter et al found that $C_{RS}$ continued to improve even at a PEEP of 15 cm $H_2O$ when a physiologic $V_T$ (5-7 mL/kg) was used.[11] Therefore, the negative effects of PEEP were $V_T$-dependent and largely avoidable. These findings from 1978 presaged lung protective ventilation practices in the early 2000s. What essentially escaped the focus of the pulmonary critical care profession for decades was a sense of historical reflection. Specifically, the use of supra-physiologic $V_T$ predated the advent of PEEP, and although initially used for treating postoperative atelectasis, it quickly was incorporated into standard mechanical ventilation practice. Even after its introduction in 1967, it took another decade before the relative contributions of PEEP and $V_T$ were investigated. In practical terms, from 1967 until publication of the seminal NIH ARDSNet ARMA trial in 2000,[12] mechanical ventilation practices generally relied on a supra-physiologic $V_T$ with relatively low PEEP and high $FiO_2$ to manage ARDS, with sobering results in terms of iatrogenic lung injury.

## DIFFERENT APPROACHES TO SETTING PEEP

Since the early 1970s, divergent PEEP strategies typically focused on "optimizing" either oxygenation or $C_{RS}$. Another approach that gained widespread acceptance was using the "least PEEP" necessary to ensure adequate arterial oxygen tension (e.g., partial pressure of oxygen, $PaO_2$, of approximately 70 mmHg) while avoiding excessive hyperoxia, barotrauma, and hemodynamic compromise.[13] Although these words evoke advocacy for low PEEP, it essentially argued against using PEEP to "optimize" oxygenation as was advocated by "super-PEEP" adherents at that time.[14] In essence, the $FiO_2$/PEEP table used in the NIH ARDSNet ARMA study was largely consistent with the least PEEP philosophy, as it attempted to balance the benefits and risks of PEEP with the risks of hyperoxia while maintaining a reasonable $PaO_2$ (55-80 mmHg).[12] In the early, exudative phase of ARDS when the lungs typically are most amenable to recruitment, ARDSNet-guided PEEP is increased aggressively to stabilize oxygenation, then just as aggressively titrated downward to find the

minimum PEEP needed to maintain modest oxygenation goals. In the early 1990s, the "open lung ventilation" (OLV) strategy heralded a shift in focus toward lung protection. The first iteration advocated briefly recruiting the lungs with pressure ventilation at 55 cm $H_2O$ and PEEP of 16 cm $H_2O$. This was followed by reducing tidal driving pressure to < 20 cm $H_2O$ to prevent stretch-related injury and inverse-ratio ventilation titrated to an intrinsic PEEP of 16 cm $H_2O$ to prevent sheer-related injury.[15] Since then, OLV had been modified to incorporate traditional inspiratory:expiratory ratios with low $V_T$ and external PEEP. PEEP is titrated to prevent de-recruitment by using a decremental trial that adjusts PEEP to 2 cm $H_2O$ above the level when deterioration in either oxygenation or $C_{RS}$ becomes apparent.

However, when reviewing OLV studies, one discovers that the mean optimal PEEP was only 10-12 cm $H_2O$ or had resulted only in modest reductions in mean PEEP from approximately 12 to 9 cm $H_2O$. This raises the question of whether this approach offers any advantage over incrementally upward PEEP adjustments. For context, large clinical trials of ARDS that combined higher PEEP with low $V_T$ using either oxygenation- or mechanics-based titration protocols consistently reported day 1 mean PEEP levels of approximately 14 to 16 cm $H_2O$.[16-18] Unfortunately, a recent large, multicenter, randomized, controlled trial of OLV reported a higher mortality with OLV compared to the ARDSNet ARMA strategy.[19] Although important unresolved questions about this study remain, its impact is likely that OLV will be used only as rescue therapy.

A newer approach has been titrating PEEP to maintain an end-expiratory transpulmonary pressure between 0 and 10 cm $H_2O$, where transpulmonary pressure is equal to PEEP minus esophageal pressure at end expiration. The authors of a pilot study found that the transpulmonary pressure-guided strategy resulted in both a higher mean PEEP and mean $PaO_2/FiO_2$ (18 cm $H_2O$ and 280 mmHg, respectively) compared to the ARDSNet ARMA strategy (12 cm $H_2O$ and 191 mmHg, respectively), both of which were achieved at an $FiO_2$ < 0.60.[20] From a practical standpoint, this invasive technique is not necessary to manage most ARDS cases, but might be useful in managing cases complicated by morbid obesity or abdominal compartment syndrome. However, even in these cases, PEEP can be titrated empirically, measuring intra-abdominal pressure as a guide. Other evidence garnered from the literature also may help answer the following question: After a half century of treating ARDS with PEEP, what range typically is needed in most cases? The authors of early physiologic studies speculated that by improving FRC and $C_{RS}$, PEEP moved tidal ventilation onto the steep portion of the inflation pressure-volume (P-V) curve (i.e., above the lower inflection point, or LIP).[4,5] This concept was supported by other studies, which found that found setting PEEP 3 cm $H_2O$ above LIP markedly improved oxygenation and that the average LIP was approximately 9 ± 3 cm $H_2O$, or a set PEEP of approximately 12 cm $H_2O$.[21,22] Data culled from 16 trials totaling 197 discreet LIP measurements revealed a median LIP of 10 (interquartile range of 8 to 3) cm $H_2O$, which translates into PEEP settings between 11 and 16 cm $H_2O$.[23] The authors of that review also found six additional studies that reported mean values of LIP between 8 and 11 cm $H_2O$ with a subsequent corresponding PEEP of 11-14 cm $H_2O$.

Setting PEEP to prevent alveolar collapse also has been advocated based on the findings from CT studies. Increased dorsal lung densities are believed to represent compressive atelectasis from the weight of the overlying edematous lung. Setting a minimal PEEP of 11-14 cm $H_2O$ was proposed to keep the dependent lung zones open at end expiration.[24] This was based on the sternovertebral height of a supine adult (12-25 cm) and the average tissue density in ARDS of 0.7 gm/cm$^3$, which produces a PEEP range of 8-18 cm $H_2O$. It's particularly noteworthy that even following a recruitment maneuver, subsequent consequential de-recruitment was reported only when PEEP was < 10 cm $H_2O$.[25]

## SUMMARY

If one adheres to a "least PEEP" philosophy, the evidence suggests that for most patients with ARDS, targeting PEEP between 10 and 16 cm $H_2O$ probably is sufficient in all but the most severe presentations. (In our institution, we estimate this to occur in no more than 15-20% of cases). In those relatively infrequent occurrences, PEEP levels > 20 cm $H_2O$ using a fixed driving pressure of 15-20 cm $H_2O$ should be attempted to stabilize FRC and gas exchange.

This can be justified based on several observations gleaned over the past half century. First, the very early exudative phase of ARDS (initial 48 hours) is characterized by congestive atelectasis and peripheral airspace obstruction from pulmonary edema that has not yet solidified. During this period, the lungs are more amenable to recruitment and displacement of pulmonary edema out of the airspaces. Second, these cases are typified by

sustained, pronounced, compressive forces emanating from both abnormal chest wall compliance and superimposed hydrostatic pressure (from edematous overlying lung tissue) favoring lung collapse. In these situations, some combination of high or super PEEP, prone positioning, and judicious use of alveolar recruitment maneuvers is indicated. This should be part of the clinician's first-line armamentarium in treating intractable hypoxemia in unusually severe presentations of ARDS. ■


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## ABSTRACT & COMMENTARY

# Critical Illness-related Corticosteroid Insufficiency: What's New?


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**Dr. Radigan reports no financial relationships relevant to this field of study.**



SYNOPSIS: For critically ill patients with sepsis, septic shock, acute respiratory distress syndrome, and major trauma, a multispecialty task force of 16 international experts developed evidence-based recommendations for the diagnosis of corticosteroid insufficiency and use of corticosteroids in the ICU.

SOURCE: Annane D, Pastores SM, Rochwerg B, et al. Guidelines for the diagnosis and management of critical illness-related corticosteroid insufficiency (CIRCI) in critically ill patients (Part I): Society of Critical Care Medicine (SCCM) and European Society of Intensive Care Medicine (ESICM) 2017. *Crit Care Med* 2017;45:2078-2088.

Although there was a 2008 consensus statement for the diagnosis and management of critical illness-related corticosteroid insufficiency (CIRCI) in adult and pediatric patients, there has been a growing need to further update the concept, diagnosis, and management of CIRCI. A multispecialty task force of 16 international experts in critical care medicine, endocrinology, and guideline methods from the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM) were chosen to update the recommendations. Experts reviewed the 2008 recommendations and examined an updated systematic review of pertinent studies from 2008-2017. Experts formulated recommendations using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology. The strength of each recommendation was classified as strong or conditional. Furthermore, the evidence was rated from very low to high and based on study design, risk of bias within the study, the consistency of the results, and the directness and precision of the evidence. An approved recommendation required the agreement of 80% of the members of the task force.

The experts were not able to reach an agreement on a single test that would consistently diagnose CIRCI. Although the team made no recommendation regarding whether to use a delta cortisol (change in baseline cortisol at 60 minutes of < 9 µg/dL) after cosyntropin 250 µg administration or a random plasma cortisol of < 10 µg/dL, it did not recommend using plasma-free cortisol or salivary cortisol level (conditional, low quality of evidence). The team recommended that treatment should include intravenous (IV) hydrocortisone < 400 mg/day for ≥ 3 days in patients with septic shock who are not responsive to fluid and needing moderate to high doses of vasopressor support (conditional, low quality of evidence). The team also recommended the use of IV methylprednisolone 1 mg/kg/day in patients with moderate to severe acute respiratory distress syndrome (ARDS; i.e., $PaO_2/FiO_2$ < 200) within at least 14 days of onset (conditional, moderate quality of evidence). Corticosteroids were not recommended for adult patients with sepsis without shock (conditional recommendation, moderate quality of evidence) or patients with major trauma (conditional, low quality of evidence).

## ■ COMMENTARY

CIRCI is widely recognized as a disorder of dysregulated systemic inflammation that results from inadequate intracellular glucocorticoid-mediated anti-inflammatory activity that is out of proportion to the severity of a patient's critical illness. This systemic inflammation is due to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, altered cortisol metabolism, and tissue resistance to corticosteroids and is thought to lead to increased morbidity, ICU length of stay, and mortality.[1,2] As there remains substantial controversy over the diagnosis and treatment of CIRCI, the SCCM and the ESICM have updated the 2008 guidelines.

Accurately diagnosing adrenal insufficiency or relative adrenal insufficiency in critically ill patients has been a challenge. In 2016, the Surviving Sepsis Campaign guidelines suggested not using the adrenocorticotropic stimulation test to assess appropriateness for treatment with hydrocortisone and recommended IV hydrocortisone at a dose of 200 mg per day if adequate fluid resuscitation and vasopressor therapy are unable to restore hemodynamic stability.[3] After a detailed review of all the data, the multispecialty task force also remained in disagreement regarding a single test to diagnosis CIRCI but suggested that a delta cortisol (change in baseline cortisol at 60 minutes of < 9 µg/dL) after cosyntropin administration and a random plasma cortisol of < 10 µg/DL may be considered. They also suggested that patients with septic shock who are not responsive to fluid and needing moderate to high doses of vasopressor support be treated with IV hydrocortisone < 400 mg/day for ≥ 3 days at full dose.

Shortly after these recommendations were released, results from the ADRENAL trial were published.[4] In this international, pragmatic, double-blind, parallel-group, randomized, controlled study, investigators assigned patients with septic shock who were undergoing mechanical ventilation to either continuous infusion of hydrocortisone 200 mg daily or placebo for seven days or until death or discharge from the ICU. It should be noted that this particular study required less stringent enrollment criteria and included all ventilated patients who had been treated with vasopressors or inotropic agents for four hours or more. Although there was no difference in 90-day mortality, patients who received hydrocortisone experienced a more rapid resolution of shock, shorter time to ICU discharge, earlier cessation of the initial episode of mechanical ventilation, and a lower incidence of blood transfusion compared to placebo.

The task force also recommended considering IV methylprednisolone 1 mg/kg/day in early ARDS patients (within seven days of onset of ARDS with $PaO_2/FiO_2$ of < 200) and methylprednisolone 2 mg/kg/day in late ARDS patients (after day 6 of onset) with slow tapering over the following 13 days. This recommendation was affected by a relatively recent individual patient data analysis of four of the largest trials evaluating prolonged methylprednisolone in early and late ARDS, which revealed a benefit

to corticosteroids with improved survival and decreased duration of mechanical ventilation without concerning side effects.[5] Since glucocorticoids may blunt the febrile response, it also was recommended to maintain optimal infection surveillance to ensure prompt identification and treatment of infection for patients undergoing glucocorticoid treatment. Despite this recommendation, many practitioners are not strong proponents of the routine administration of glucocorticoids in ARDS until there is an adequately powered, randomized, placebo-controlled trial demonstrating a mortality benefit and further detailing the indication, timing, duration, and appropriate dosing of corticosteroids in this setting. Currently, this recommendation from the team likely would benefit from further ongoing investigation. In conclusion, there is no single test that can consistently diagnose CIRCI. Although the task force recommends against use of corticosteroids in patients with sepsis but without shock, treatment with IV hydrocortisone < 400 mg/day for ≥ 3 days at full dose should be considered in patients with septic shock who are not responsive to fluid and needing moderate- to high-dose vasopressor support. Although mortality benefits are not seen consistently across the literature in these situations, there may be other benefits, such as faster resolution of shock and shorter ICU lengths of stay. The task force also recommends the use of IV methylprednisolone 1 mg/kg/day in patients with moderate to severe ARDS ($PaO_2/FiO_2$ < 200) within 14 days of onset, but consideration should be made on a case-by-case basis, strongly weighing the benefits and risks of such a therapy. ■

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ABSTRACT & COMMENTARY

# ECMO vs. Prone Position in ARDS: The Curious Rejection of Evidence-based Practice


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SYNOPSIS: Despite credible evidence from a large, randomized, controlled trial and numerous meta-analyses demonstrating improved outcomes, prone position is seldom attempted prior to initiating extracorporeal membrane oxygenation to treat severe acute respiratory distress syndrome.



SOURCE: Li X, Scales DC, Kavanagh BP. Unproven and expensive before proven and cheap — Extracorporeal membrane oxygenation vs. prone position in ARDS. *Am J Respir Crit Care Med* 2018 Jan 9. doi: 10.1164/rccm.201711-2216CP. [Epub ahead of print].


The authors of this retrospective investigation examined 17 studies involving 672 patients who received extracorporeal membrane oxygenation (ECMO) between 1997 and 2017 for severe acute respiratory distress syndrome (ARDS). Overall, 15 studies were published after 2010. These studies represented only 28% of those meeting inclusion criteria because only correspondence with those study investigators could confirm whether a prone position (PP) trial preceded ECMO initiation. Only 208 of 672 patients received PP prior to ECMO. Interestingly, more patients received PP prior to publication of the landmark 2013 PROSEVA study, which showed that PP decreased 28-day and 90-day mortality than after: 124/220 vs. 84/452, respectively ($P$ < 0.05). Li et al were unable to ascertain from their inquiries why so few patients receiving ECMO after 2013 did not first receive a trial of PP.

## ■ COMMENTARY

The justification for ECMO in ARDS is based largely on the 2009 CESAR trial[1] and the ANZ-ECMO case series during the H1N1 influenza pandemic. Unfortunately, neither study provided high-level evidence that would advocate using this extraordinarily invasive and costly

therapy that carries greater risks than PP.[2] The CESAR trial did not use explicit, well-defined methods, particularly regarding mechanical ventilation in the control group.[2] In essence, ECMO at a single treatment center was compared to ill-defined, usual care practice at referral hospitals. Moreover, in contrast to other multi-center, randomized, controlled trials of ARDS, the authors of the CESAR trial didn't publish detailed mechanical ventilation data from the first three to seven study days. Thus, the degree to which lung protective ventilation was achieved remains unknown. However, it's telling that only 70% of the control group received treatment by low volume-low pressure ventilation "at any time" compared to 93% of those randomized to receive ECMO. Numerous studies strongly suggest that mortality risk in ARDS increases when tidal volume exceeds 6 mL/kg and plateau pressure exceeds 30 cm $H_2O$ or driving pressure exceeds 15 cm $H_2O$. Therefore, it is impossible to accurately assess mortality differences reported in the CESAR trial, as in large measure these differences may have reflected failure to provide adequate lung protective ventilation. So why is there such a discrepancy between using a simple, highly effective, and economically prudent therapy supported by high-level evidence in favor of one that doesn't? Perhaps the contemporaneous publication of the CESAR trial with the H1N1 influenza pandemic may have generated an illusion of superiority (or suspension of skepticism), engendered in part by emotionally fraught circumstances in dealing with a particularly severe form of influenza. Another aspect that illuminates this discussion relates to the extraordinary advancement in our understanding of lung recruitment that began approximately two decades ago. In severe ARDS, recruiting the dorsal-caudal lung while in the supine position (primarily responsible for severe refractory hypoxemia) requires brief exposure to threshold opening pressures of 40-50 cm $H_2O$ with a positive end-expiratory pressure (PEEP) of 20-30 cm $H_2O$. This is of interest because a cursory review of studies cited by Li et al reveals that, when reported, mean PEEP prior to ECMO was 12-16 cm $H_2O$, with plateau pressures of 30-35 cm $H_2O$. Therefore, this strategy alone would not be expected to substantially improve gas exchange. Moreover, it also perpetuates the impression (or bias) that ECMO is the only viable therapeutic alternative in these circumstances. Incorporating PP enhances the recruiting and stabilizing effects of plateau pressure and PEEP by adding ~5 cm $H_2O$ of transpulmonary pressure while also improving ventilation-perfusion relationships, global alveolar stability, and secretion mobilization regardless of whatever recruitment might be achieved.[3] However, it's easier to manage severe ARDS with ECMO than it is to implement mechanics-based treatment strategies using these techniques. ECMO becomes all the more seductive if it's readily available and also generates considerable revenue. Clinician angst from unfamiliarity is a substantial barrier to implementing PP. This continues to be an issue at my institution, despite 20 years of experience with PP and employing both respiratory care practitioners and nurses who are highly competent in its practice. Essentially, it remains a physician leadership issue, as those experienced in using PP are not hesitant to use it. There is always trepidation when first using PP, which dissipates as experience increases. Thus, the problem essentially is a circular one. In addition, as long as strong financial incentives to pursue ECMO exist, the initial uneasiness to pursue PP in the treatment of ARDS is unlikely to change.

Finally, we've devised an effective strategy to prevent overuse of ECMO by first requiring at least 16 hours of bundled therapies to reverse refractory hypoxemia, including: tidal volume of < 6 mL/kg with a minimum PEEP of 16 cm $H_2O$ in combination with PP, neuromuscular blockade, inhaled vasodilators, and, in some instances, full alveolar recruitment maneuvers (the caveat: absence of heart failure or contraindications to these therapies). We have found that such an approach prior to referral to an ECMO center is both fiscally sound and clinically prudent. ■

REFERENCES


1. Peek GJ, Mugford M, Tiruvoipati R, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): A multicentre randomized controlled trial. *Lancet* 2009;374:1351-1363.
2. Morris AH, Hirshberg E, Miller RR 3rd, et al. Counterpoint: Efficacy of extracorporeal membrane oxygenation in 2009 Influenza A(H1N1). Sufficient evidence? *Chest* 2010;138:778-784.
3. Kallet RH. A comprehensive review of prone positioning in acute respiratory distress syndrome. *Respir Care* 2015;60:1660-1688.

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## CME/CE QUESTIONS

1. **Which of the following is *false* regarding positive end-expiratory pressure (PEEP) titration strategies in acute respiratory distress syndrome (ARDS)?**
   a. The NIH ARDSNet ARMA approach titrates PEEP to keep a $PaO_2$ of 55-80 mmHg.
   b. The original open lung ventilation (OLV) approach used an inverse ratio to keep intrinsic PEEP at 16 cm $H_2O$.
   c. The current OLV strategy adjusts PEEP by using a decremental PEEP trial.
   d. The "least PEEP" method advocates increasing PEEP whenever $PaO_2$ reaches 70 mmHg.

2. **All of the following statements regarding PEEP in ARDS are true *except*:**
   a. PEEP prevents lung de-recruitment.
   b. PEEP indirectly causes lung recruitment by simultaneously increasing plateau pressure.
   c. PEEP directly causes lung recruitment.
   d. Using a physiologic tidal volume with PEEP helps prevent lung overdistension.

3. **In patients with septic shock who are not responsive to fluid and needing moderate-to high-dose vasopressor support, treatment should include:**
   a. IV fludrocortisone 50 mcg daily.
   b. IV hydrocortisone < 400 mg/day for ≥ 3 days.
   c. IV hydrocortisone < 200 mg/day for > 7 days.
   d. None of the above

4. **Which of the following statements is *false* regarding the use of prone position (PP) prior to initiating extracorporeal membrane oxygenation (ECMO) in ARDS?**
   a. A trial of PP was not attempted before initiating ECMO in most published studies.
   b. Only 31% of patients received a trial of PP prior to ECMO.
   c. Fewer patients underwent a PP trial preceding ECMO after publication of the PROSEVA study.
   d. More patients underwent a PP trial preceding ECMO after publication of the PROSEVA study.

5. **Which of the following statements is *true* regarding the CESAR trial of ECMO in ARDS?**
   a. The control arm of the CESAR trial essentially represented usual care practice at referring hospitals.
   b. The control arm of the CESAR trial used the NIH ARDSNetwork ventilator protocol.
   c. The ECMO arm of the CESAR trial used an open lung ventilation strategy.
   d. In the CESAR trial, PP was used to verify the appropriateness of proceeding with ECMO.

## CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- identify relevant topics in the practice of critical care medicine;
- utilize recommendations from current clinical guidelines; and
- manage common critically ill patient and ICU administration scenarios.